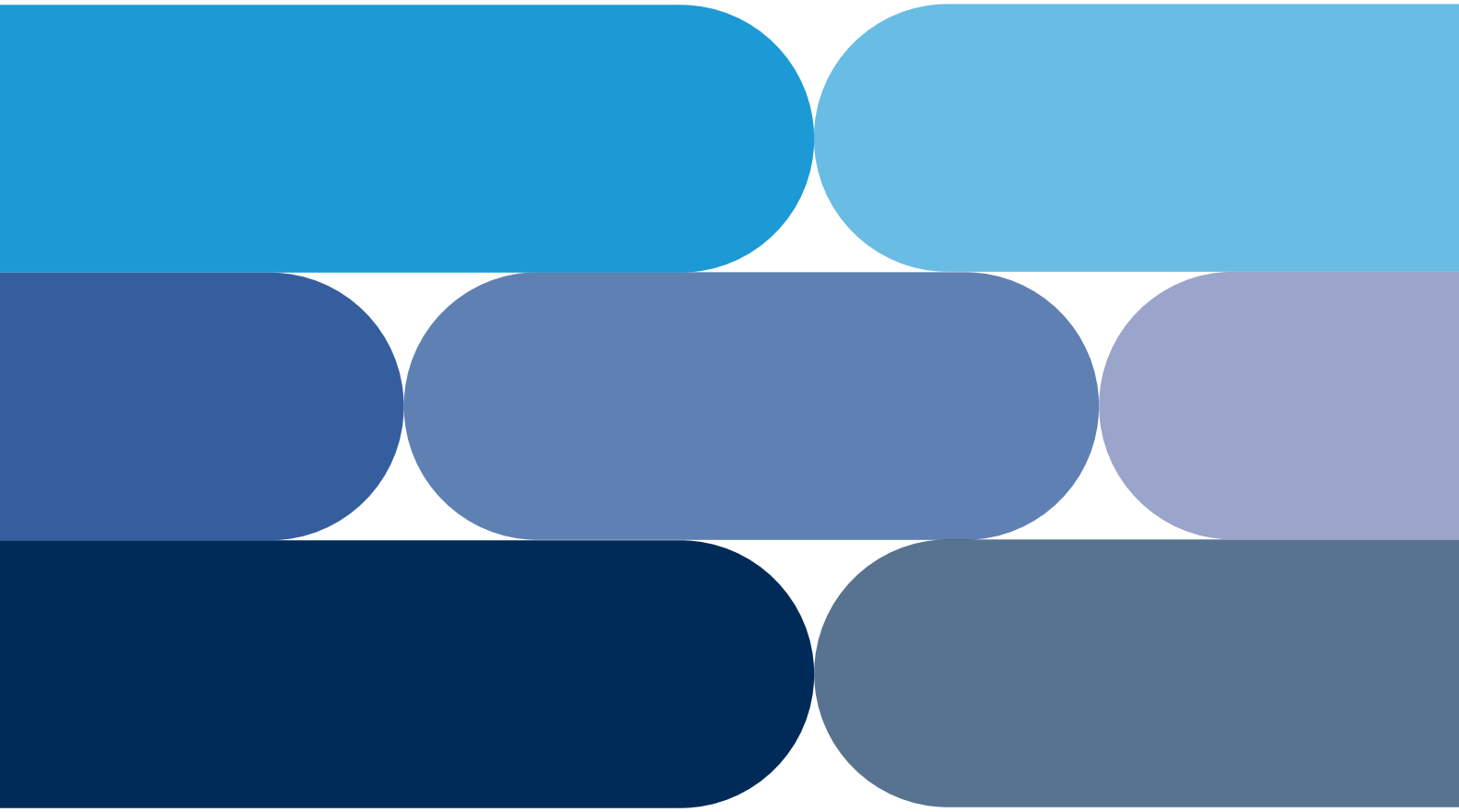
WHO Global Benchmarking Tool (GBT)

for Evaluation of National Regulatory System of Medical Products

Revision VI



World Health Organization

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Revision VI

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Contents

Introduction

The World Health Organization (WHO) considers medical products and other health technologies one of the six building blocks of health systems. Unlike many other commodities, however, end users and health care workers are typically not in a position to judge the quality of medical products. It is therefore essential that the interests and safety of the public be entrusted to a regulatory body responsible for ensuring the quality, safety, and efficacy of medical products throughout the product life cycle.

Regulatory systems play a key role in assuring the quality, safety, and efficacy of medical products. Effective, efficient and transparent regulatory systems are consequently an essential component of overall health systems and contribute to desired public health outcomes and to innovation and investment. In contrast, inefficient regulatory systems can be a barrier to access of safe, effective and quality medical products.

WHO has played a pivotal role in supporting countries to strengthen their regulatory systems, a role implicitly mandated by the WHO constitution and elaborated explicitly in various World Health Assembly (WHA) resolutions. Most notable of these is Resolution WHA 67.20 that addresses strengthening regulatory systems for medical products adopted in May 2014 .

The benchmarking of regulatory systems referred to in Resolution WHA 67.20 implies a structured and documented process by which Member States (MSs) can identify and address gaps with the goal of reaching a level of regulatory oversight commensurate with a stable, well-functioning and integrated regulatory system.

The use of the WHO global benchmarking tool (GBT) is the primary means by which WHO assesses regulatory systems for the regulation of medical products. The tool and benchmarking methodology enable WHO and regulatory authorities to identify areas of strength as well as areas for improvement; facilitate the formulation of an institutional development plan (IDP) to build upon strengths and address identified gaps; to aid in the prioritization of investments in IDP implementation; and to help monitor progress.

WHO began assessing regulatory systems in 1997 using a set of indicators designed to assess the regulatory program for vaccines. Since that time, several tools and revisions have been introduced, and the regulatory systems of over 150 countries have been benchmarked.

The development of a unified WHO GBT for the assessment of medicine and vaccine programmes began in 2013 following a mapping of benchmarking tools internal and external to WHO with a view to ensuring policy coherence, maximizing regulatory outcomes and reducing burden on regulatory authorities.

The benchmarking policy and methodology were the subject of two international consultations in January and December 2015, respectively. The GBT revision VI was also the subject of a public consultation and extensive expert consultation in 2018. Importantly, GBT revision VI was integrated with the medical regulatory systems assessment tools developed by the WHO Regional Office for the Americas/Pan American Health Organization (AMR/PAHO).

The GBT replaces all tools previously used by WHO, representing the first truly ‘global’ tool for benchmarking regulatory systems. The GBT is designed to evaluate the overarching regulatory framework and the component regulatory functions e.g. clinical trial oversight through a series of sub-indicators that may also be grouped and examined according to nine cross-cutting categories or themes, for example, quality and risk management system. Fact sheets have been developed for each sub-indicator to guide the benchmarking team and ensure consistency in the evaluation, documentation and rating of the sub-indicator.

The GBT also incorporates the concept of ‘maturity level’ or ML (adapted from ISO 9004), allowing WHO and regulatory authorities to assess the overall ‘maturity’ of the regulatory system on a scale of 1 (existence of some elements of regulatory system) to 4 (operating at advanced level of performance and continuous improvement).

A benchmarking manual is available to help users to understand and apply the policy, methodology and process to be followed and completed for benchmarking of regulatory system of medical products.

The GBT revision VI (for medicines and vaccines) is available in four UN official languages of English, French, Spanish and Russian.

The GBT is supported by a computerized platform to facilitate the benchmarking, including the calculation of maturity levels. The computerized GBT (cGBT) is available, upon request, to Member States and organizations working with WHO under the Coalition of Interested Parties (CIP).

All queries related to GBT should be sent to WHO Regulatory Systems Strengthening Team at nra_admin@who.int.

Acknowledgements

The World Health Organization (WHO) would like to thank all Member States, the donor community, technical partners, entities, individuals, and staff who over the years contributed to the establishment and maintenance of the global benchmarking tool including its fact sheets, and who continue to do so, thereby ensuring the continued success ad sustainability of the WHO regulatory system strengthening programme. We are indebted to you all. Without your support this work would not have been possible.

01

National Regulatory System (RS): Indicators and Fact Sheets

WHO Global Benchmarking Tool (GBT) for Evaluation of National Regulatory System of Medical Products

01. National Regulatory System (RS): Indicators and Fact Sheets

Function:	01 — NATIONAL REGULATORY SYSTEM (RS)
Description:	The National Regulatory System provides the framework that supports the World Health Organization (WHO) recommended regulatory functions. The National Regulatory Authority (NRA) is the institution in charge of assuring the quality, safety, and efficacy of medical products as well as ensuring the relevance and accuracy of product information. A sustainable, well-functioning regulatory system will ensure an independent and competent oversight of medical products.
Indicator:	**RS01 Legal provisions, regulations and guidelines required to define regulatory framework of national regulatory system (RS)**
Objective:	The objective of this indicator is to ensure that the legal basis defining the regulatory framework for the national regulatory system exists. The assessor should identify how the different pieces of the legislation are drafted and to know which organizations and institutions are consulted during this process, including the public, industry, non-governmental organizations and other interested parties. The assessor should identify the cases where the relevant legal provisions have been defined but the regulations have not been enacted and published, which may lead to legal uncertainty, misunderstanding or misinterpretation. The regulatory system functions should be supported by appropriate and promulgated legislation.
Category:	01. Legal provisions, regulations and guidelines
Sub Indicator:	**RS01.01: Legal provision and regulations define the medical products that should be regulated.**
Maturity Level:	1
Scope:	1. Medicines 2. Vaccines
Description:	The assessor should identify within the existing legislation and institutional regulations, the scope of regulatory activities and products that should be regulated. Existing definitions for regulated medical products (e.g., medicines, biological products, and medical devices) should be used. It is not necessary to have a single (standalone) drug law; however, a promulgated and enforced law should exist. If the base laws and regulations refer to the need for complementary regulation, it is important to access that information.
Objective:	The objective of this sub-indicator is to ensure the existence of legislation and institutional regulations that define the products that should be regulated. It is important to set up the scope and mandate of the regulatory agency in charge of regulating medical products in the country.
Requirement:	Scope of regulated medical products
Evidence to review:	The assessor should request for and review: 1. Promulgated legal provisions and regulations that define the medical products that should be regulated.
References:	1. National drug regulatory legislation: guiding principles for small drug regulatory authorities. In: WHO Expert Committee on Specifications for Pharmaceutical Preparations:

	thirty-fifth report. World Health Organization; 1999: Annex 8 (WHO Technical Report Series, No. 885)., (1), (http://apps.who.int/medicinedocs/documents/s21964en/s21964en.pdf) 2. Guidelines for national authorities on quality assurance for biological products. In: WHO Expert Committee on Biological Standardization: forty-second report. World Health Organization; 1992: Annex 2 (WHO Technical Report Series, No. 822), (2), (http://www.who.int/biologicals/publications/trs/areas/biological_products/WHO_TRS_822_A2.pdf) 3. Regulation and licensing of biological products in countries with newly developing regulatory authorities. In: WHO Expert Committee on Biological Standardization: forty-fifth report. World Health Organization; 1995: Annex 1 (WHO Technical Report Series, No. 858), (3), (http://www.who.int/bloodproducts/publications/WHO_TRS_858_A1.pdf) 4. How to develop and implement a national drug policy, Second edition. WHO, 2001., (116), (http://apps.who.int/medicinedocs/pdf/s2283e/s2283e.pdf)
Framework:	Structure/Foundation/Input
Rating Scale:	➜ NOT IMPLEMENTED (NI): There are no legal provisions or regulations defining the medical products that should be regulated. ➜ ONGOING IMPLEMENTATION (OI): There are some legal provisions and regulations or although they do not exist, demonstrable steps have been taken towards developing them. ➜ PARTIALLY IMPLEMENTED (PI): The legal provisions and regulations defining the medical products that should be regulated were recently developed as draft but not yet promulgated and enforced. ➜ IMPLEMENTED (I): The legal provisions and regulations defining the medical products are promulgated and enforced.
Limitations and remarks:	▪ In a short time, it may not be possible for the assessor to review all aspects that this indicator includes. Preferably the country profile or other documents that provide a good description of the regulatory landscape in the country should be studied beforehand. ▪ Scoring this sub-indicator as "not applicable NA" is excluded (i.e. this sub-indicator will always apply for all benchmarked NRAs).
Sub Indicator:	**RS01.02: Legal provision and regulations define the institutions that are involved as part of the regulatory system, as well as their mandates, functions, roles, responsibilities and enforcement powers.**
Maturity Level:	1
Scope:	1. Medicines 2. Vaccines
Description:	The assessor should identify the legislation and regulations that define all institutions involved in medical product regulation including the relevant regulatory functions for each institution. The regulatory functions covered will depend on the scope of the regulatory system. The regulations should provide a clear mandate and define functions, roles, responsibilities and enforcement powers for each regulatory function in order to avoid overlapping of the respective empowerments. In the case of an assessment of a framework with multiple regulatory authorities, the sub-indicator should be fulfilled by each regulatory authority as well as any regional institution or authority. If different organizations at different level of the state are involved the assessor should review how the linkage among the organizations is defined in the law.
Objective:	The objective of this sub-indicator is to ensure that the legislation and institutional regulations provide clear mandates, functions, roles, responsibilities and enforcement powers for each section in order to avoid overlap of the respective empowerments. The same principle is applied if more than one institution is involved, or if different entities at different levels of the state are involved.
Requirement:	Institutions involved in the regulatory system

Evidence to review:	The assessor should request for and review: 1. List of agencies or authorities participating in the regulation of medical products, and the mandate for each. 2. Promulgated legal provisions and regulations establishing the regulatory system and defining the mandate for each of the institutions involved in the regulatory system. 3. Duties, responsibilities, level of competencies, mandates and enforcement powers established for each institution. 4. Documents that demonstrate that the role and scope of each institution is clear to all involved, especially when there are complementary or shared responsibilities.
References:	1. Guidelines for national authorities on quality assurance for biological products. In: WHO Expert Committee on Biological Standardization: forty-second report. World Health Organization; 1992: Annex 2 (WHO Technical Report Series, No. 822), (2), (http://www.who.int/biologicals/publications/trs/areas/biological_products/WHO_TRS_822_A2.pdf) 2. National Drug Regulatory Legislation: guiding principles for small drug regulatory authorities. In: WHO Expert Committee on Specifications on Pharmaceutical Preparations: thirty- fifth report. World Health Organization; 1999: Annex 8 (WHO Technical Report Series, No. 885)., (78), (http://apps.who.int/medicinedocs/documents/s21964en/s21964en.pdf) 3. Regulation and licensing of biological products in countries with newly developing regulatory authorities. In: WHO Expert Committee on Biological Standardization: forty-fifth report. Geneva: World Health Organization; 1995: Annex 1 (WHO Technical Report Series, No. 858), (3), (http://www.who.int/bloodproducts/publications/WHO_TRS_858_A1.pdf) 4. How to develop and implement a national drug policy, Second edition. WHO, 2001., (116), (http://apps.who.int/medicinedocs/pdf/s2283e/s2283e.pdf)
Framework:	Structure/Foundation/Input
Rating Scale:	➔ NOT IMPLEMENTED (NI): There are no legal provisions or regulations defining the institutions involved as part of the regulatory system. ➔ ONGOING IMPLEMENTATION (OI): There might be legal provisions and regulations defining the institutions involved as part of the regulatory system for some institutions but not all, or although they do not exist, demonstrable steps have been taken towards developing them. ➔ PARTIALLY IMPLEMENTED (PI): The legal provisions and regulations defining the institutions involved as part of the regulatory system were recently developed as draft but not yet published officially. ➔ IMPLEMENTED (I): The legal provisions and regulations defining the institutions involved as part of the regulatory system are published and available.
Limitations and remarks:	Scoring this sub-indicator as "not applicable NA" is excluded (i.e. this sub-indicator will always apply for all benchmarked NRAs).
Sub Indicator:	**RS01.03: When more than one institution or authority is involved in regulatory oversight, the regulations should define administrative arrangements and the channels of communication and coordination.**
Maturity Level:	2
Scope:	1. Medicines 2. Vaccines
Description:	The assessor should verify the availability and implementation of regulations defining channels of coordination among different institutions when the National Regulatory Authority (NRA) is represented by more than one institution or authority. The assessor should verify that there are well-defined administrative mechanisms for clear coordination among the different institutions in order to avoid overlap of the respective empowerments. If different organizations at different levels of the state are involved, the assessor should review how the exchange of information is established and implemented.

Objective:	The objective of this sub-indicator is to ensure that the regulations define mechanisms for communication, coordination and management of regulatory activities and processes when more than one institution or authority is involved in the national regulatory system. If different entities at different levels of the state are involved, the same principle is applied.
Requirement:	Defined channels of coordination and an administrative mechanism
Evidence to review:	The assessor should request for and review: 1. List of agencies or authorities participating in the regulation of medical products and the mandate for each. 2. Published regulations defining the channels of coordination and an administrative mechanism when more than one institution or authority is involved in regulatory activities. 3. Record of communications and other related evidence that shows coordination and proper exchange of information. 4. Identified focal points for the purpose of coordination and exchange of information.
References:	
Framework:	Structure/Foundation/Input
Rating Scale:	➜ NOT IMPLEMENTED (NI): There are no regulations defining the administrative arrangements and the channels of communication and coordination when more than one institution or authority is involved in regulatory activities. ➜ ONGOING IMPLEMENTATION (OI): There might be regulations defining the administrative arrangements and the channels of communication and coordination for some institutions or authorities but not for all, or although they do not exist, demonstrable steps have been taken towards developing them. ➜ PARTIALLY IMPLEMENTED (PI): The regulations defining the administrative arrangements and the channels of communication and coordination were recently developed as draft but not yet published officially. ➜ IMPLEMENTED (I): The regulations defining the administrative arrangements and the channels of communication and coordination, when more than one institution or authority is involved in regulatory activities, are published and available.
Limitations and remarks:	
Sub Indicator:	**RS01.04: All regulatory entities (central and decentralized ones) follow non- contradictory regulations, standards, guidelines and procedures.**
Maturity Level:	3
Scope:	1. Medicines 2. Vaccines
Description:	The assessor should understand, for the different administrative levels, the policy and administrative organization for each of the organizational structures, as well as their responsibilities and mandates. The assessor should verify if legislation defines whether activities are centralized or whether they have been decentralized to other agencies or authorities (states, provinces, others). If decentralized, assessor should verify that they follow non-contradictory regulations, standards, guidelines, and procedures. Assessor should check the availability and implementation of such non-contradictory regulations, standards, guidelines and procedures in all levels of the regulatory bodies. In addition, there should be a mechanism in place to manage the possible changes to any related regulations, standards, guidelines and procedures. Guidelines for regulatory activities should be developed and/or adopted and regularly updated. All regulatory bodies should apply these guidelines.
Objective:	The objective of this indicator is to ensure that activities conducted by decentralized entities follow updated regulations, standards, guidelines, and procedures that are in agreement with the central authority of the country. This ensures that regardless of the entity or place where

	regulatory activities are taking place, the same principles and standards will be followed by all relevant parties. It also allows those regulatory bodies to have clarity on their roles and responsibilities.
Requirement:	Updated and non-contradictory regulations, standards, guidelines and procedures for all regulatory bodies.
Evidence to review:	The assessor should request for and review: 1. List of all regulatory bodies (central and decentralized ones) participating in the regulation of medical products and the mandate for each. 2. The legislation and regulations that establish that all regulatory bodies (central and decentralized ones) should follow the same regulations, standards, guidelines, and procedures. 3. The identity of the individual or group responsible for monitoring of adherence to these principles (item2) 4. Documented evidence that procedures and mechanisms are in place to manage changes and inform all involved parties. 5. Documented evidence that procedures and mechanisms are in place to ensure guidelines are developed, regularly updated and available to all regulatory bodies.
References:	1. National drug regulatory legislation: guiding principles for small drug regulatory authorities. In: WHO Expert Committee on Specifications for Pharmaceutical Preparations: thirty-fifth report. Geneva: World Health Organization; 1999: Annex 8 (WHO Technical Report Series, No. 885) (1) (http://apps.who.int/medicinedocs/documents/s21964en/s21964en.pdf) 2. Guidelines for national authorities on quality assurance for biological products. In: WHO Expert Committee on Biological Standardization: forty-second report. World Health Organization; 1992: Annex 2 (WHO Technical Report Series, No. 822), (2), (http://www.who.int/biologicals/publications/trs/areas/biological_products/WHO_TRS_822_A2.pdf) 3. Regulation and licensing of biological products in countries with newly developing regulatory authorities. In: WHO Expert Committee on Biological Standardization: forty-fifth report. Geneva: World Health Organization; 1995: Annex 1 (WHO Technical Report Series, No. 858), (3), (http://www.who.int/bloodproducts/publications/WHO_TRS_858_A1.pdf) 4. How to develop and implement a national drug policy, Second edition. WHO, 2001., (116), (http://apps.who.int/medicinedocs/pdf/s2283e/s2283e.pdf)
Framework:	Structure/Foundation/Input
Rating Scale:	➜ NOT IMPLEMENTED (NI): There are no legal provisions or regulations defining the regulatory bodies (central and decentralized ones) involved as part of the regulatory system. ➜ ONGOING IMPLEMENTATION (OI): There might be legal provision and regulations defining the regulatory bodies (central and decentralized ones) involved as part of the regulatory system for some institutions but not all, or although they do not exist, demonstrable steps have been taken towards developing them. ➜ PARTIALLY IMPLEMENTED (PI): The legal provisions and regulations defining the regulatory bodies (central and decentralized ones) involved as part of the regulatory system were recently developed as draft but not yet published officially. ➜ IMPLEMENTED (I): The legal provisions and regulations defining the regulatory bodies (central and decentralized ones) involved as parts of the regulatory system are published and available.
Limitations and remarks:	
Sub Indicator:	**RS01.05: Legal provisions and relevant regulations to take actions on recall, suspension, withdrawal and/or destruction of substandard and falsified (SF) medical products.**
Maturity Level:	1

Scope:	1. Medicines 2. Vaccines
Description:	The assessor should verify the availability of legal provisions and regulations supporting regulatory enforcement actions related to SF medical products, including recall, suspension, withdrawal and/or destruction. In addition, the assessor should ensure that the NRA has authority to withhold or withdraw products from the market as well as from use in clinical trials.
Objective:	The objective of this indicator is to ensure that adequate provisions and mechanisms exist and have been enacted to handle actions on recall, suspension, withdrawal and/or destruction of SF medical products. This should include their destruction and a requirement for the manufacturers, distributors, or marketing authorization holders to participate in the recall of unsafe, defective or inappropriately labelled products. Possible actions include the suspension of a marketing authorization, the recall of certain batches, issuance of warnings in national drugs bulletins, or issuance of a separate warning sent out to a list of institutions and key persons dealing with handling of medical products. NRA should have authority to withdraw products from the market and from clinical development or clinical trials.
Requirement:	Legal provisions and/or regulations for regulatory actions against SF medical products.
Evidence to review:	The assessor should request for and review: 1. Promulgated and enforced legal provisions and regulations to take actions on recall, suspension, withdrawal and/or destruction of SF medical products. 2. Guidance for manufacturers, importers, exporters and distributors on how to handle a recall including product destruction. 3. Procedures for handling quality defects (e.g., notifications of suspected quality defects or batch recalls by the company) including, focal points, defined responsibilities, deadlines and records. 4. List of recalls performed and documented reports.
References:	
Framework:	Structure/Foundation/Input
Rating Scale:	➜ NOT IMPLEMENTED (NI): There are no legal provisions or regulations to take actions on recall, suspension, withdrawal and/or destruction of SF medical products. ➜ ONGOING IMPLEMENTATION (OI): There might be some legal provisions and regulations to take actions on recall, suspension, withdrawal and/or destruction of some SF medical products but not all, or although they do not exist, demonstrable steps have been taken towards developing them. ➜ PARTIALLY IMPLEMENTED (PI): The legal provisions and regulations to take actions on recall, suspension, withdrawal and/or destruction of SF medical products were recently developed as draft but not yet published officially. ➜ IMPLEMENTED (I): The legal provisions and regulations to take actions on recall, suspension, withdrawal and/or destruction of SF medical products are published and available.
Limitations and remarks:	▪ Market Surveillance and Control (MC) function ▪ Regulatory Inspection (RI) function ▪ Scoring this sub-indicator as "not applicable NA" is excluded (i.e. this sub-indicator will always apply for all benchmarked NRAs).
Sub Indicator:	**RS01.06: Legal provisions and regulations define requirements of transparency and dissemination of information to the public and relevant stakeholders.**
Maturity Level:	2
Scope:	1. Medicines 2. Vaccines

Description:	The assessor should check whether the legal basis requires the mandated institutions to provide information to public and relevant stakeholders. The assessor should verify whether legislation and regulations are publicly available, and that channels of communication exist for this purpose.
Objective:	The objective of this sub-indicator is to ensure that legislation, regulations and other relevant information are publicly available. This public availability will ensure that those governed by the regulations, as well as society in general, can be aware of the information and utilize it as appropriate. In order to perform adequately and in a timely manner, the NRA should have proper channels of communication in order to respond to the needs, obligations and priorities.
Requirement:	Legal provisions for transparency and dissemination of information.
Evidence to review:	The assessor should request for and review: 1. Laws, regulations, other regulatory provisions, methodologies, and procedures establishing that legislation and regulations are to be made public. 2. Public information from websites or in official bulletins or other legal publications. 3. Evidence for the availability and use of electronic or other platforms or means that allow external communications regarding the regulations. 4. Direct forms of dissemination such as letters and emails. 5. Documentation of feedback after dissemination and publication (e.g., acknowledgments of receipt, complaints, or questions).
References:	National drug regulatory legislation: guiding principles for small drug regulatory authorities. In: WHO Expert Committee on Specifications for Pharmaceutical Preparations: thirty-fifth report. Geneva: World Health Organization; 1999: Annex 8 (WHO Technical Report Series, No. 885) (1) (http://apps.who.int/medicinedocs/documents/s21964en/s21964en.pdf) 2. Guidelines for national authorities on quality assurance for biological products. In: WHO Expert Committee on Biological Standardization: forty-second report. WorldHealth Organization; 1992: Annex 2 (WHO Technical Report Series, No. 822), (2), (http://www.who.int/biologicals/publications/trs/areas/biological_products/WHO_TRS_822_A2.pdf) 3. Regulation and licensing of biological products in countries with newly developing regulatory authorities. In: WHO Expert Committee on Biological Standardization: forty-fifth report. Geneva: World Health Organization; 1995: Annex 1 (WHO Technical Report Series, No. 858), (3), (http://www.who.int/bloodproducts/publications/WHO_TRS_858_A1.pdf) 4. How to develop and implement a national drug policy, Second edition. WHO, 2001., (116), (http://apps.who.int/medicinedocs/pdf/s2283e/s2283e.pdf) 5. Good governance for medicines: Model framework. Updated version 2014. WHO (110) (https://www.who.int/medicines/areas/governance/ggm_modelframe_updated/en/)
Framework:	Structure/Foundation/Input
Rating Scale:	➜ NOT IMPLEMENTED (NI): There are no legal provisions or regulations to define requirements of transparency and dissemination of information to the public and relevant stakeholders. ➜ ONGOING IMPLEMENTATION (OI): The legal provisions and regulations to define requirements for transparency and dissemination of information to the public and relevant stakeholders were recently developed as draft but not yet published officially and implemented. ➜ PARTIALLY IMPLEMENTED (PI): There are legal provisions and regulation to define requirements for transparency and dissemination of information to the public and relevant stakeholders, and these were recently published and/or implemented. ➜ IMPLEMENTED (I): The legal provisions and regulations to define requirements of transparency and dissemination of information to the public and relevant stakeholders are published and available.
Limitations and remarks:	

Sub Indicator:	**RS01.07: Development of the regulations involves the NRA responsible for their implementation and enforcement.**
Maturity Level:	1
Scope:	1. Medicines 2. Vaccines
Description:	The assessor should verify that legislation and regulations ensure that the responsibilities, qualifications, rights and roles of each party are defined and recognized (including those of medical practitioners, pharmacists and the NRA). They also create the legal basis enabling the regulatory control of activities such as drug manufacture, import, export, marketing, prescribing, dispensing and distribution. The legal provisions also should establish the legal basis for enforcement of such laws and regulations. The purpose of the legislation is therefore the same as that of the drug policy: to ensure that only safe, effective, quality drugs are produced, imported and distributed, and that these drugs are made available, managed effectively, and used appropriately. When writing the law, the practicalities of future enforcement should be kept in mind. If there are no strategies, facilities and resources for implementation and enforcement, legislation on its own will achieve nothing. A law with modest aims and objectives that is properly enforced is preferable to a more comprehensive one that cannot be implemented. As a good practice, development of the legal provisions should involve the regulatory authority responsible for their implementation and enforcement. In addition, the assessor should check if suitable timelines for the implementation of newly adopted regulations and guidelines are practiced. The suggested timeline for adoption of new internationally recognized guidelines (e.g., guidelines from World Health Organization (WHO) or International Conference on Harmonization) ranges from 6 to 12 months; however, it is recognized that guideline implementation, might be extended over a longer period.
Objective:	The objective of this sub-indicator is to ensure that the development of the legal provisions involves the regulatory authority responsible for their implementation and enforcement. A well-formulated enforcement strategy is one that provides correct incentives for the regulated subjects as well as appropriate guidelines for enforcement. Furthermore, the enforcement strategy should be designed to minimize both the monitoring effort and the costs for the regulated subjects and the public sector. The importance of the enforcement phase is to ensure the quality and effectiveness of regulatory policy and delivery, to reduce the overall level of regulatory burdens imposed on businesses and citizens, and to increase incentives for compliance by private actors.
Requirement:	Involvement of the regulatory system in the development of regulations
Evidence to review:	The assessor should request for and review: 1. Legal provisions supporting different regulatory activities; 2. Records of process.
References:	1. National drug regulatory legislation: guiding principles for small drug regulatory authorities. In: WHO Expert Committee on Specifications for Pharmaceutical Preparations: thirty-fifth report. Geneva: World Health Organization; 1999: Annex 8 (WHO Technical Report Series, No. 885) (1) (http://apps.who.int/medicinedocs/documents/s21964en/s21964en.pdf) 2. Guidelines for national authorities on quality assurance for biological products. In: WHO Expert Committee on Biological Standardization: forty-second report. World Health Organization; 1992: Annex 2 (WHO Technical Report Series, No. 822), (2), (http://www.who.int/biologicals/publications/trs/areas/biological_products/WHO_TRS_822_A2.pdf) 3. Regulation and licensing of biological products in countries with newly developing regulatory authorities. In: WHO Expert Committee on Biological Standardization: forty-fifth report. Geneva: World Health Organization; 1995: Annex 1 (WHO Technical Report Series, No. 858), (3), (http://www.who.int/bloodproducts/publications/WHO_TRS_858_A1.pdf) 4. How to develop and implement a national drug policy, Second edition. WHO, 2001., (116), (http://apps.who.int/medicinedocs/pdf/s2283e/s2283e.pdf)

Framework:	Structure/Foundation/Input
Rating Scale:	➜ NOT IMPLEMENTED (NI): There is no evidence that the development of regulations involve the regulatory authority responsible for their implementation and enforcement. ➜ ONGOING IMPLEMENTATION (OI): There is no evidence but demonstrable steps have been taken towards this. ➜ PARTIALLY IMPLEMENTED (PI): The regulatory authority responsible for its implementation has developed a draft but it has not yet been promulgated and enforced. ➜ IMPLEMENTED (I): The regulations are developed with the involvement of the regulatory authority responsible for their implementation and enforcement.
Limitations and remarks:	Scoring this sub-indicator as "not applicable NA" is excluded (i.e. this sub-indicator will always apply for all benchmarked NRAs).
Sub Indicator:	**RS01.08: The NRA consults or involves specific sectors of the civil society (such as non-governmental organizations (NGOs) representing health professionals, industry, consumers and patients) during the development or adoption of regulations and guideline.**
Maturity Level:	3
Scope:	1. Medicines 2. Vaccines
Description:	The assessor should verify the development and application of a public and civil society consultation process prior to issuance of guidelines related to different regulatory activities. Specifically, assessor should: 1. Check whether the current and applicable legal and methodological bases for thedevelopment of regulations in the country require the participation of the NRA, industry, representatives of the health sector, patients, and NGOs. 2. Check whether a procedure is established to officially circulate or publish drafts in consultation with the public, the NRA, industry, representatives of the health sector, patients, and NGOs. 3. Assess evidence of how existing regulations were drafted, preferably those that were approved more than one year ago. Evaluate the extent to which they were circulated, and input was received from the NRA, industry, representatives of the health sector, patients, and NGOs. 4. Assess evidence that the time provided for consultation with the public, the NRA, industry, representatives of the health sector, patients, and NGOs was sufficient for review and response. 5, Assess evidence for the existence of suitable timelines for the implementation of newly adopted regulations and guidelines. Preferably, these timelines should be specified in the public consultation process. The suggested timeline for adoption of new internationally recognized guidelines (e.g. WHO and International Conference on Harmonization guidelines) ranges from 6 to 12 months; however, it is recognized that the guideline implementation might be extended over a longer period.
Objective:	The objective of this indicator is to confirm that the regulations are developed through an interactive and participative process involving, among others, the NRA, industry, representatives of the health sector, patients, and NGOs. Assessor should note that the participants may vary according to the draft regulation or guideline under consideration; however, the consultation process ideally should be open to the public in accordance with good regulatory practices (GRP). As part of an open and transparent public policy, the development of regulations demands the participation of the general public as well as those regulated. From the earliest stages of developing a regulatory provision, consideration must be given to the viewpoints of those who must follow the standards that are set, those who are impacted by them, and those in general society. If regulations are approved without input from the key stakeholders involved, it is doubtful that they will be fully understood or successfully implemented.

Requirement:	Consults or involves specific sectors for the development or adoption of the guidelines
Evidence to review:	The assessor should request for and review: 1. Procedures for public and civil society consultation along with published drafts of guidelines; 2. Laws, regulations, guidelines, methodologies, or procedures establishing how regulations are prepared, who is invited to participate in the process, and who is consulted before approval; 3. Institutional records on the preparation of regulations and consultations carried out.
References:	1. National drug regulatory legislation: guiding principles for small drug regulatory authorities. In: WHO Expert Committee on Specifications for Pharmaceutical Preparations: thirty-fifth report. Geneva: World Health Organization; 1999: Annex 8 (WHO Technical Report Series, No. 885) (1) (http://apps.who.int/medicinedocs/documents/s21964en/s21964en.pdf) 2. Guidelines for national authorities on quality assurance for biological products. In: WHO Expert Committee on Biological Standardization: forty-second report. World Health Organization; 1992: Annex 2 (WHO Technical Report Series, No. 822), (2), (http://www.who.int/biologicals/publications/trs/areas/biological_products/WHO_TRS_822_A2.pdf) 3. Regulation and licensing of biological products in countries with newly developing regulatory authorities. In: WHO Expert Committee on Biological Standardization: forty-fifth report. Geneva: World Health Organization; 1995: Annex 1 (WHO Technical Report Series, No. 858), (3), (http://www.who.int/bloodproducts/publications/WHO_TRS_858_A1.pdf) 4. How to develop and implement a national drug policy, Second edition. WHO, 2001., (116), (http://apps.who.int/medicinedocs/pdf/s2283e/s2283e.pdf)
Framework:	"Structure/Foundation/Input"
Rating Scale:	➜ NOT IMPLEMENTED (NI): There is no evidence the NRA consults or involves specific sectors of the civil society (such as NGOs representing health professionals, industry, consumers and patients) during the development or adoption of regulations and guidelines. ➜ ONGOING IMPLEMENTATION (OI): There is no evidence but demonstrable steps have been taken towards this. ➜ PARTIALLY IMPLEMENTED (PI): The regulatory authority responsible for its implementation has developed a draft but it has not yet been promulgated and enforced. ➜ IMPLEMENTED (I): There is documented evidence the NRA consults or involves specific sectors of the civil society (such as NGOs representing health professionals, industry, consumers and patients) during the development or adoption of regulations and guidelines.
Limitations and remarks:	▪ The participation of all parties identified will vary depending on the type of regulation. The assessor should be mindful of why some may be excluded from the process for certain regulations. ▪ Scoring this sub-indicator as "not applicable NA" is excluded (i.e. this sub-indicator will always apply for all benchmarked NRAs).
Sub Indicator:	**RS01.09: A guideline on complaints and appeals against regulatory decisions is available to the public.**
Maturity Level:	3
Scope:	1. Medicines 2. Vaccines
Description:	The assessor should review if the possibility to appeal regulatory decisions, including those related to enforcement and inspection activities, is a fundamental aspect of the law. An efficient and effective enforcement system must provide readily accessible and transparent means for receiving complaints and appeals against regulatory decisions. The NRA should have implemented guidelines on review, evaluation, communication of complaints and appeals against regulatory decisions.

Objective:	The objective of this sub-indicator is to ensure that a mechanism exists to appeal regulatory decisions.
Requirement:	Complaints and appeals against regulatory decisions
Evidence to review:	The assessor should request for and review: 1. Guidelines for complaints and appeals related to different regulatory decisions.
References:	1. National drug regulatory legislation: guiding principles for small drug regulatory authorities. In: WHO Expert Committee on Specifications for Pharmaceutical Preparations: thirty-fifth report. Geneva: World Health Organization; 1999: Annex 8 (WHO Technical Report Series, No. 885) (1) (http://apps.who.int/medicinedocs/documents/s21964en/s21964en.pdf) 2. Guidelines for national authorities on quality assurance for biological products. In: WHO Expert Committee on Biological Standardization: forty-second report. World Health Organization; 1992: Annex 2 (WHO Technical Report Series, No. 822), (2), (http://www.who.int/biologicals/publications/trs/areas/biological_products/WHO_TRS_822_A2.pdf) 3. Regulation and licensing of biological products in countries with newly developing regulatory authorities. In: WHO Expert Committee on Biological Standardization: forty-fifth report. Geneva: World Health Organization; 1995: Annex 1 (WHO Technical Report Series, No. 858), (3), (http://www.who.int/bloodproducts/publications/WHO_TRS_858_A1.pdf) 4. How to develop and implement a national drug policy, Second edition. WHO, 2001., (116), (http://apps.who.int/medicinedocs/pdf/s2283e/s2283e.pdf)
Framework:	Structure/Foundation/Input
Rating Scale:	➜ NOT IMPLEMENTED (NI): There is no guideline available on complaints and appeals against regulatory decisions. ➜ ONGOING IMPLEMENTATION (OI): There is no evidence of a guideline on complaints and appeals against regulatory decisions, but demonstrable steps have been taken towards its development. ➜ PARTIALLY IMPLEMENTED (PI): There is a draft guideline on complaints and appeals against regulatory decisions but it is not yet implemented. ➜ IMPLEMENTED (I): There is a documented and implemented guideline on complaints and appeals against regulatory decisions.
Limitations and remarks:	Scoring this sub-indicator as "not applicable NA" is excluded (i.e. this sub-indicator will always apply for all benchmarked NRAs).
Indicator:	**RS02 Arrangement for effective organization and good governance.**
Objective:	The objective of this indicator is to ensure that arrangements for effective organization and good governance are in place. Good governance is an essential factor for economic growth and sustainable development at all levels and within all sectors of society. The term Good Governance is increasingly used to emphasize the need for governance to operate with due regard for the rule of law and especially in a manner that is free of corruption. There is also growing consensus on the major characteristics of good governance. Good governance is participatory, consensus-oriented, accountable, transparent, responsive, effective, efficient, equitable, inclusive, and follows the rule of law.
Category:	02. Organization and governance
Sub Indicator:	**RS02.01: The structure and line of authority among, and within, all institutions that participate in the regulatory system is defined, documented and implemented.**
Maturity Level:	3
Scope:	1. Medicines 2. Vaccines

Description:	The assessor should verify that legislation or institutional regulation defines the structure and line of authority among, and within, all institutions that participate in the regulatory system. If more than one institution is involved, the legislation or institutional regulation should provide for clear coordination and avoid overlap of the regulatory activities. If different organizations at different level of the state are involved, the assessor should review the linkage among the organizations and evaluate how the exchange of information is established and implemented.
Objective:	The objective of this sub-indicator is to ensure that the structure and line of authority among, and within, all institutions that participate in the regulatory system is implemented to ensure coordination and to avoid overlap of the respective empowerments.
Requirement:	Structure and line of authority
Evidence to review:	The assessor should request for and review: 1. Institutional founding documents along with evidence of implementation through procedures and respective records; 2. Organizational chart of NRA. 3. Procedures and human resources record forms of members and staff of the authority, their terms of reference and duration of office.
References:	1. National drug regulatory legislation: guiding principles for small drug regulatory authorities. In: WHO Expert Committee on Specifications for Pharmaceutical Preparations: thirty-fifth report. Geneva: World Health Organization; 1999: Annex 8 (WHO Technical Report Series, No. 885) (1) (http://apps.who.int/medicinedocs/documents/s21964en/s21964en.pdf) 2. Guidelines for national authorities on quality assurance for biological products. In: WHO Expert Committee on Biological Standardization: forty-second report. World Health Organization; 1992: Annex 2 (WHO Technical Report Series, No. 822), (2), (http://www.who.int/biologicals/publications/trs/areas/biological_products/WHO_TRS_822_A2.pdf) 3. Regulation and licensing of biological products in countries with newly developing regulatory authorities. In: WHO Expert Committee on Biological Standardization: forty-fifth report. Geneva: World Health Organization; 1995: Annex 1 (WHO Technical Report Series, No. 858), (3), (http://www.who.int/bloodproducts/publications/WHO_TRS_858_A1.pdf) 4. How to develop and implement a national drug policy, Second edition. WHO, 2001., (116), (http://apps.who.int/medicinedocs/pdf/s2283e/s2283e.pdf) 5. Good governance for medicines: Model framework. Updated version 2014. WHO (110) (https://www.who.int/medicines/areas/governance/ggm_modelframe_updated/en/)
Framework:	Structure/Foundation/Input
Rating Scale:	➜ NOT IMPLEMENTED (NI): The structure and line of authority among, and within, all institutions that participate in the regulatory system is not defined, documented and implemented. ➜ ONGOING IMPLEMENTATION (OI): There is no evidence that the structure and line of authority among, and within, all institutions that participate in the regulatory system are defined, documented and implemented but demonstrable steps have been taken towards its development. ➜ PARTIALLY IMPLEMENTED (PI): There is a draft defining the structure and line of authority among, and within, all institutions that participate in the regulatory system but it is not yet implemented. ➜ IMPLEMENTED (I): The structure and line of authority among, and within, all institutions that participate in the regulatory is defined, documented and implemented.
Limitations and remarks:	Scoring this sub-indicator as "not applicable NA" is excluded (i.e. this sub-indicator will always apply for all benchmarked NRAs).

Sub Indicator:	**RS02.02: Channels of communication and decision-making are clearly established among the structures, institutions, and departments forming the NRA.**
Maturity Level:	3
Scope:	1. Medicines 2. Vaccines
Description:	The assessor should verify the existence and the actual use of communication and decision makings channels among different structures, institutions, and departments forming the NRA.
Objective:	The objective of this sub-indicator is to ensure that channels of communication and decision-making are clearly established among the structures, institutions, and departments forming the NRA. Supporting documentation should include the definitions for roles and responsibilities for each section, mechanisms for communication and coordination, and protocols for information and resource sharing. Collaborative agreements can assist in avoiding overlap and the duplication of efforts.
Requirement:	Communication and decision-making channels
Evidence to review:	The assessor should request for and review: 1. Documentation for communication channels and decision making-process among the structures, institutions, and departments; 2. Evidence of implementation through procedures and respective records.
References:	1. National drug regulatory legislation: guiding principles for small drug regulatory authorities. In: WHO Expert Committee on Specifications for Pharmaceutical Preparations: thirty-fifth report. Geneva: World Health Organization; 1999: Annex 8 (WHO Technical Report Series, No. 885) (1) (http://apps.who.int/medicinedocs/documents/s21964en/s21964en.pdf) 2. Guidelines for national authorities on quality assurance for biological products. In: WHO Expert Committee on Biological Standardization: forty-second report. World Health Organization; 1992: Annex 2 (WHO Technical Report Series, No. 822), (2), (http://www.who.int/biologicals/publications/trs/areas/biological_products/WHO_TRS_822_A2.pdf) 3. Regulation and licensing of biological products in countries with newly developing regulatory authorities. In: WHO Expert Committee on Biological Standardization: forty-fifth report. Geneva: World Health Organization; 1995: Annex 1 (WHO Technical Report Series, No. 858), (3), (http://www.who.int/bloodproducts/publications/WHO_TRS_858_A1.pdf) 4. How to develop and implement a national drug policy, Second edition. WHO, 2001., (116), (http://apps.who.int/medicinedocs/pdf/s2283e/s2283e.pdf)
Framework:	Structure/Foundation/Input
Rating Scale:	➔ NOT IMPLEMENTED (NI): Channels of communication and decision-making are not clearly established among the structures, institutions, and departments that form the NRA. ➔ ONGOING IMPLEMENTATION (OI): There is no evidence that channels of communication and decision-making are established among the structures, institutions, and departments that form the NRA, but demonstrable steps have been taken towards their development. ➔ PARTIALLY IMPLEMENTED (PI): There is a draft defining channels of communication and decision-making among the structures, institutions, and departments that form the NRA, but it is not yet implemented. ➔ IMPLEMENTED (I): Channels of communication and decision-making among the structures, institutions, and departments that form the NRA are clearly defined, documented and implemented.
Limitations and remarks:	Scoring this sub-indicator as "not applicable NA" is excluded (i.e. this sub-indicator will always apply for all benchmarked NRAs).

Sub Indicator:	**RS02.03: Scientific and advisory committees exist to advise the NRA on topics of scientific and regulatory interest and on future objectives and strategies.**
Maturity Level:	3
Scope:	1. Medicines 2. Vaccines
Description:	The assessor should verify that: 1. there are legal provisions granting the NRA authority to convene outside experts and committees; 2. the scope of existing legal provisions authorizes the NRA to determine: a. the functions of the outside experts and committees; b. their role in the decision-making process; c. the circumstances under which they should be convened; 3. the NRA uses this authority to convene outside experts and committees
Objective:	The objective of this indicator is to ensure that the legal basis exists to convene outside experts and expert committees, to define their functions, (in particular, their role in the NRA decision-making process) and to define the circumstances under which they should be convened. Science and technology are evolving at a dizzying pace. Therefore, issues must be handled by multidisciplinary teams and it is impossible for the NRAs to have all the expertise needed to handle all issues. For this reason, it is highly recommended to have external experts and committees of experts available to help with the regulatory decision-making process. Nevertheless, advisory and scientific committees should not be considered as mandatory for the regulatory work. In this context, it should be noted that advisory and scientific committees add financial and administrative burden on the regulatory system. Legislation should give the NRA the authority to convene them in well-defined circumstances.
Requirement:	Scientific/advisory committees
Evidence to review:	The assessor should request for and review: 1. Laws, regulations, decrees, agreements, and other legal provisions conferring authority on the NRA to convene outside experts and expert committees, to define their functions, especially in the decision-making process, and to define the circumstances under which they should be convened. 2. Records, proceedings, and any other documents showing that the NRA makes use of the authority granted by the legislation.
References:	1. National drug regulatory legislation: guiding principles for small drug regulatory authorities. In: WHO Expert Committee on Specifications for Pharmaceutical Preparations: thirty-fifth report. Geneva: World Health Organization; 1999: Annex 8 (WHO Technical Report Series, No. 885) (1) (http://apps.who.int/medicinedocs/documents/s21964en/s21964en.pdf) 2. Guidelines for national authorities on quality assurance for biological products. In: WHO Expert Committee on Biological Standardization: forty-second report. World Health Organization; 1992: Annex 2 (WHO Technical Report Series, No. 822), (2), (http://www.who.int/biologicals/publications/trs/areas/biological_products/WHO_TRS_822_A2.pdf) 3. Regulation and licensing of biological products in countries with newly developing regulatory authorities. In: WHO Expert Committee on Biological Standardization: forty-fifth report. Geneva: World Health Organization; 1995: Annex 1 (WHO Technical Report Series, No. 858), (3), (http://www.who.int/bloodproducts/publications/WHO_TRS_858_A1.pdf) 4. How to develop and implement a national drug policy, Second edition. WHO, 2001., (116), (http://apps.who.int/medicinedocs/pdf/s2283e/s2283e.pdf)
Framework:	Structure/Foundation/Input

Rating Scale:	➔ NOT IMPLEMENTED (NI): Scientific and advisory committees to advise the NRA on topics of scientific and regulatory interest and future objectives and strategies are not used or documented. ➔ ONGOING IMPLEMENTATION (OI): There is no evidence that scientific and advisory committees to advise the NRA on topics of scientific and regulatory interest and future objectives and strategies are used but demonstrable steps have been taken towards their implementation. ➔ PARTIALLY IMPLEMENTED (PI): There is a draft defining scientific and advisory committees to advise the NRA on topics of scientific and regulatory interest and future objectives and strategies, but it is not yet implemented. ➔ IMPLEMENTED (I): Scientific and advisory committees to advise the NRA on topics of scientific and regulatory interest and future objectives and strategies are used and documented.
Limitations and remarks:	Advisory and scientific committees, formed or external or internal experts should not be considered as mandatory for the regulatory work. Therefore, if there is a duly documented political or legal decision against the participation of outside experts and committees (e.g., due to their administrative and/or financial burden), this indicator should be rated Not Applicable. However, in this case, which is exceptional indeed, the assessor should verify the availability of internal personnel with the expertise needed to take over the required regulatory activities without the need, for internal or external, expert committees. Availability of terms of reference for experts and expert committees would provide additional guidance to the assessor.
Sub Indicator:	**RS02.04: Independence of NRA from researchers, manufacturers, distributors and wholesalers, as well as from the procurement system.**
Maturity Level:	2
Scope:	1. Medicines 2. Vaccines
Description:	The assessor should identify documented evidence that demonstrates the independence of NRA decision-making from researchers, manufacturers, distributors, wholesalers as well as from procurement institutions involved in acquiring different medical products. For example, the control laboratory of a manufacturer must not perform the quality testing on behalf of the NRA when quality testing is deemed necessary by the NRA (e.g. for the purpose of post-marketing surveillance or NRA lot release, if applicable). Another example is that the decision-making bodies should not include or be influenced by experts who represent institutions interested in marketing of medical products. If the Ministry of Health or other governmental authority is responsible for procuring medical products in the country, documented evidence should be provided that NRA decision- making is independent from the organization or office that is responsible for procuring the products. Aspects to consider when assessing whether the objectives of the indicator have been met: 1. Determine whether the duties assigned to the NRA include research, manufacture, or distribution of medical products; 2. Examine the hierarchical level of the NRA and verify that the NRA is independent of those involved in research, manufacturing, and distribution of product.
Objective:	The objective of this indicator is to ensure that, consistently over time, the NRA operates independently of researchers, producers, distributors and other regulated parties. In order to discharge its duties fairly, the NRA must be independent of those regulated entities. Thus, the NRA may not be engaged in the activities that it regulates and may not be at a hierarchal level that is subordinate to those institutions that perform regulated activities. In some countries, the NRA historically has been responsible for manufacturing vaccines, which placed the NRA in the position of being judge and party to the matters before it, and thus compromising its independence and impartiality. Independence of the NRA decision-making process from influence by institutions,

	societies, and industries which may have direct or indirect interest in the NRA decisions is one of the key elements regarding the safe use of medical products and protection of public health.
Requirement:	Independence of NRA
Evidence to review:	The assessor should request for and review: 1. Organizational chart of the national regulatory system; 2. Functioning organizational chart of the NRA; 3. Documents defining mission and functions of the organizations within the national regulatory system.
References:	1. National drug regulatory legislation: guiding principles for small drug regulatory authorities. In: WHO Expert Committee on Specifications for Pharmaceutical Preparations: thirty-fifth report. Geneva: World Health Organization; 1999: Annex 8 (WHO Technical Report Series, No. 885) (1) (http://apps.who.int/medicinedocs/documents/s21964en/s21964en.pdf) 2. Guidelines for national authorities on quality assurance for biological products. In: WHO Expert Committee on Biological Standardization: forty-second report. World Health Organization; 1992: Annex 2 (WHO Technical Report Series, No. 822), (2), (http://www.who.int/biologicals/publications/trs/areas/biological_products/WHO_TRS_822_A2.pdf) 3. Regulation and licensing of biological products in countries with newly developing regulatory authorities. In: WHO Expert Committee on Biological Standardization: forty-fifth report. Geneva: World Health Organization; 1995: Annex 1 (WHO Technical Report Series, No. 858), (3), (http://www.who.int/bloodproducts/publications/WHO_TRS_858_A1.pdf) 4. How to develop and implement a national drug policy, Second edition. WHO, 2001., (116), (http://apps.who.int/medicinedocs/pdf/s2283e/s2283e.pdf)
Framework:	Structure/Foundation/Input
Rating Scale:	➔ NOT IMPLEMENTED (NI): There is no evidence that the NRA is independent from researchers, manufacturers, distributors and wholesalers, as well as from the procurement system. ➔ ONGOING IMPLEMENTATION (OI): There is no evidence that the NRA is independent from researchers, manufacturers, distributors and wholesalers, as well as from the procurement system; however, demonstrable steps toward this have been taken. ➔ PARTIALLY IMPLEMENTED (PI): There is evidence that some steps have been taken to establish the independence of NRA from researchers, manufacturers, distributors and wholesalers, as well as the procurement system, but it is not yet implemented. ➔ IMPLEMENTED (I): There is documented evidence the NRA is independent from researchers, manufacturers, distributors and wholesalers, as well as from the procurement system.
Limitations and remarks:	▪ In case the manufacturer is part of the structure of the National Regulatory System, this must be taken into consideration when evaluating the independency. It is important to maintain good collaboration and communication between industry and academia while maintaining the independence of the regulatory system. Regulatory authorities (including national control laboratories) may be involved in scientific research activities. However, these research activities should not entail any ▪ conflict of interest with respect to regulatory oversight. Internal researchers with no conflicts of interest are not meant to be addressed by this sub-indicator and scoring the sub-indicator as "not implemented" should be excluded (unless justified for some other reason). On the other hand, if the regulatory authority is involved in research activities which conflict with the mandate to regulate medical products, the sub-indicator should be scored as "not implemented". ▪ Scoring this sub-indicator as "not applicable NA" is excluded (i.e. this sub-indicator will always apply for all benchmarked NRAs).
Indicator:	**RS03 Strategic plan with clarified objective in place.**
Objective:	The objective of this indicator is to ensure that the NRA has implemented and updated

	its strategic plan, including general objectives that are broken down into specific targets for various regulatory functions, and that are provided with defined time periods for implementation. The NRA should also ensure that adherence to the strategic plan is monitored periodically. Based on its mission and vision, and in accordance with the government's policy, the NRA should adopt a coherent development strategy, update the strategy periodically, and monitor its implementation. This requires the availability of a detailed institutional development plan, including targets and deadlines, which complements the NRA strategy as stated in the NRA strategic plan. Setting a NRA strategy involves a complex process of development, implementation and monitoring. First, the strategy development process results in the formulation of the strategic plan. Second, activities aimed at achieving strategic objectives are implemented by the various entities of the NRA. Finally, the effect of these activities is monitored, and the regulatory work is adjusted if necessary. Throughout the process, careful planning and the involvement of the related parties are needed; at all times, the political dynamics have to be considered. A strategic plan without an implementation plan (also called institutional development plan) remains a dead document. Careful planning of the implementation steps and activities necessary to arrive at the expected outcome is important throughout the process. As evident, there are various types of plans. The first is probably the strategic plan (which may come under a higher national drug and medicine policy) to develop the strategic objectives themselves. After the strategic plan has been adopted, an implementation plan (also called institutional development plan or master plan) is needed; this implementation plan typically covers a 3 to 5-year period. This plan details the various activities for each of the strategic objectives. The implementation plan spells out what needs to be done and who is responsible, and then estimates the budget and proposes a time frame. If resources are insufficient without external input, a set of priority activities should be identified that can be executed within the existing resources. The implementation plan can be broken down into individual annual work plans for the NRA as a whole, or for the various units and departments.
Category:	03. Policy and strategic planning
Sub Indicator:	**RS03.01: A national drug policy, aligned with health policy, exists and is implemented.**
Maturity Level:	4
Scope:	1. Medicines 2. Vaccines
Description:	The assessor should verify the existence of national drug policy. A national drug policy, presented and printed as an official government statement, is important because it acts as a formal record of aspirations, aims, decisions and commitments. Without such a formal policy document, there may be no general overview of what is needed. As a result, some government measures may conflict with others because the various goals and responsibilities are not clearly defined and understood. The policy document should be developed through a systematic process that incudes consultation with all interested parties. In this process the objectives must be defined, priorities must be set, strategies must be developed, and commitments must be built. A national drug policy cannot bedeveloped in a vacuum; it must fit within the framework of a particular health care system, a national health policy and, perhaps, a programme of health sector reform. The goals of the national drug policy should always be consistent with broader health objectives, and policy implementation should help to achieve those broader objectives.
Objective:	The objective of this sub-indicator is to ensure that a national drug policy aligned with the health policy exists and it is implemented. A national drug policy is a commitment to a goal and a guide for action. It defines and prioritizes the medium to long-term goals set by the government for the pharmaceutical sector and identifies the main strategies for attaining them. It provides a framework within which the activities of the pharmaceutical sector can be coordinated. The policy covers both the public and the private sectors and

	involves all the main actors in the pharmaceutical field. A national drug policy is needed for many reasons. The most important are: to present a formal record of values, aspirations, aims, decisions and medium to long-term government commitments; to define the national goals and objectives for the pharmaceutical sector; to set priorities; to identify the strategies needed to meet those objectives; to identify the various actors responsible for implementing the main components of the policy; and to create a forum for national discussions on these issues.
Requirement:	National drug policy/national medicines policy
Evidence to review:	The assessor should request for and review: 1. National drug policy; 2. National health policy; 3. Evidence for implementation of the drug policy.
References:	1. National drug regulatory legislation: guiding principles for small drug regulatory authorities. In: WHO Expert Committee on Specifications for Pharmaceutical Preparations: thirty-fifth report. Geneva: World Health Organization; 1999: Annex 8 (WHO Technical Report Series, No. 885) (1) (http://apps.who.int/medicinedocs/documents/s21964en/s21964en.pdf) 2. Guidelines for national authorities on quality assurance for biological products. In: WHO Expert Committee on Biological Standardization: forty-second report. World Health Organization; 1992: Annex 2 (WHO Technical Report Series, No. 822), (2), (http://www.who.int/biologicals/publications/trs/areas/biological_products/WHO_TRS_822_A2.pdf) 3. Regulation and licensing of biological products in countries with newly developing regulatory authorities. In: WHO Expert Committee on Biological Standardization: forty-fifth report. Geneva: World Health Organization; 1995: Annex 1 (WHO Technical Report Series, No. 858), (3), (http://www.who.int/bloodproducts/publications/WHO_TRS_858_A1.pdf) 4. How to develop and implement a national drug policy, Second edition. WHO, 2001., (116), (http://apps.who.int/medicinedocs/pdf/s2283e/s2283e.pdf)
Framework:	Structure/Foundation/Input
Rating Scale:	➜ NOT IMPLEMENTED (NI): A national drug policy, aligned with health policy is not defined, documented and implemented. ➜ ONGOING IMPLEMENTATION (OI): There is no evidence that a national drug policy, aligned with health policy, exists and is implemented but demonstrable steps have been taken towards its development. ➜ PARTIALLY IMPLEMENTED (PI): There is a draft defining a national drug policy, aligned with health policy but it is not yet implemented. ➜ IMPLEMENTED (I): A national drug policy, aligned with health policy is defined, documented and implemented.
Limitations and remarks:	National drug policy is the term broadly used, however national medicines policy can also be found. In some countries the national drug policy can go to the cabinet or parliament for endorsement. In others, the policy will remain an administrative document that serves as a basis for implementation plans and changes in the law and regulations. In some countries the entire national drug policy document has become law. Although this is a powerful demonstration of political commitment, it can also cause problems, as future adjustments to the policy may become difficult. It is therefore recommended that only certain enabling components of the policy are incorporated into law, without too many operational details. Scoring this sub-indicator as "not applicable NA" is excluded (i.e. this sub-indicator will always apply for all benchmarked NRAs).
Sub Indicator:	**RS03.02: The NRA has established and declared its vision, mission and strategic priorities.**
Maturity Level:	3

Scope:	1. Medicines 2. Vaccines
Description:	The assessor should verify: 1. The existence of legal provisions establishing that the NRA must have a Board, Management Committee, or administrative leadership body. 2. That the functions of the Board, Management Committee or administrative body include the establishment and/or adoption of strategic development plans. 3. That such an administrative body exists in practice, that the administrative body is functioning, and that it approves and monitors the institution's strategic development plans.
Objective:	The objective of this sub-indicator is to ensure that the NRA has established and declared its vision, mission and strategic priorities. The general objectives of the national drug policy are access, quality and objective use. The policy should balance the various goals and objectives, and thus create a complete and consistent entity. For example, one objective is to provide access to assured source of medicines. Additionally, strategic development plans set out the means to achieve short, medium, and long-term goals, and to channel resources and activities toward achievement of same.
Requirement:	Vision, mission and strategic priorities
Evidence to review:	The assessor should request for and review: 1. Published or unpublished legal provisions on the leadership levels within the NRA; 2. Records, for the last three-time periods, of the proceedings of the administrative body that is responsible for adopting the institution's strategic development plans; 3. Organizational chart or other NRA document describing the Board or other administrative body.
References:	1. National drug regulatory legislation: guiding principles for small drug regulatory authorities. In: WHO Expert Committee on Specifications for Pharmaceutical Preparations: thirty-fifth report. Geneva: World Health Organization; 1999: Annex 8 (WHO Technical Report Series, No. 885) (1) (http://apps.who.int/medicinedocs/documents/s21964en/s21964en.pdf) 2. Guidelines for national authorities on quality assurance for biological products. In: WHO Expert Committee on Biological Standardization: forty-second report. World Health Organization; 1992: Annex 2 (WHO Technical Report Series, No. 822), (2), (http://www.who.int/biologicals/publications/trs/areas/biological_products/WHO_TRS_822_A2.pdf) 3. Regulation and licensing of biological products in countries with newly developing regulatory authorities. In: WHO Expert Committee on Biological Standardization: forty-fifth report. Geneva: World Health Organization; 1995: Annex 1 (WHO Technical Report Series, No. 858), (3), (http://www.who.int/bloodproducts/publications/WHO_TRS_858_A1.pdf) 4. How to develop and implement a national drug policy, Second edition. WHO, 2001., (116), (http://apps.who.int/medicinedocs/pdf/s2283e/s2283e.pdf)
Framework:	Structure/Foundation/Input
Rating Scale:	➔ NOT IMPLEMENTED (NI): The NRA has not established and declared its vision, mission and strategic priorities. ➔ ONGOING IMPLEMENTATION (OI): There is no evidence that the NRA has established and declared its vision, mission and strategic priorities but demonstrable steps have been taken towards its development. ➔ PARTIALLY IMPLEMENTED (PI): There is a draft document defining the NRA vision, mission and strategic priorities. ➔ IMPLEMENTED (I): There is documented evidence that the NRA has established and declared its vision, mission and strategic priorities.

Limitations and remarks:	▪ The terminology for collegial administrative bodies and institutional strategic development plans may vary from country to country. ▪ Scoring this sub-indicator as "not applicable NA" is excluded (i.e. this sub-indicator will always apply for all benchmarked NRAs).
Sub Indicator:	**RS03.03: A plan for achieving strategic objectives is developed, implemented and regularly updated.**
Maturity Level:	3
Scope:	1. Medicines 2. Vaccines
Description:	The assessor should verify that: 1. There are institutional strategic development plans and that they are updated (check last three versions or past three years). 2. The plan contains general and specific objectives, includes all basic regulatory functions, and establishes deadlines for carrying out actions or achieving expected results. 3. There is periodic monitoring of compliance with the plan.
Objective:	The objective of this indicator is to ensure that the NRA has implemented and updated its development plan, including the plan's general objectives that define specific targets and time periods for various regulatory functions. The NRA should also ensure that adherence to the development plan is monitored periodically. Based on its mission and vision, and in accordance with the government's policy, the NRA should adopt a coherent development strategy that is periodically updated and should then monitor its implementation. This requires the existence of an institutional development plan, as well as a strategy, including targets and deadlines, for following the plan.
Requirement:	Plan for achieving strategic objectives
Evidence to review:	The assessor should request for and review: 1. The NRA's institutional development plans and their updates; 2. The NRA's annual plans; 3. Documents that describe the general and specific objectives and measurement indicators; 4. periodic reports on compliance with the plans and objectives (which should be completed on at least an annual basis).
References:	1. National drug regulatory legislation: guiding principles for small drug regulatory authorities. In: WHO Expert Committee on Specifications for Pharmaceutical Preparations: thirty-fifth report. Geneva: World Health Organization; 1999: Annex 8 (WHO Technical Report Series, No. 885) (1) (http://apps.who.int/medicinedocs/documents/s21964en/s21964en.pdf) 2. Guidelines for national authorities on quality assurance for biological products. In: WHO Expert Committee on Biological Standardization: forty-second report. World Health Organization; 1992: Annex 2 (WHO Technical Report Series, No. 822), (2), (http://www.who.int/biologicals/publications/trs/areas/biological_products/WHO_TRS_822_A2.pdf) 3. Regulation and licensing of biological products in countries with newly developing regulatory authorities. In: WHO Expert Committee on Biological Standardization: forty-fifth report. Geneva: World Health Organization; 1995: Annex 1 (WHO Technical Report Series, No. 858), (3), (http://www.who.int/bloodproducts/publications/WHO_TRS_858_A1.pdf) 4. How to develop and implement a national drug policy, Second edition. WHO, 2001., (116), (http://apps.who.int/medicinedocs/pdf/s2283e/s2283e.pdf)
Framework:	Structure/Foundation/Input
Rating Scale:	➔ NOT IMPLEMENTED (NI): The NRA has not developed, implemented or regularly updated a plan for achieving strategic objectives. ➔ ONGOING IMPLEMENTATION (OI): There is no evidence that the NRA has developed,

	implemented or regularly updated a plan for achieving strategic objectives, but demonstrable steps have been taken towards its development. ➜ PARTIALLY IMPLEMENTED (PI): There is a draft document defining a plan for achieving strategic objectives. ➜ IMPLEMENTED (I): There is documented evidence that the NRA has developed, implemented and regularly updated a plan for achieving strategic objectives.
Limitations and remarks:	Scoring this sub-indicator as "not applicable NA" is excluded (i.e. this sub-indicator will always apply for all benchmarked NRAs).
Sub Indicator:	**RS03.04: Documented policies, procedures and mechanisms, including written criteria, are established for recognition and reliance on decisions of other NRAs (if applicable).**
Maturity Level:	2
Scope:	1. Medicines 2. Vaccines
Description:	The assessor should identify if there are provisions or written criteria for recognition and reliance on other NRAs. The assessor should check the criteria, provisions, procedures, and decision-making processes related to this recognition process, along with a list of recognized NRAs.
Objective:	The objective of this sub-indicator is to ensure there are documented policies, procedures and mechanisms in place for recognition and reliance on other NRAs. For example, some countries will not have the mechanisms and resources that enable them to assess the medicines applications with their own expertise; such countries may use a system or mechanism of recognizing decisions of other NRAs. In that case the country may recognize certificates, reports or decisions from the foreign NRA (e.g. in the country of origin of the product) or from the WHO prequalification process. Other examples may include the functions such as regulatory inspections, clinical trials oversight, and lot release. If this is the case, the assessor should verify that written provisions and procedures are established that define who is allowed to recognize decisions, reports or certificates from other authorities. For this purpose, the NRA should create a list of the NRAs that may be recognized.
Requirement:	Recognition and reliance on other NRA's decisions
Evidence to review:	The assessor should request for and review: 1. Documentation for the mechanisms and procedures for recognition and reliance on other NRA's decisions; 2. Documentation for the policy that defines the criteria for recognition of foreign NRA inspections or regulatory decisions; 3. A list of recognized NRAs and supporting records.
References:	1. National drug regulatory legislation: guiding principles for small drug regulatory authorities. In: WHO Expert Committee on Specifications for Pharmaceutical Preparations: thirty-fifth report. Geneva: World Health Organization; 1999: Annex 8 (WHO Technical Report Series, No. 885) (1) (http://apps.who.int/medicinedocs/documents/s21964en/s21964en.pdf) 2. Guidelines for national authorities on quality assurance for biological products. In: WHO Expert Committee on Biological Standardization: forty-second report. World Health Organization; 1992: Annex 2 (WHO Technical Report Series, No. 822), (2), (http://www.who.int/biologicals/publications/trs/areas/biological_products/WHO_TRS_822_A2.pdf) 3. Regulation and licensing of biological products in countries with newly developing regulatory authorities. In: WHO Expert Committee on Biological Standardization: forty-fifth report. Geneva: World Health Organization; 1995: Annex 1 (WHO Technical Report Series, No. 858), (3), (http://www.who.int/bloodproducts/publications/WHO_TRS_858_A1.pdf) 4. How to develop and implement a national drug policy, Second edition. WHO, 2001., (116), (http://apps.who.int/medicinedocs/pdf/s2283e/s2283e.pdf)

Framework:	Structure/Foundation/Input
Rating Scale:	➜ NOT IMPLEMENTED (NI): The NRA has not established documented policies, procedures and mechanisms with written criteria for recognition and reliance on other NRA's decisions (if applicable). ➜ ONGOING IMPLEMENTATION (OI): There is no evidence that the NRA has established documented policies, procedures and mechanisms with written criteria for recognition and reliance on other NRA's decisions (if applicable) but demonstrable steps have been taken towards its development. ➜ PARTIALLY IMPLEMENTED (PI): There is a draft document defining documented policies, procedures and mechanisms with written criteria for recognition and reliance on other NRA's decisions (if applicable) ➜ IMPLEMENTED (I): There is documented evidence that the NRA has developed, implemented or regularly updated documented policies, procedures and mechanisms, with written criteria, for recognition and reliance on other NRA's decisions (if applicable)
Limitations and remarks:	If the country has enough resources to conduct all regulatory oversight with internal resources, this sub-indicator is not applicable.
Sub Indicator:	**RS03.05: The NRA is promoting good regulatory practices (GRPs).**
Maturity Level:	4
Scope:	1. Medicines 2. Vaccines
Description:	The assessor should evaluate if the NRA promotes, establishes and applies the principles of GRP to the regulation of medical products in different functions and areas. The principles on which regulatory systems may be established and by which they may be evaluated are legality, impartiality, consistency, proportionality, flexibility, effectiveness, efficiency, clarity and transparency.
Objective:	The objective of this sub-indicator is to ensure the NRA applies the principles of GRP to the regulation of medical products. GRPs are built on a foundation of transparency, good governance and sound policy-making. Public confidence in health products depends on confidence in the integrity of regulatory oversight. In order to meet their objectives of promoting and protecting public health, national regulatory authorities need to carry out their functions based on this set of principles. GRPs help to ensure that national regulatory systems, and international regulatory cooperation programmes, remain relevant, current and flexible as technology evolves and unforeseen needs and emergencies occur.
Requirement:	GRP
Evidence to review:	The assessor should request for and review: 1. Policies and regulations outlining the application of the principles of GRPs in the oversight of medical products; 2. Documents that provide examples of the application of the principles of GRPs.
References:	1. National drug regulatory legislation: guiding principles for small drug regulatory authorities. In: WHO Expert Committee on Specifications for Pharmaceutical Preparations: thirty-fifth report. Geneva: World Health Organization; 1999: Annex 8 (WHO Technical Report Series, No. 885) (1) (http://apps.who.int/medicinedocs/documents/s21964en/s21964en.pdf) 2. Guidelines for national authorities on quality assurance for biological products. In: WHO Expert Committee on Biological Standardization: forty-second report. World Health Organization; 1992: Annex 2 (WHO Technical Report Series, No. 822), (2), (http://www.who.int/biologicals/publications/trs/areas/biological_products/WHO_TRS_822_A2.pdf) 3. Regulation and licensing of biological products in countries with newly developing

	regulatory authorities. In: WHO Expert Committee on Biological Standardization: forty-fifth report. Geneva: World Health Organization; 1995: Annex 1 (WHO Technical Report Series, No. 858), (3), (http://www.who.int/bloodproducts/publications/WHO_TRS_858_A1.pdf) 4. How to develop and implement a national drug policy, Second edition. WHO, 2001., (116), (http://apps.who.int/medicinedocs/pdf/s2283e/s2283e.pdf) 5. Good regulatory practices: guidelines for national regulatory authorities for medical products., (112), (http://digicollection.org/whoqapharm/p/about/) and (http://apps.who.int/medicinedocs/en/)
Framework:	"Structure/Foundation/Input"
Rating Scale:	➔ NOT IMPLEMENTED (NI): The NRA is not promoting the principles of GRP. ➔ ONGOING IMPLEMENTATION (OI): There is no documented evidence the NRA is promoting the principles of GRP, but demonstrable steps have been taken towards its development. ➔ PARTIALLY IMPLEMENTED (PI): There is a draft document defining the principles of GRP. ➔ IMPLEMENTED (I): There is documented evidence that the NRA is promoting and applying accepted principles of GRP.
Limitations and remarks:	Scoring this sub-indicator as "not applicable NA" is excluded (i.e. this sub-indicator will always apply for all benchmarked NRAs).
Indicator:	**RS04 Regulatory system is supported with leadership and crisis management plans.**
Objective:	The objective of this indicator is to ensure that national regulatory authorities have the appropriate tools and institutional framework for co-coordinated action for management of crises. Getting a clear operational picture of the development of the crisis is the basis for decision-making both at operational and strategic levels. What happened, how many people are or might be affected, what are the issues at stake, how might the crisis develop, and what are the means in the operational field are a series of questions that leadership needs for making decisions. The complexities of modern crises often require the involvement of many actors, above and beyond emergency services. This approach demands effective coordination for a successful outcome. The need for coordination also raises significant public governance challenges, as crisis management functions are often exercised at sub-national levels but coordinated at the centers of governments. The capacity to coordinate crisis management is a fundamental element of good governance, as it tests the government's capacity to provide, in a timely manner, the appropriate responses required to protect citizens and businesses and to mitigate the impact of disasters. Crisis managers need to adapt their approaches to deal with a variety of different stakeholders that may have different interests, priorities, and values.
Category:	04. Leadership and crisis management
Sub Indicator:	**RS04.01: Leadership ensures that the strategic priorities and objectives are well known and communicated throughout the NRA.**
Maturity Level:	4
Scope:	1. Medicines 2. Vaccines
Description:	The assessor should verify that the strategic priorities and objectives are defined and implemented. In the case of crisis management, harmonized systems and situation reports from all active operational entities should be gathered at a centralized location in order to inform the crisis cell (i.e., the group composed of high level officials designated to be in charge and to respond, handle and manage crisis situations). Information and communication systems, as well as standard reporting protocols among the emergency

	response network, enable easier analysis and raise awareness of the situation. Ongoing work to address the challenge of public health emergencies has increasingly recognized the important role that public communication plays in their effective management.
Objective:	The objective of this sub-indicator is to confirm that strategic priorities and objectives are issued by senior management or the head of the institution. In addition, the assessor should verify that a development plan exists, and its implementation is supported by the senior management.
Requirement:	Strategic priorities and objectives communication
Evidence to review:	The assessor should request for and review: 1. Documents that verify that strategic priorities and objectives are available, distributed to different organizational levels and understood by the staff; 2. Records of relevant communications.
References:	1. National drug regulatory legislation: guiding principles for small drug regulatory authorities. In: WHO Expert Committee on Specifications for Pharmaceutical Preparations: thirty-fifth report. Geneva: World Health Organization; 1999: Annex 8 (WHO Technical Report Series, No. 885) (1) (http://apps.who.int/medicinedocs/documents/s21964en/s21964en.pdf) 2. Guidelines for national authorities on quality assurance for biological products. In: WHO Expert Committee on Biological Standardization: forty-second report. World Health Organization; 1992: Annex 2 (WHO Technical Report Series, No. 822), (2), (http://www.who.int/biologicals/publications/trs/areas/biological_products/WHO_TRS_822_A2.pdf) 3. Regulation and licensing of biological products in countries with newly developing regulatory authorities. In: WHO Expert Committee on Biological Standardization: forty-fifth report. Geneva: World Health Organization; 1995: Annex 1 (WHO Technical Report Series, No. 858), (3), (http://www.who.int/bloodproducts/publications/WHO_TRS_858_A1.pdf) 4. How to develop and implement a national drug policy, Second edition. WHO, 2001., (116), (http://apps.who.int/medicinedocs/pdf/s2283e/s2283e.pdf)
Framework:	Structure/Foundation/Input
Rating Scale:	➜ NOT IMPLEMENTED (NI): The strategic priorities and objectives are neither known nor communicated throughout the NRA. ➜ ONGOING IMPLEMENTATION (OI): There is no evidence that strategic priorities and objectives are known and communicated throughout the NRA, but demonstrable steps have been taken towards its development. ➜ PARTIALLY IMPLEMENTED (PI): There is a draft document defining the strategic priorities and objectives and how to communicate them through the NRA. ➜ IMPLEMENTED (I): There is documented evidence that the strategic priorities and objectives are known and communicated throughout the NRA.
Limitations and remarks:	Scoring this sub-indicator as “not applicable NA” is excluded (i.e. this sub-indicator will always apply for all benchmarked NRAs).
Sub Indicator:	**RS04.02: A rapid alert system to for managing the threats by SF medical products and for recalling these products from the market.**
Maturity Level:	2
Scope:	1. Medicines 2. Vaccines
Description:	The assessor should verify the existence of a nationwide rapid alert system to manage and react to SF medical products whenever and wherever identified. Such rapid alerts may or may not include an order to recall the concerned product or batch; however, the option

	for either limited or nationwide recalls should be available. In addition to product recalls, other possible actions in association with the rapid alert include, but are not limited to, suspension of distribution, quarantine in place, and importation alert. Furthermore, the rapid alert (with or without recall) may be associated with suspension or withdrawal of the marketing authorization for the related product. In addition, the rapid alert system may entail different levels of implementation (and accordingly communication), for example, national level, state level, district level, main store, and others throughout the organizations involved in the distribution channel. The assessor should also review the related roles and responsibilities, points of contact, communication channels, and decision trees, including representative examples of rapid alerts issued over the last few years.
Objective:	The objective of this sub-indicator is to confirm the existence of a rapid alert system that is able to manage threats posed by SF medical products and ensure a timely and proportionate response. The existence of SF medical products is an unacceptable risk to public health because they have the potential to harm patients and undermine confidence in medical products, healthcare professionals and health systems.
Requirement:	Management system of SF medical products
Evidence to review:	The assessor should request for and review: 1. Regulations and documented procedures that address the management of threats by SF medical products and recalls of such products from the market; 2. Number of complaints received; 3. Number of recalled medical products; 4. Documentation that information is publicly available, that the media used (web page, official gazette or other NRA bulletin) are appropriate, and that the information is maintained and updated on a regular basis; 5. Guidance given to manufacturers, importers, exporters and distributors on management of recalls, including the destruction of product; 6. Procedures and related records for handling quality defects (e.g., notifications of suspected quality defects and company batch recalls) 7. List of recalls performed and documented reports; 8. Procedures and records of the rapid alert system including responsibilities, points of contact, communication channels and decision trees.
References:	1. National drug regulatory legislation: guiding principles for small drug regulatory authorities. In: WHO Expert Committee on Specifications for Pharmaceutical Preparations: thirty-fifth report. Geneva: World Health Organization; 1999: Annex 8 (WHO Technical Report Series, No. 885) (1) (http://apps.who.int/medicinedocs/documents/s21964en/s21964en.pdf) 2. Guidelines for national authorities on quality assurance for biological products. In: WHO Expert Committee on Biological Standardization: forty-second report. World Health Organization; 1992: Annex 2 (WHO Technical Report Series, No. 822), (2), (http://www.who.int/biologicals/publications/trs/areas/biological_products/WHO_TRS_822_A2.pdf) 3. Regulation and licensing of biological products in countries with newly developing regulatory authorities. In: WHO Expert Committee on Biological Standardization: forty-fifth report. Geneva: World Health Organization; 1995: Annex 1 (WHO Technical Report Series, No. 858), (3), (http://www.who.int/bloodproducts/publications/WHO_TRS_858_A1.pdf) 4. How to develop and implement a national drug policy, Second edition. WHO, 2001., (116), (http://apps.who.int/medicinedocs/pdf/s2283e/s2283e.pdf)
Framework:	Structure/Foundation/Input
Rating Scale:	➔ NOT IMPLEMENTED (NI): There is no evidence of a rapid alert system to react to and to manage threats by SF medical products. ➔ ONGOING IMPLEMENTATION (OI): There is no evidence of a rapid alert system to react to and to manage threats by SF medical products; however, demonstrable steps have been taken towards its development.

	➔ PARTIALLY IMPLEMENTED (PI): There is a draft document defining a rapid alert system to react to and to manage threats by SF medical products. ➔ IMPLEMENTED (I): There is documented evidence of a rapid alert system to react to and to manage threats by SF medical products.
Limitations and remarks:	Scoring this sub-indicator as "not applicable NA" is excluded (i.e. this sub-indicator will always apply for all benchmarked NRAs).
Sub Indicator:	**RS04.03: A rapid alert and recall system based on documented communication to the appropriate level of the distribution channel and with a feedback mechanism.**
Maturity Level:	3
Scope:	1. Medicines 2. Vaccines
Description:	The assessor should verify how the alert and recall system works, focusing on communications to the appropriate level across the distribution channel along with the confirmatory feedback mechanism. In a timely process, the decision taken by the NRA should be shared appropriately and should state the severity of the defect. Communications should be given to the entire supply chain and to all stakeholders using the fastest mode of communication available, which may include email, telephone, fax, text or other appropriate means. Immediately after the decision to recall has been made, the licensee, or representative of licensee where the product is marketed, should inform the concerned regulatory authorities in the country in which any affected product batches were distributed. Further actions on recall should be undertaken according to the recall class and a feedback mechanism should be established.
Objective:	The objective of this sub-indicator is to ensure a system is in place to recall from the market, promptly and effectively, products known or suspected to be defective. Recall is an action taken to withdraw and remove the medical products from distribution or use. The process should include corrective actions taken for deficiencies reported on quality, safety or efficacy. Recall operations should be capable of being initiated promptly down to the required level in the distribution channel and a feedback mechanism should be in place.
Requirement:	A rapid alert and recall system
Evidence to review:	The assessor should request for and review: 1. Rapid alert and recall procedures along with the associated records and communications; 2. List of recalls, examples of recalls and recall notifications.
References:	1. National drug regulatory legislation: guiding principles for small drug regulatory authorities. In: WHO Expert Committee on Specifications for Pharmaceutical Preparations: thirty-fifth report. Geneva: World Health Organization; 1999: Annex 8 (WHO Technical Report Series, No. 885) (1) (http://apps.who.int/medicinedocs/documents/s21964en/s21964en.pdf) 2. Guidelines for national authorities on quality assurance for biological products. In: WHO Expert Committee on Biological Standardization: forty-second report. World Health Organization; 1992: Annex 2 (WHO Technical Report Series, No. 822), (2), (http://www.who.int/biologicals/publications/trs/areas/biological_products/WHO_TRS_822_A2.pdf) 3. Regulation and licensing of biological products in countries with newly developing regulatory authorities. In: WHO Expert Committee on Biological Standardization: forty-fifth report. Geneva: World Health Organization; 1995: Annex 1 (WHO Technical Report Series, No. 858), (3), (http://www.who.int/bloodproducts/publications/WHO_TRS_858_A1.pdf) 4. How to develop and implement a national drug policy, Second edition. WHO, 2001., (116), (http://apps.who.int/medicinedocs/pdf/s2283e/s2283e.pdf)
Framework:	Process

Rating Scale:	➜ NOT IMPLEMENTED (NI): There is no evidence of a rapid alert and recall system based on documented communication to the appropriate level of the distribution channel and with a feedback mechanism. ➜ ONGOING IMPLEMENTATION (OI): There is no evidence of a rapid alert and recall system based on documented communication to the appropriate level of the distribution channel, but demonstrable steps have been taken towards its development. ➜ PARTIALLY IMPLEMENTED (PI): There is a draft document defining a rapid alert and recall system based on documented communication to the appropriate level of the distribution channel. ➜ IMPLEMENTED (I): There is documented evidence of a rapid alert and recall system based on documented communication to the appropriate level of the distribution channel and with a feedback mechanism.
Limitations and remarks:	Scoring this sub-indicator as "not applicable NA" is excluded (i.e. this sub-indicator will always apply for all benchmarked NRAs).
Sub Indicator:	**RS04.04: Recall system based on documented confirmation that appropriate, batch-traceable action and/or destruction has been undertaken when necessary.**
Maturity Level:	3
Scope:	1. Medicines 2. Vaccines
Description:	The assessor should verify the existence of documentation which covers the regulatory decisions related to product recalls, and which can provide sufficient evidence that proper actions have been taken. There should be written procedures describing the actions to be taken, including the need to consider a recall in the case of a complaint concerning a possible product defect. If a product defect is discovered or suspected in a batch, consideration should be given to whether other batches should be checked to determine whether they have been also affected. In particular, other batches that may contain reprocessed product from the defective batch should be investigated. Where necessary, appropriate follow-up action, possibly including product recall, should be taken after investigation and evaluation of the complaint. All decisions made, and all measures taken as a result of a complaint or detection of unqualified products should be recorded and referenced to the corresponding batch records. Complaints records should be regularly reviewed for any indication of specific or recurring problems that require attention and that might justify the recall of marketed products. The competent authorities should be informed if a manufacturer or other relevant stakeholder is considering action following possibly faulty manufacture, product deterioration, or detection of any other serious quality problems with a product.
Objective:	The objective of this sub-indicator is to ensure that a recall system exists, and the progress of the recall process is monitored and recorded. Records include the disposition of the batches and/or destruction when necessary.
Requirement:	Recall system based on documented confirmation
Evidence to review:	The assessor should request for and review: 1. Documented evidence of the fate of recalled batches; 2. Documentation of reconciliation and recalls success rate (i.e. comparison of actual recalled units versus distributed ones within a certain timeframe).
References:	1. National drug regulatory legislation: guiding principles for small drug regulatory authorities. In: WHO Expert Committee on Specifications for Pharmaceutical Preparations: thirty-fifth report. Geneva: World Health Organization; 1999: Annex 8 (WHO Technical Report Series, No. 885) (1) (http://apps.who.int/medicinedocs/documents/s21964en/s21964en.pdf) 2. Guidelines for national authorities on quality assurance for biological products. In: WHO Expert Committee on Biological Standardization: forty-second report. World Health Organization; 1992: Annex 2 (WHO Technical Report Series, No. 822), (2), (http://

	www.who.int/biologicals/publications/trs/areas/biological_products/WHO_TRS_822_A2.pdf) 3. Regulation and licensing of biological products in countries with newly developing regulatory authorities. In: WHO Expert Committee on Biological Standardization: forty-fifth report. Geneva: World Health Organization; 1995: Annex 1 (WHO Technical Report Series, No. 858), (3), (http://www.who.int/bloodproducts/publications/WHO_TRS_858_A1.pdf) 4. How to develop and implement a national drug policy, Second edition. WHO, 2001., (116), (http://apps.who.int/medicinedocs/pdf/s2283e/s2283e.pdf) 5. WHO good manufacturing practices for pharmaceutical products: main principles (51) (http://digicollection.org/whoqapharm/p/about/) and (http://apps.who.int/medicinedocs/en/)
Framework:	"Structure/Foundation/Input"
Rating Scale:	➔ NOT IMPLEMENTED (NI): There is no evidence of a recall system based on documented confirmation that appropriate, batch-traceable action and/or destruction has been undertaken when necessary. ➔ ONGOING IMPLEMENTATION (OI):There is no evidence of a recall system based on documented confirmation that appropriate, batch-traceable action and/or destruction has been undertaken when necessary; however, demonstrable steps have been taken towards its development. ➔ PARTIALLY IMPLEMENTED (PI): There is a draft document defining a recall system based on documented confirmation that appropriate, batch-traceable action and/or destruction has been undertaken when necessary. ➔ IMPLEMENTED (I): There is documented evidence of a recall system based on documented confirmation that appropriate, batch-traceable action and/or destruction has been undertaken when necessary.
Limitations and remarks:	Scoring this sub-indicator as "not applicable NA" is excluded (i.e. this sub-indicator will always apply for all benchmarked NRAs).
Sub Indicator:	**RS04.05: Written criteria to cover circumstances in which the routine regulatory processes may not have to be followed in relation to crises and emergencies linked to a risk management plan.**
Maturity Level:	3
Scope:	1. Medicines 2. Vaccines
Description:	The assessor should verify the existence of a risk management plan ready to be implemented in circumstances in which the routine regulatory processes may not be followed when responding to crises and emergencies (e.g. outbreaks, force majeure, and medical product shortages). In addition, the criteria should be defined in a written document to describe management of crises and emergencies. A crises and emergencies plan is a course of action developed to mitigate the damage caused by those events that could endanger an organization's ability to function. Such a plan should include measures that provide for the safety of personnel and, if possible, property and facilities. It should also include provisions to assess the severity of an incident and to implement steps to eliminate the problem. Development of the plan begins with a vulnerability assessment. The results of the assessment will show: 1. The likelihood of a situation occurring; 2. The means that are available to stop or prevent the situation; 3. The potential responses to a given situation. From this analysis, appropriate crisis and emergency management procedures can be established. At the planning stage, it is important to employ a multidisciplinary team approach. Communication, training and periodic drills will ensure adequate performance if the plan must be carried out.
Objective:	The objective of this sub-indicator is to ensure that procedures related to NRA response to relevant crises and emergencies have been developed, documented and tested prior

	to the occurrence of an event. Such procedures should be developed according to a risk management plan. An important element of any system for the prevention of major incidents is the establishment of an emergency plan. Crises and emergencies plans seek to minimize the consequences of a crisis or emergency and require the timely application of defined procedures by people with adequate training and resources.
Requirement:	Crises and Emergencies Plan
Evidence to review:	The assessor should request for and review: 1. Regulatory risk management plan to cover circumstances in which the routine regulatory processes may not be followed when responding to crises and emergencies; 2. Written documents that describe the process; 3. Any records of crises management.
References:	1. National drug regulatory legislation: guiding principles for small drug regulatory authorities. In: WHO Expert Committee on Specifications for Pharmaceutical Preparations: thirty-fifth report. Geneva: World Health Organization; 1999: Annex 8 (WHO Technical Report Series, No. 885) (1) (http://apps.who.int/medicinedocs/documents/s21964en/s21964en.pdf) 2. Guidelines for national authorities on quality assurance for biological products. In: WHO Expert Committee on Biological Standardization: forty-second report. World Health Organization; 1992: Annex 2 (WHO Technical Report Series, No. 822), (2), (http://www.who.int/biologicals/publications/trs/areas/biological_products/WHO_TRS_822_A2.pdf) 3. Regulation and licensing of biological products in countries with newly developing regulatory authorities. In: WHO Expert Committee on Biological Standardization: forty-fifth report. Geneva: World Health Organization; 1995: Annex 1 (WHO Technical Report Series, No. 858), (3), (http://www.who.int/bloodproducts/publications/WHO_TRS_858_A1.pdf) 4. How to develop and implement a national drug policy, Second edition. WHO, 2001., (116), (http://apps.who.int/medicinedocs/pdf/s2283e/s2283e.pdf)
Framework:	Structure/Foundation/Input
Rating Scale:	➜ NOT IMPLEMENTED (NI): There is no evidence of written criteria to cover circumstances in which the routine regulatory processes may not be followed in relation to crises and emergencies. ➜ ONGOING IMPLEMENTATION (OI): There is no evidence of written criteria to cover circumstances in which the routine regulatory processes may not have to be followed in relation to crises and emergencies, but demonstrable steps have been taken towards its development. ➜ PARTIALLY IMPLEMENTED (PI): There is a draft document defining written criteria to cover circumstances in which the routine regulatory processes may not have to be followed in relation to crises and emergencies. ➜ IMPLEMENTED (I): There is documented evidence of written criteria to cover circumstances in which the routine regulatory processes may not have to be followed in relation to crises and emergencies.
Limitations and remarks:	If routine regulatory processes are mandatory in all circumstance based on the regulation, the assessor should review how the country can handle an emergency condition in a timely manner, for example, by providing additional staff and resources that allow regulatory activities to be conducted under emergency conditions.
Indicator:	**RS05 Quality management systems (QMS) including the risk management principles are applied and realized.**
Objective:	The objective of this indicator is to confirm whether the NRA has implemented the main principles of a Quality Management System (QMS) which includes the application of risk

	management principles for all regulatory functions and which has been updated to include the required documentation. QMS is a valuable tool that helps NRAs to achieve greater credibility for their decisions and greater stability in their operations, to include systematic planning, control, and improved quality in all processes throughout all regulatory functions, and to ensure a comprehensive approach for all.
Category:	05. Quality and risk management system
Sub Indicator:	**RS05.01: Top management demonstrates commitment and leadership to develop and implement quality management system (QMS).**
Maturity Level:	3
Scope:	1. Medicines 2. Vaccines
Description:	The commitment and leadership with respect to QMS is demonstrated by: 1. taking accountability for the effectiveness of the QMS; 2. ensuring that the quality policy and quality objectives are established for the QMS and that they are compatible with the visions, mandates and strategic directions of the organization; 3. ensuring the integration of the QMS requirements into the organization's business processes; 4. promoting the use of the process approach and risk-based thinking; 5. ensuring that the resources needed for the QMS are available; 6. communicating the importance of effective quality management and of conformance to the QMS requirements; 7. ensuring that the QMS achieves its intended results; 8. engaging, directing and supporting persons to contribute to the effectiveness of the QMS; 9. promoting continuous QMS improvement; 10. supporting other relevant management roles to demonstrate their leadership as it applies to their areas of responsibility.
Objective:	The objective of this sub-indicator is to confirm the commitment and leadership from top management that is required for the proper development, implementation and maintenance of the QMS.
Requirement:	Leadership and commitment
Evidence to review:	The assessor should request for and review: 1. Documentation of the resources (financial, human, infrastructure, and equipment) allocated for the development, implementation and maintenance of QMS; 2. Communication aids that convey to all staff levels the importance of effective QMS 3. Documentation for top management involvement in the monitoring, review and continuous improvement of QMS.
References:	1. Quality management systems — Requirements. International Standard ISO 9001:2015. International Organization for Standardization, 2015 sub-clause 5.1.1., (4), (https://www.iso.org/iso-9001-quality-management.html)
Framework:	Structure/Foundation/Input
Rating Scale:	➜ ONGOING IMPLEMENTATION (OI): There is no evidence that top management demonstrates commitment and leadership to develop and implement QMS, but demonstrable steps have been taken in this direction. ➜ PARTIALLY IMPLEMENTED (PI): Some resources (financial, human, infrastructure and equipment) have been allocated for the development, implementation, and maintenance of QMS. ➜ IMPLEMENTED (I): There is documented evidence that top management demonstrate commitment and leadership to develop and implement QMS.

Limitations and remarks:	Scoring this sub-indicator as "not applicable NA" is excluded (i.e. this sub-indicator will always apply for all benchmarked NRAs).
Sub Indicator:	**RS05.02: Quality policy, objectives, scope and action plans for establishment of the QMS are in place and communicated to all levels.**
Maturity Level:	3
Scope:	1. Medicines 2. Vaccines
Description:	The assessor should verify that top management has established, implemented and maintained a quality policy that: 1. is appropriate to the purpose and context of the NRA and supports its strategic direction; 2. provides a framework for setting quality objectives; 3. includes a commitment to satisfy applicable requirements; 4. includes a commitment to continued improvement of the QMS; 5. is communicated to all levels across the organization. The assessor should verify that the quality policy: 1. Is available and is maintained as documented information; 2. is communicated, understood and applied within the NRA; 3. is available to relevant interested parties, as appropriate. The assessor should verify that the NRA has established quality objectives for functions, levels and processes needed for the QMS. The quality objectives should: 1. be consistent with the quality policy; 2. be measurable; 3. take into account applicable requirements; 4. be relevant for conformity of products and services and for enhancement of customer satisfaction; 5. be monitored; 6. be communicated; 7. be updated as appropriate. The NRA should maintain documented information on the quality objectives. When NRA is planning how to achieve its quality objectives, the NRA should determine: 1. what will be done; 2. what resources will be required; 3. who will be responsible; 4. when it will be completed; 5. how the results will be evaluated.
Objective:	The objective of this sub-indicator is to confirm that a policy statement to support QMS is issued by senior management or the head of institution, that a development plan exists, and that implementation of the plan is supported by senior management. The quality policy should be communicated to all levels across the organization.
Requirement:	Quality policy, objectives, scope, and action plans
Evidence to review:	The assessor should request for and review: 1. Evidence that the quality policy is available, distributed to different levels of the organization and understood by the staff; 2. Evidence that quality objectives are documented and communicated to all levels; 3. Evidence that there is agreement on the scope of QMS application; 4. Evidence that the action plan for QMS establishment and maintenance is available and regularly updated.
References:	1. Quality management systems — Requirements. International Standard ISO 9001:2015. International Organization for Standardization, 2015 sub-clause 5.2.1, 5.2.2 , 6.2., (4), (https://www.iso.org/iso-9001-quality-management.html)

Framework:	"Structure/Foundation/Input"
Rating Scale:	➔ NOT IMPLEMENTED (NI): The NRA has no quality policy for the establishment of the QMS. ➔ ONGOING IMPLEMENTATION (OI): The NRA is taking steps toward the quality policy for the establishment of a QMS and there is documented evidence of this. ➔ PARTIALLY IMPLEMENTED (PI): The quality policy for the establishment of the QMS was recently established, a quality system policy was implemented less than a year ago, or there is a QMS, but it does not yet cover all regulatory functions. ➔ IMPLEMENTED (I): The NRA has all of the aforementioned elements, and consistently maintains documentation of the results of related activities over time.
Limitations and remarks:	Scoring this sub-indicator as "not applicable NA" is excluded (i.e. this sub-indicator will always apply for all benchmarked NRAs).
Sub Indicator:	**RS05.03: Organizational chart, with roles and responsibilities to establish the QMS are defined and in place.**
Maturity Level:	3
Scope:	1. Medicines 2. Vaccines
Description:	The assessor should verify that top management assign the responsibility and authority for: 1. ensuring that the QMS conforms to the requirements of international standards; 2. ensuring that the processes are delivering their intended outputs; 3. reporting on the performance of the QMS and on opportunities for improvement, in particular to top management; 4. ensuring the promotion of customer focus throughout the NRA; 5. ensuring that the integrity of the QMS is maintained when changes to the QMS are planned and implemented.
Objective:	The objective of this sub-indicator is to confirm that top management ensures that responsibilities and authorities for relevant roles are assigned, communicated, understood, and followed within the NRA in order to establish and maintain the QMS.
Requirement:	Organizational roles, responsibilities and authorities
Evidence to review:	The assessor should identify the entities that are in place to establish, implement or maintain the QMS. The different responsibilities should be identified and assigned. So, the assessor should check and evaluate that the: 1. Organizational chart is documented and authorized; 2. Responsibilities & authorities for processes are assigned; 3. Job descriptions that include roles, responsibilities, and authorities for each block in the organizational chart have been written and approved
References:	Quality management systems — Requirements. International Standard ISO 9001:2015. International Organization for Standardization, 2015 sub-clause 5.3., (4), (https://www.iso.org/iso-9001-quality-management.html)
Framework:	"Structure/Foundation/Input"
Rating Scale:	➔ NOT IMPLEMENTED (NI): There are no defined roles and responsibilities (with or without organizational chart) to establish the QMS. ➔ ONGOING IMPLEMENTATION (OI): There is no organizational chart, with defined roles and responsibilities to establish the QMS, but demonstrable steps have been taken towards its development. ➔ PARTIALLY IMPLEMENTED (PI): The organizational chart, with defined roles and responsibilities to establish the QMS, was recently developed.

	➔ IMPLEMENTED (I): There is an organizational chart, with defined roles and responsibilities, and the QMS is established.
Limitations and remarks:	Scoring this sub-indicator as "not applicable NA" is excluded (i.e. this sub-indicator will always apply for all benchmarked NRAs).
Sub Indicator:	**RS05.04: Enough competent staff is assigned to develop, implement and maintain the QMS.**
Maturity Level:	3
Scope:	1. Medicines 2. Vaccines
Description:	The assessor should verify whether the NRA: 1. Has determined the adequate number of staff to implement and maintain QMS; 2. Has determined the necessary competence of NRA personnel doing work that affects the performance and effectiveness of the QMS; 3. Has ensured that these personnel are competent on the basis of appropriate education, training, skills and experience; 4. Has taken actions to acquire the necessary competence, and evaluate the effectiveness of the actions taken, where applicable; 5. Has retained appropriate documented information as evidence of competence.
Objective:	The objective of this sub-indicator is to ensure the NRA provides the human resources (i.e., with respect to number and competence of personnel) necessary for the effective implementation of its QMS and for the operation and control of its processes. Necessary competence for personnel performing work significantly influences the work output and outcome.
Requirement:	Human resources and competency
Evidence to review:	The assessor should evaluate and verify if adequate competent (i.e., with respect to education, training, skills and experience) human resources has been designated and assigned to develop, implement and maintain QMS. The assessor should check and evaluate the following: 1. Criteria for the necessary personnel competence (e.g., competency matrix for each function); 2. Staff training plan (addressing recruitment, on-the-job training and other actions to achieve the necessary competencies); 3. Appropriate training records and system for retention of these records.
References:	1. Quality management systems — Requirements. International Standard ISO 9001:2015. International Organization for Standardization, 2015 sub-clause 7.1.2, 7.2., (4), (https://www.iso.org/iso-9001-quality-management.html)
Framework:	"Structure/Foundation/Input"
Rating Scale:	➔ NOT IMPLEMENTED (NI): The NRA does not have adequate competent staff (education, training, skills and experience) to develop, implement and maintain the QMS. ➔ ONGOING IMPLEMENTATION (OI): The NRA has recently developed the plan to recruit adequate competent staff; however, the plan has not been implemented. ➔ PARTIALLY IMPLEMENTED (PI): The NRA recently recruited the adequate number of the staff to develop, implement and maintain the QMS and their training programmes or competency building activities are ongoing. ➔ IMPLEMENTED (I): The NRA has had a sustained number of competent staff (education, training, skills and experience) assigned to develop, implement and maintain the QMS.

Limitations and remarks:	▪ Applicable actions can include, for example, the provision of training to, the mentoring of, or the reassignment of currently employed personnel, as well as the hiring or). ▪ contracting of competent personal. Regarding effectiveness of training please refer to sub-indicator RS05.14 ▪ Scoring this sub-indicator as "not applicable NA" is excluded (i.e. this sub-indicator will always apply for all benchmarked NRAs
Sub Indicator:	**RS05.05: The NRA establishes mechanisms to continually improve the QMS.**
Maturity Level:	4
Scope:	1. Medicines 2. Vaccines
Description:	Continuous improvement is a constant theme of a QMS. QMS continuous improvement can be achieved through different complementary approaches including, for example, management review, customer feedback, and process and product evaluation. The NRA should continually work to improve the adequacy and effectiveness of the QMS. The NRA should consider the results of analyses and evaluations, and the outputs from management reviews, to determine if there are needs or opportunities that should be addressed as part of continual improvement.
Objective:	The objective of this sub-indicator is to ensure that the NRA establishes, implements, maintains and continually improves the QMS. The NRA should identify the processes needed for developing and maintaining the QMS and should adopt the mechanisms necessary to ensure continued improvement.
Requirement:	Continual improvement
Evidence to review:	The assessor should evaluate and verify whether the NRA has established, documented and implemented a QMS, and has worked continually to improve its effectiveness through management review. The assessor should check and evaluate the following: 1. mechanisms of QMS monitoring and evaluation and ways for figuring out and addressing identified gaps; 2. availability of resources needed for QMS continual improvement; 3. availability of documentation related to addressing risks, opportunities and outputs from management review; 4. availability of documents that describe processes for QMS and regulatory system evaluation and that identify processes that require optimization; 5. availability of documents to improve the processes and address QMS gaps.
References:	1. Quality management systems — Requirements. International Standard ISO 9001:2015. International Organization for Standardization, 2015 sub-clause 10.3., (4), (https://www.iso.org/iso-9001-quality-management.html)
Framework:	"Structure/Foundation/Input"
Rating Scale:	➔ NOT IMPLEMENTED (NI): The NRA has no QMS. ➔ ONGOING IMPLEMENTATION (OI): The NRA is taking steps toward the establishment of a QMS and there is documented evidence of this. ➔ PARTIALLY IMPLEMENTED (PI): The NRA's QMS and its system of documentation were recently established, one of the systems was implemented less than a year ago, or there is a QMS, but it does not yet cover all regulatory functions. ➔ IMPLEMENTED (I): The NRA has established mechanisms to continually improve the QMS and consistently maintains documentation of the results of related activities over time.

Limitations and remarks:	Scoring this sub-indicator as "not applicable NA" is excluded (i.e. this sub-indicator will always apply for all benchmarked NRAs).
Sub Indicator:	**RS05.06: The NRA has identified its regulatory processes, determined their interactions and defined the methods needed to control these processes.**
Maturity Level:	4
Scope:	1. Medicines 2. Vaccines
Description:	The assessor should verify that the NRA determines the processes needed for the QMS and their application. The NRA should: 1. determine the regulatory inputs required and the outputs expected; 2. determine the sequence (i.e. regulatory workflow including all related steps assigned to each unit within NRA and those assigned to other stakeholders e.g. industry) and interactions among these processes; 3. determine and apply the criteria and methods (including monitoring, measurements and related performance indicators) needed to ensure the effective operation and control of these processes; 4. determine the resources needed for these processes and ensure their availability; 5. assign the responsibilities and authorities for these processes; 6. address the risks and opportunities; 7. evaluate these processes and implement any changes needed to ensure that these processes achieve their intended results; 8. improve the processes and the QMS. To the extent necessary, the NRA should: 1. maintain documented information to support the operation of its processes; 2. retain documented information to provide confidence that the processes are being carried out as planned. The NRA should apply controls to the design and development process to ensure that: 1. the results to be achieved are defined; 2. reviews are conducted to evaluate the ability of the results of design and development actions to meet requirements; 3. verification activities are conducted to ensure that the design and development of the regulatory outputs (e.g. approved marketing authorizations) meet the input requirements (e.g., marketing authorization standards and regulations); 4. validation activities are conducted to ensure that the resulting products and services (e.g. laboratory testing) meet the requirements for the specified application or intended use (e.g. pharmacopeial standards); 5. necessary actions are taken on problems determined during the reviews or verification and validation activities; 6. documented information of these activities is retained. The NRA should implement production and service provisions under controlled conditions. Controlled conditions should include, as applicable: 1. the availability of documented information that define: a) the characteristics of the products to be produced, the services to be provided, or the activities to be performed; b) the results to be achieved; 2. the availability and use of suitable monitoring and measuring resources; 3. the implementation of monitoring and measurement activities at appropriate stages to verify that criteria for control of processes or outputs, and acceptance criteria for products and services, have been met; 4. the use of suitable infrastructure and environment for the operation of processes; 5. the appointment of competent personnel with any required qualifications; 6. the validation, and periodic revalidation, of the ability to achieve planned results of the processes for production and service provision, where the resulting output cannot be verified by subsequent monitoring or measurement; 7. the implementation of actions to prevent human error; 8. the implementation of release, delivery and post-delivery activities.

	Design and development reviews, verifications and validations have distinct purposes. They can be conducted separately or in any combination, as is suitable for the products and services of the organization.
Objective:	The objective of this sub-indicator is to confirm the organization has established, implemented and maintained a design and development process that is appropriate to ensure the subsequent provision of products and services. The NRA should establish methods and tools to monitor proper implementation.
Requirement:	Operation
Evidence to review:	The assessor should request and review evidence for: 1. availability of processes list; 2. availability of different regulatory processes flowcharts including process controls and interactions with other processes.
References:	1. Quality management systems — Requirements. International Standard ISO 9001:2015. International Organization for Standardization, 2015 sub-clause 4.4, 8.3, 8.5.1., (4), (https://www.iso.org/iso-9001-quality-management.html)
Framework:	"Structure/Foundation/Input"
Rating Scale:	➜ NOT IMPLEMENTED (NI): The NRA has not identified its regulatory processes. ➜ ONGOING IMPLEMENTATION (OI): The NRA is taking steps toward the establishment of its regulatory processes and there is documented evidence of this. ➜ PARTIALLY IMPLEMENTED (PI): The NRA has recently identified its regulatory processes, determined their interactions and defined the methods needed to control these processes. ➜ IMPLEMENTED (I): The NRA has identified its regulatory processes and determined their interactions, and there is documented evidence that the regulatory processes are under control.
Limitations and remarks:	▪ The implementation of this requirement can be evaluated with more detail under each function. ▪ Scoring this sub-indicator as "not applicable NA" is excluded (i.e. this sub-indicator will always apply for all benchmarked NRAs).
Sub Indicator:	**RS05.07: Requirements for documentation management as well as traceability of regulatory activities are established.**
Maturity Level:	2
Scope:	1. Medicines 2. Vaccines
Description:	The assessor should verify the NRA's QMS includes: 1. documented information required by the applicable International Standard; 2. documented information determined by the organization to be necessary for the effectiveness of the QMS. The assessor should check that the NRA, when creating and updating documented information, ensures that: 1. identifications and descriptions (e.g. a title, date, author, or reference number) are appropriate; 2. format (e.g., language, software version, and graphics) and media (e.g. paper or electronic) are appropriate; 3. reviews and approvals are suitable and adequate. The assessor should verify that documented information required by the QMS and by the applicable International Standard should be controlled to ensure that information is: 1. available and suitable for use, where and when it is needed; 2. adequately protected (e.g. from loss of confidentiality, improper use, or loss of integrity). With respect to the control of documented information, the assessor should check that the

	NRA addresses the following activities, as applicable: 1. distribution, access, retrieval and use; 2. storage and preservation, including preservation of legibility; 3. control of changes (e.g. version control); 4. retention and disposition. The assessor should confirm that documented information of external origin that the NRA considers to be necessary for QMS planning and operation is appropriately identified and controlled. The assessor should verify that documented information retained as evidence of conformity is protected from unintended alterations. Procedures should identify those personnel who have permission and authority to view and change the documented information, and those personnel who have permission only to view the documented information.
Objective:	The objective of this sub-indicator is to ensure the NRA has a suitable document control procedure for the organization, identification, storage, protection, retrieval, retention, and disposition of documents (i.e., procedures and records).
Requirement:	Documented information
Evidence to review:	The assessor should evaluate and verify this requirement by reviewing: 1. Record control procedures; 2. Record control system, including identification of records, safeguard of records, retrieval of records, retention of records for defined periods, and destruction of obsolete records; 3. Mechanisms for ensuring traceability of different regulatory activities; 4. Examples of records; 5. Records access, archiving, retention, and disposition.
References:	1. Quality management systems — Requirements. International Standard ISO 9001:2015. International Organization for Standardization, 2015 sub-clause 7.5., (4), (https://www.iso.org/iso-9001-quality-management.html)
Framework:	"Structure/Foundation/Input"
Rating Scale:	➜ NOT IMPLEMENTED (NI): The NRA has no requirements for documentation management or cannot trace its regulatory activities and decisions. ➜ ONGOING IMPLEMENTATION (OI): The NRA is taking steps toward the establishment of its requirements for documentation management and traceability of regulatory activities; however, there is no documented evidence for this. ➜ PARTIALLY IMPLEMENTED (PI): The NRA has recently identified its requirements for documentation management and traceability of regulatory activities. ➜ IMPLEMENTED (I): The NRA has identified its requirements for documentation management and traceability of regulatory activities and there is documented evidence of the same
Limitations and remarks:	The extent of documented information for a QMS can differ from one organization to another due to: 1. the size of NRA and the scope of its mandate with respect to types of activities, processes, products and services; 2. the complexity of processes and their interactions; 3. the competence of personnel; 4. technical resources and technologies available. Records must remain legible and identifiable throughout their retention period. Scoring this sub-indicator as "not applicable NA" is excluded (i.e. this sub-indicator will always apply for all benchmarked NRAs).
Sub Indicator:	**RS05.08: External and internal issues including relevant potential risks are defined and assessed periodically for proper risk mitigation.**
Maturity Level:	4

Scope:	1. Medicines 2. Vaccines
Description:	The assessor should verify that the NRA monitors and reviews information about external and internal issues. Issues can include positive and negative factors or conditions for consideration. Understanding the external context can be facilitated by considering issues arising from legal, technological, competitive, market, cultural, social and economic environments, whether international, national, regional or local. Understanding the internal context can be facilitated by considering issues related to values, culture, knowledge and performance of the organization. The assessor should confirm the NRA considers the issues and requirements referred to the organization when planning for the QMS. The risks and opportunities need to be addressed in order to: 1. give assurance that the QMS can achieve its intended result(s); nization or its customers. 2. enhance desirable effects; 3. prevent, or reduce, undesired effects; 4. achieve improvement. The assessor should verify the NRA has planned: 1. actions to address these risks and opportunities; 2. steps to: a) integrate and implement the actions into its QMS processes; b) evaluate the effectiveness of these actions. The assessor should check that actions taken to address risks and opportunities are proportionate to the potential impact on the conformity of products and services. Options to address risks can include avoiding risks, taking risks in order to pursue an opportunity, eliminating the risk source, changing the likelihood or consequences of the risk, sharing the risk, or retaining risk by informed decision. Opportunities can lead to the adoption of new practices, launching new products, addressing new customers, building partnerships, and using new technology and other desirable and viable possibilities to address the needs of the organization or its customers.
Objective:	The objective of this sub-indicator is to ensure the organization determines external and internal issues that are relevant to its purpose and strategic direction and that may affect its ability to achieve the intended QMS result. When planning for the QMS, the NRA should consider the issues and requirements and determine the risks and opportunities that need to be addressed in the context of the organization. The NRA should identify issues that may eventually impact the regulatory performance in a negative way and develop actions and steps needed to implement the mitigation strategy. Such strategies can provide assurance that the QMS can achieve its intended results.
Requirement:	Actions to address risk and opportunities
Evidence to review:	The assessor should evaluate and verify the integration of this requirement by reviewing: 1. Evidence for identification of potential risks for each process, and for creation of a list of potential risks; 2. Methodology and SOPs for risk analysis with examples of some potential risks (e.g., calculations of likelihood and severity and creation of risk index); 3. Evidence for availability of risk mitigation action plan or strategy to control the potential risks based on its risk assessment.
References:	1. Quality management systems — Requirements. International Standard ISO 9001:2015. International Organization for Standardization , 2015 sub-clause 6.1, 4.1., (4), (https://www.iso.org/iso-9001-quality-management.html)
Framework:	"Structure/Foundation/Input"
Rating Scale:	➔ NOT IMPLEMENTED (NI): The NRA has not identified or prioritized potential risks or defined essential processes for risk mitigation. ➔ ONGOING IMPLEMENTATION (OI): The NRA is taking steps towards the identification and prioritization of potential risks and defining essential processes for risk mitigation,

	and there is documented evidence of this. ➔ PARTIALLY IMPLEMENTED (PI): The NRA has recently identified and prioritized potential risks, defined essential processes and developed SOPs for risk analysis and risk mitigation plan. ➔ IMPLEMENTED (I): The NRA has identified and prioritized potential risks, defined essential processes, and implemented SOPs for risk analysis. There is a mitigation action plan or strategy to control the potential risks based on its risk assessment.
Limitations and remarks:	Scoring this sub-indicator as "not applicable NA" is excluded (i.e. this sub-indicator will always apply for all benchmarked NRAs).
Sub Indicator:	**RS05.09: The externally provided products and services relevant to regulatory activities are controlled through established mechanisms.**
Maturity Level:	3
Scope:	1. Medicines 2. Vaccines
Description:	The assessor should verify that the organization has determined the controls to be applied to externally provided processes, products and services when: 1. products and services from external providers are intended for incorporation into the organization's own products and services; 2. products and services are provided directly to the customers by external providers on behalf of the organization; 3. a process, or part of a process, is provided by an external provider as a result of a decision by the NRA. The NRA should retain documented information of these activities and any necessary actions arising from the evaluations. The NRA should ensure that externally provided processes, products and services do not adversely affect the NRA's ability to consistently deliver conforming products and services to its customers. The assessor should verify the NRA should: 1. ensure that externally provided processes remain within the control of its QMS; 2. define both the controls that it intends to apply to an external provider and those that it intends to apply to the resulting output; 3. take into consideration: a) the potential impact of the externally provided processes, products and services on the organization's ability to consistently meet customer and applicable statutory and regulatory requirements; b) the effectiveness of the controls applied by the external provider; 4. determine the verification steps, or other activities, necessary to ensure that the externally provided processes, products and services meet requirements. The NRA should ensure the adequacy of requirements prior to their communication to the external provider. The NRA should communicate to external providers its requirements for: 1. the processes, products and services to be provided; 2. the approval of: a) products and services; b) methods, processes and equipment; c) the release of products and services; 3. competence, including any required personnel qualifications, and the need to establish terms of reference addressing confidentiality and potential conflicts of interest (as per RS06.04 and RS09.06); 4. the external providers' interactions with the NRA; 5. the controls and monitoring of the external providers' performance that will be applied by the NRA; 6. verification or validation activities.

Objective:	The objective of this sub-indicator is to confirm the NRA ensures that externally provided processes, products and services conform to requirements. The NRA should determine and apply criteria for the evaluation, selection, performance monitoring, and re- evaluation of external providers. These criteria should be based on their ability to provide processes or products and services in accordance with established requirements. An example of externally provided services is outsourced laboratory testing which should ideally be controlled through a quality agreement (with defined roles and responsibilities) between the responsible unit within the NRA (contract giver) and the external laboratory (contract acceptor). Another example of externally provided product is the information provided by the regulated sector. In the latter example, it should be noted that some of the main outputs from an NRA include those that establish parameters, rules and services for regulated industry, and thus these actors from the regulated sector can be considered both as suppliers and customers of the NRA services. This depends on the direction of the workflow. In all cases, as part of the QMS establishment within the NRA, services, products and customers should be well-defined and controlled.
Requirement:	Control of externally provided process, products and services
Evidence to review:	The assessor should evaluate and verify this requirement by reviewing: 1. List of externally provided products and services (e.g., tests, audits, or assessments) that are relevant to regulatory activities; 2. Availability of criteria for selection, evaluation, and re-evaluation of suppliers and outsourcing organizations; 3. Availability of list of approved suppliers and outsourcing organizations; 4. Availability of evaluation records of suppliers and outsourced organizations.
References:	1. Quality management systems — Requirements. International Standard ISO 9001:2015. International Organization for Standardization, 2015 sub-clause 8.4., (4), (https://www.iso.org/iso-9001-quality-management.html)
Framework:	"Structure/Foundation/Input"
Rating Scale:	➜ NOT IMPLEMENTED (NI): The NRA does not have a list of regulatory-relevant externally-provided products and services. ➜ ONGOING IMPLEMENTATION (OI): The NRA does not have a list of regulatory-relevant externally-provided products and services, but there are some demonstrable steps. ➜ PARTIALLY IMPLEMENTED (PI): The NRA has recently identified the list of regulatory-relevant externally-provided products and services. ➜ IMPLEMENTED (I): The NRA has a list of regulatory-relevant externally-provided products and services, has defined criteria for selection, evaluation, and re-evaluation of suppliers and outsourcing organizations, and has records of evaluations.
Limitations and remarks:	
Sub Indicator:	**RS05.10: A mechanism to evaluate the satisfaction of internal and external customers and other interested parties is in place for system improvement.**
Maturity Level:	4
Scope:	1. Medicines 2. Vaccines
Description:	The assessor should verify that the NRA monitors customers' perceptions of the degree to which their needs and expectations have been fulfilled. The NRA should determine the methods for obtaining, monitoring and reviewing this information. Mapping or identifying the customers and other stakeholder is essential for the proper implementation of this sub-indicator. Examples of monitoring customer perceptions can include customer surveys, customer feedback on delivered products and services, meetings with customers, market-share analysis, compliments, and warranty claims.

Objective:	The objective of this sub-indicator is to ensure the organization implements an effective customer satisfaction process to record and evaluate outcomes. Effective arrangements for communicating customer feedback and complaints should be in place.
Requirement:	Customer satisfaction
Evidence to review:	The assessor should evaluate and verify the implantation of this requirement by reviewing: 1. Results of customer satisfaction measurement by means of surveys, complaints analysis and claims analysis; 2. Actions taken with each unsatisfied customer (complaints or claims).
References:	1. Quality management systems — Requirements. International Standard ISO 9001:2015. International Organization for Standardization, 2015 sub-clause 9.1.2., (4), (https://www.iso.org/iso-9001-quality-management.html)
Framework:	"Output".
Rating Scale:	➜ NOT IMPLEMENTED (NI): The NRA does not perform customer satisfaction measurement by means of surveys, complaints analysis and claims analysis. ➜ ONGOING IMPLEMENTATION (OI): The NRA does not perform customer satisfaction measurement by means of surveys, complaints analysis and claims analysis, but there are some demonstrable steps taken towards this end. ➜ PARTIALLY IMPLEMENTED (PI): The NRA has recently implemented customer satisfaction measurement by means of surveys, complaints analysis and claims analysis. ➜ MPLEMENTED (I): There is documented evidence that the NRA performs customer satisfaction measurement by means of surveys, complaints analysis and claims analysis and that actions are taken to deal with unsatisfied customers.
Limitations and remarks:	Scoring this sub-indicator as "not applicable NA" is excluded (i.e. this sub-indicator will always apply for all benchmarked NRAs).
Sub Indicator:	**RS05.11: Internal and external audits of the QMS are established and conducted at planned intervals.**
Maturity Level:	3
Scope:	1. Medicines 2. Vaccines
Description:	The assessor should verify that the NRA: 1. plans, establishes, implements and maintains an audit programme which specifies the frequency, methods, responsibilities, planning, and reporting requirements, and which takes into consideration the importance of the processes concerned, changes affecting the NRA, and the results of previous audits; 2. defines the audit criteria and scope for each audit; 3. selects auditors and conducts audits to ensure objectivity and impartiality of the audit process; 4. ensures that the results of the audits are reported to relevant management; 5. takes appropriate correction and corrective actions without undue delay; 6. retains documented information as evidence of the implementation of the audit programme and the audit results.
Objective:	The objective of this sub-indicator is to ensure that internal and external audits are planned at regular intervals to provide information on whether the QMS conforms to the organization's own requirements and is effectively implemented and maintained.
Requirement:	Internal audit

Evidence to review:	The assessor should evaluate and verify implementation of auditing system by reviewing: 1. Internal audit procedures; 2. Audit schedules; 3. Records of auditors' qualifications and competence; 4. Audit records; 5. Root cause analyses and corrective actions to prevent recurrence of non-conformities.
References:	1. Quality management systems — Requirements. International Standard ISO 9001:2015. International Organization for Standardization, 2015 sub-clause 9.2 (4) (https://www.iso.org/iso-9001-quality-management.html) 2. ISO 19011: 2018 Guidelines for auditing management systems., International Organization for Standardization., (117), (https://www.iso.org/standard/70017.html)
Framework:	"Process"
Rating Scale:	➜ NOT IMPLEMENTED (NI): The NRA has not established internal and external audits of the QMS at planned intervals. ➜ ONGOING IMPLEMENTATION (OI): The NRA has not established internal and external audits of the QMS at planned intervals, but some demonstrable steps have been taken. ➜ PARTIALLY IMPLEMENTED (PI): The NRA has recently established internal and external audits of the QMS at planned intervals but these are not yet implemented. ➜ IMPLEMENTED (I): There is documented evidence that the NRA has established and implemented internal and external audits of the QMS at planned intervals
Limitations and remarks:	Scoring this sub-indicator as "not applicable NA" is excluded (i.e. this sub-indicator will always apply for all benchmarked NRAs).
Sub Indicator:	**RS05.12: Corrections, corrective actions, and other actions for risk mitigation and overall improvement, are implemented and documented and their effectiveness is verified.**
Maturity Level:	4
Scope:	1. Medicines 2. Vaccines
Description:	The assessor should verify that when a nonconformity occurs, including any arising from complaints, the NRA should: 1. react to the nonconformity and, as applicable: a) take action to control and correct it; b) deal with the consequences; 2. evaluate the need for action to eliminate the cause of the nonconformity, in order that it does not recur or occur elsewhere, by: a) reviewing and analyzing the nonconformity; b) determining the causes of the nonconformity; c) determining if similar nonconformities exist or could potentially occur; 3. implement any action needed; 4. review the effectiveness of any corrective action taken; 5. Update, if necessary, risks and opportunities determined during planning; 6. make any required changes to the QMS. Corrective actions should be appropriate taking into consideration the effects of the nonconformities encountered. The NRA should retain documented information as evidence of: 1. the nature of the nonconformities and any subsequent actions taken; 2. the results of any corrective action
Objective:	The objective of this sub-indicator is to ensure the NRA determines and selects opportunities for improvement and implements any necessary actions to meet customer requirements and enhance customer satisfaction. These should include improving products and services to meet requirements and to address future needs and

	expectations, as well as correcting, preventing or reducing undesired effects. The goal of these actions is to improve the performance and effectiveness of the QMS. Examples of improvement can include correction, corrective action, continual improvement, breakthrough change, innovation and re-organization.
Requirement:	Non-conformity, correction and corrective action
Evidence to review:	The assessor should evaluate and verify the status of corrective actions and actions for risk mitigation and for overall improvement, as well as the implementation of these actions and documentation of their effectiveness. The assessor should request for and review: 1. Evidence of implementing corrections, corrective actions & preventive actions; 2. Corrections and corrective action procedures with example of records; 3. Preventive action procedures with examples of records, if any.
References:	1. Quality management systems — Requirements. International Standard ISO 9001:2015. International Organization for Standardization, 2015 sub-clause 10.2., (4), (https://www.iso.org/iso-9001-quality-management.html)
Framework:	"Process"
Rating Scale:	➔ NOT IMPLEMENTED (NI): The NRA has not implemented corrections, corrective actions, and other actions to mitigate risks. ➔ ONGOING IMPLEMENTATION (OI): The NRA has not implemented corrections, corrective actions, and other actions to mitigate risks, but some demonstrable steps have been taken. ➔ PARTIALLY IMPLEMENTED (PI): The NRA has recently implemented corrections, corrective actions, and other actions to mitigate risks but these are not documented. ➔ IMPLEMENTED (I): The NRA has implemented and documented corrections, corrective actions, and other actions for risk mitigation and overall improvement. The effectiveness of these actions is verified.
Limitations and remarks:	Scoring this sub-indicator as "not applicable NA" is excluded (i.e. this sub-indicator will always apply for all benchmarked NRAs).
Sub Indicator:	**RS05.13: Top management reviews and documents the organization's QMS at planned intervals (i.e., management review).**
Maturity Level:	4
Scope:	1. Medicines 2. Vaccines
Description:	The assessor should verify that management reviews should be planned and carried out taking into consideration: 1. the status of actions from previous management reviews; 2. changes in external and internal issues that are relevant to the QMS; 3. information on the performance and effectiveness of the QMS, including trends in: a. customer satisfaction and feedback from relevant interested parties; b. the extent to which quality objectives have been met; c. process performance and conformity of products and services; d. nonconformities and corrections, corrective actions and preventive actions; e. monitoring and measurement results; f. audit results; g. the performance of external providers; 4. the adequacy of resources; 5. the effectiveness of actions taken to address risks and opportunities; 6. opportunities for improvement. The outputs of the management review should include decisions and actions related to: 1. opportunities for improvement;

	2. any need for changes to the QMS; 3. resources need. The organization should retain documented information as evidence of the results of management reviews.
Objective:	The objective of this sub-indicator is to ensure that top management reviews the organization's QMS at planned intervals, to ensure its continued suitability, adequacy, effectiveness and alignment with the strategic direction of the organization.
Requirement:	Management review
Evidence to review:	The assessor should evaluate and verify that top management monitors the QMS at planned intervals by review of the following: 1. Management review procedures; actions), 2. Management review periodicity; 3. Management review records; 4. Management review inputs (e.g., audit results and customer satisfaction reports) as well as outputs (e.g., decisions, corrections, corrective actions and preventive
References:	1. Quality management systems — Requirements. International Standard ISO 9001:2015. International Organization for Standardization, 2015 sub-clause 9.3., (4), (https://www.iso.org/iso-9001-quality-management.html)
Framework:	"Structure/Foundation/Input"
Rating Scale:	➜ NOT IMPLEMENTED (NI): The NRA top management does not review and document the organization's QMS at planned intervals (i.e., management review). ➜ ONGOING IMPLEMENTATION (OI): The NRA top management does not review and document the organization's QMS at planned intervals (i.e., management review), but some demonstrable steps have been taken. ➜ PARTIALLY IMPLEMENTED (PI): The NRA has recently implemented management reviews at planned intervals, but these are not documented. ➜ IMPLEMENTED (I): The NRA top management reviews and documents the organization's QMS at planned intervals (i.e., management review).
Limitations and remarks:	Scoring this sub-indicator as "not applicable NA" is excluded (i.e. this sub-indicator will always apply for all benchmarked NRAs).
Sub Indicator:	**RS05.14: A mechanism is established to evaluate and demonstrate the effectiveness of training activities.**
Maturity Level:	4
Scope:	1. Medicines 2. Vaccines
Description:	The assessor should verify the NRA reviews and evaluates whether planned training meets their objectives. In addition, NRA should evaluate the learning effectiveness of trained staff.
Objective:	The objective of this sub-indicator is to ensure the NRA has established a mechanism to evaluate and demonstrate the effectiveness of training activities. For the purpose of this sub-indicator, training is not confined to QMS training activities but extends to all training activities (e.g., technical, management, and soft (i.e., interpersonal)) skills. Training is one of the key elements for building and developing personnel competencies. In order to ensure proper conduct of training programs, training evaluations must be performed. Training evaluations may cover single or multiple trainings, with or without focus on individual trainees. Pre and/or post training examination is one form of evaluation of individual training effectiveness. Other evaluation mechanisms include, for

	example, evaluation of the individual and overall performance of trainees, and evaluation of behavioral changes in the trainees. Training effectiveness evaluation is essential for ensuring that training objectives are met, and that participating staff has benefited from it.
Requirement:	Competency and training
Evidence to review:	The assessor should evaluate and verify the effectiveness of training by reviewing: 1. Standard operating procedures (SOPs) for evaluation of the effectiveness of the training and actions taken; 2. Samples of training evaluation records and analyses.
References:	1. Quality management systems — Requirements. International Standard ISO 9001:2015. International Organization for Standardization, 2015 sub-clause 7., (4), (https://www.iso.org/iso-9001-quality-management.html)
Framework:	"Output"
Rating Scale:	➜ NOT IMPLEMENTED (NI): There is no mechanism established to evaluate and demonstrate the effectiveness of training activities. ➜ ONGOING IMPLEMENTATION (OI): Records to evaluate and demonstrate the effectiveness of training activities have not been implemented; however some demonstrable steps have been taken. ➜ PARTIALLY IMPLEMENTED (PI): Documentation to evaluate and demonstrate the effectiveness of training activities has been recently implemented. ➜ IMPLEMENTED (I): Records to evaluate and demonstrate the effectiveness of training activities are available and maintained over time.
Limitations and remarks:	Scoring this sub-indicator as "not applicable NA" is excluded (i.e. this sub-indicator will always apply for all benchmarked NRAs).
Indicator:	**RS06 Human resources to perform regulatory activities.**
Objective:	The objective of this indicator is to ensure that all entities within an NRA are adequately resourced with a trained, experienced and skilled workforce that is empowered to fully perform their regulatory functions. This will ensure that regulatory processes and activities are performed in accordance with international best practices. The government should take responsibility for planning and overseeing the development of the necessary human resources. The strategies chosen should realistically reflect the needs and capacity of the country, and an adequate budget should be allocated. Consideration of the following aspects will help to ensure the development of a human resources policy that is supportive of the national drug policy and national regulatory system implementation. Planning should be initiated at an early stage and should consider short, medium and longer-term needs. A quantitative analysis of the human resources needed (including a realistic estimate of the attrition rate) may help to set priorities. Financial planning should match the financial resources with priority needs. Good planning and appropriate lead times will help to ensure that sufficient number of competent staff is available. Plans should include a career development policy and measures to retain staff in the service. The assessor should evaluate this general approach for the NRA by reviewing the human resources chapters of each regulatory functions and the education, skills, experience and training of the staff employed to perform the regulatory activities
Category:	06. Resources (HR, FR, infrastructure and equipment)
Sub Indicator:	**RS06.01: The NRA has the power to select and recruit its own staff following documented procedures based on its own written criteria (i.e., education, training, skills and experience).**
Maturity Level:	4

Scope:	1. Medicines 2. Vaccines
Description:	The assessor should verify the role and responsibilities of the NRA in the selection of the personnel in its workforce. Assessor should verify that the NRA is involved in the framing of the recruitment criteria as per the requirements of the job or function. Key policy issues include: 1. government responsibility for planning and overseeing the development and training of the human resources needed; 2. definitions for minimum education, training, skills and experience requirements for each category of staff; 4. career planning and team building in government service; 5. the need for external assistance (i.e., national and international).
Objective:	The objective of this sub-indicator is to ensure that human resources development policies and strategies ensure that sufficient competent and motivated personnel are available to implement the components of the national regulatory system. Lack of motivation or appropriate expertise has been a decisive factor in failures to implement an effective and efficient national regulatory system.
Requirement:	Autonomy to select and recruit its own staff
Evidence to review:	The assessor should request for and review: 1. Regulations that give power to NRA to select and hire their own staff; 2. Documented recruitment procedures that are based on its own written criteria (i.e., education, training, skills and experience).
References:	1. National drug regulatory legislation: guiding principles for small drug regulatory authorities. In: WHO Expert Committee on Specifications for Pharmaceutical Preparations: thirty-fifth report. Geneva: World Health Organization; 1999: Annex 8 (WHO Technical Report Series, No. 885) (1) (http://apps.who.int/medicinedocs/documents/s21964en/s21964en.pdf) 2. Guidelines for national authorities on quality assurance for biological products. In: WHO Expert Committee on Biological Standardization: forty-second report. World Health Organization; 1992: Annex 2 (WHO Technical Report Series, No. 822), (2), (http://www.who.int/biologicals/publications/trs/areas/biological_products/WHO_TRS_822_A2.pdf) 3. Regulation and licensing of biological products in countries with newly developing regulatory authorities. In: WHO Expert Committee on Biological Standardization: forty-fifth report. Geneva: World Health Organization; 1995: Annex 1 (WHO Technical Report Series, No. 858), (3), (http://www.who.int/bloodproducts/publications/WHO_TRS_858_A1.pdf) 4. How to develop and implement a national drug policy, Second edition. WHO, 2001., (116), (http://apps.who.int/medicinedocs/pdf/s2283e/s2283e.pdf)
Framework:	"Structure/Foundation/Input"
Rating Scale:	➜ NOT IMPLEMENTED (NI): The NRA has no power to select and recruit its own staff. ➜ ONGOING IMPLEMENTATION (OI): There is no regulation that gives NRA the power to select and recruit its own staff however some demonstrable steps have been taken. ➜ PARTIALLY IMPLEMENTED (PI): Documented procedures for recruitment based on NRA's own written criteria (i.e., education, training, skills and experience) have been recently drafted but not yet implemented. ➜ IMPLEMENTED (I): The NRA has the power to select and recruit its own staff and there are documented procedures and records based on its own written criteria (i.e., education, training, skills and experience).
Limitations and remarks:	Scoring this sub-indicator as "not applicable NA" is excluded (i.e. this sub-indicator will always apply for all benchmarked NRAs).

Sub Indicator:	**RS06.02: A periodic staff appraisal system is established to review performance and competencies, to identify training needs, and to agree on performance targets.**
Maturity Level:	4
Scope:	1. Medicines 2. Vaccines
Description:	The assessor should verify that a periodic staff appraisal system is established to review performance and competencies, to identify training needs and to agree on performance targets. For each category of personnel, the nature and extent of their involvement, as well as their roles and responsibilities should be clearly defined. This will make it possible to decide on the discipline and level of training required for each category. There should be a number of minimum educational and training requirements for each category. In addition, there is need to evaluate the competency and performance of staff members at defined intervals, to ensure the adequacy of expertise needed to perform regulatory functions.
Objective:	The practical and theoretical training of human resources involved in drug regulation, as well as the continuous updating of their skills, are key components of good NRA performance. This provides consistency and ensures that the agency's actions will be based on the latest scientific developments.
Requirement:	Assessment of human resource capability (e.g., number proportionate to tasks, possession of appropriate skills and education, identification of training needs) along with periodic staff appraisal for performance evaluation
Evidence to review:	The assessor should request for and review: 1. SOP or any written procedure to define periodic staff appraisal system, interval of evaluation and performance targets for each function; 2. List of personnel trained in the last three years; 3. Records for re- evaluation of staff.
References:	1. National drug regulatory legislation: guiding principles for small drug regulatory authorities. In: WHO Expert Committee on Specifications for Pharmaceutical Preparations: thirty-fifth report. Geneva: World Health Organization; 1999: Annex 8 (WHO Technical Report Series, No. 885) (1) (http://apps.who.int/medicinedocs/documents/s21964en/s21964en.pdf) 2. Guidelines for national authorities on quality assurance for biological products. In: WHO Expert Committee on Biological Standardization: forty-second report. World Health Organization; 1992: Annex 2 (WHO Technical Report Series, No. 822), (2), (http://www.who.int/biologicals/publications/trs/areas/biological_products/WHO_TRS_822_A2.pdf) 3. Regulation and licensing of biological products in countries with newly developing regulatory authorities. In: WHO Expert Committee on Biological Standardization: forty-fifth report. Geneva: World Health Organization; 1995: Annex 1 (WHO Technical Report Series, No. 858), (3), (http://www.who.int/bloodproducts/publications/WHO_TRS_858_A1.pdf) 4. How to develop and implement a national drug policy, Second edition. WHO, 2001., (116), (http://apps.who.int/medicinedocs/pdf/s2283e/s2283e.pdf)
Framework:	"Process"
Rating Scale:	➜ NOT IMPLEMENTED (NI): There is no SOP or any written procedure to define a periodic staff appraisal system. ➜ ONGOING IMPLEMENTATION (OI): There is no SOP or any written procedure to define a periodic staff appraisal system; however some demonstrable steps have been taken. ➜ PARTIALLY IMPLEMENTED (PI): The SOP to define periodic staff appraisal system has been recently drafted but is not yet implemented. ➜ IMPLEMENTED (I): There is a documented and implemented procedure to define periodic staff appraisal system, interval of evaluation and performance targets for each regulatory function.

Limitations and remarks:	Scoring this sub-indicator as "not applicable NA" is excluded (i.e. this sub-indicator will always apply for all benchmarked NRAs).
Sub Indicator:	**RS06.03: A documented policy or procedure for the appointment and recruitment of external experts is available.**
Maturity Level:	3
Scope:	1. Medicines 2. Vaccines
Description:	The assessor should verify that there is a policy for appointment of external experts, evaluate whether the selection process uses an unbiased selection panel, and assess whether the process is transparent. The results of such selection should be made public. When assessing whether the objectives of the indicator have been met, assessor should consider 1. whether the NRA has a documented policy for the recruitment and selection of outside experts; 2. if there is no such policy, how the NRA demonstrates the ability to base its decisions on current scientific developments; 3. whether the policy is applied.
Objective:	The objective of this sub- indicator is to ensure the NRA has a documented policy or procedure for the appointment and recruitment of external experts. This policy or procedure should have defined criteria for the selection of experts. Selection process should be conducted by a competent panel and decisions should be made public. Outside experts and expert committees are mechanisms that allow the NRA access to expertise on a particular topic. Such a practice is recommended in light of the rapid pace of progress in science and technology, which means that no NRA can have staff with sufficient first-hand, up-to-date knowledge in all fields. External experts are an extension of the NRA's staff, and therefore must meet the same requirements as in- house staff, especially given the implicit risks because they are not an internal and integral part of the NRA, and thus are not subject to the same work-related laws and regulations. Therefore, it is good regulatory practice to establish a policy with defined criteria for recruitment of experts, creation of selection panels, and publication of final decisions.
Requirement:	Recruitment of external experts
Evidence to review:	The assessor should request for and review: 1. Public information from the internet, bulletins, publications, or other official documents; 2. Supporting documentation, including notices for external experts, records of selection meetings, appointments, and contracts.
References:	1. National drug regulatory legislation: guiding principles for small drug regulatory authorities. In: WHO Expert Committee on Specifications for Pharmaceutical Preparations: thirty-fifth report. Geneva: World Health Organization; 1999: Annex 8 (WHO Technical Report Series, No. 885) (1) (http://apps.who.int/medicinedocs/documents/s21964en/s21964en.pdf) 2. Guidelines for national authorities on quality assurance for biological products. In: WHO Expert Committee on Biological Standardization: forty-second report. World Health Organization; 1992: Annex 2 (WHO Technical Report Series, No. 822), (2), (http://www.who.int/biologicals/publications/trs/areas/biological_products/WHO_TRS_822_A2.pdf) 3. Regulation and licensing of biological products in countries with newly developing regulatory authorities. In: WHO Expert Committee on Biological Standardization: forty-fifth report. Geneva: World Health Organization; 1995: Annex 1 (WHO Technical Report Series, No. 858), (3), (http://www.who.int/bloodproducts/publications/WHO_TRS_858_A1.pdf) 4. How to develop and implement a national drug policy, Second edition. WHO, 2001., (116), (http://apps.who.int/medicinedocs/pdf/s2283e/s2283e.pdf)
Framework:	"Process"

Rating Scale:	➔ NOT IMPLEMENTED (NI): There is no policy for the appointment, recruitment and selection of external experts. ➔ ONGOING IMPLEMENTATION (OI): A circulated draft of such a policy is available, or there is evidence that proposals have been made. ➔ PARTIALLY IMPLEMENTED (PI): The policy was approved recently (less than one year ago), and these concepts were only recently incorporated into experts' contracts or other documents. ➔ IMPLEMENTED (I): The NRA has and consistently applies a policy for the recruitment and selection of external experts.
Limitations and remarks:	
Sub Indicator:	**RS06.04: Documented mechanism to handle potential conflicts of interest for internal and external experts and committee members, to gather declarations of interest and to guarantee the update of these declarations for all regulatory functions.**
Maturity Level:	3
Scope:	1. Medicines 2. Vaccines
Description:	The assessor should review the procedure for declaration of interests by experts and verify whether the same criteria are applied in case of internal or external experts and committee members for all regulatory functions. Assessor should consider the following aspects when assessing whether the objectives of the indicator have been met: 1. whether there is a conduct policy for external experts and expert committees; 2. if there is such a policy, whether it establishes terms of reference regarding confidentiality and potential conflicts of interest; 3. whether the policy is applied.
Objective:	The objective of this sub-indicator is to ensure that there is a mechanism in place to manage potential conflicts of interest for internal and external experts and expert committees. Outside experts and committees on which they serve are an extension of the NRA's work; therefore, they must meet the same criteria as those applied to staff involved in regulatory functions. Since they do not work at the NRA and generally perform other tasks, potentially with and for those regulated, there is a risk of conflicts of interest that are different from those faced by civil servants. For this reason, the NRA must apply a special conflict of interest policy when hiring outside experts.
Requirement:	Managing potential conflicts of interest of internal and external experts and committee members
Evidence to review:	The assessor should request for and review: 1. Public information in the internet, bulletins, or other official documents; 2. Code of conduct for experts; 3. Contracts for external experts; 4. Expert committee rules and special exclusions; 5. Examples of declarations of interest, as well as examples of deferrals due to potential conflicts of interest
References:	1. National drug regulatory legislation: guiding principles for small drug regulatory authorities. In: WHO Expert Committee on Specifications for Pharmaceutical Preparations: thirty-fifth report. Geneva: World Health Organization; 1999: Annex 8 (WHO Technical Report Series, No. 885) (1) (http://apps.who.int/medicinedocs/documents/s21964en/s21964en.pdf) 2. Guidelines for national authorities on quality assurance for biological products. In: WHO Expert Committee on Biological Standardization: forty-second report. World Health Organization; 1992: Annex 2 (WHO Technical Report Series, No. 822), (2), (http://www.who.

	int/biologicals/publications/trs/areas/biological_products/WHO_TRS_822_A2.pdf) 3. Regulation and licensing of biological products in countries with newly developing regulatory authorities. In: WHO Expert Committee on Biological Standardization: forty-fifth report. Geneva: World Health Organization; 1995: Annex 1 (WHO Technical Report Series, No. 858), (3), (http://www.who.int/bloodproducts/publications/WHO_TRS_858_A1.pdf) 4. How to develop and implement a national drug policy, Second edition. WHO, 2001., (116), (http://apps.who.int/medicinedocs/pdf/s2283e/s2283e.pdf)
Framework:	"Process"
Rating Scale:	➜ NOT IMPLEMENTED (NI): The NRA has no internal mechanism to handle conflicts of interest for internal and external experts and committee members. ➜ ONGOING IMPLEMENTATION (OI): There is documented evidence that steps have been taken to develop a rule or policy and internal mechanisms and procedures to handle conflicts of interest, but they are not available or have not yet been implemented. ➜ PARTIALLY IMPLEMENTED (PI): A policy and mechanism to handle potential conflicts of interest were recently established (less than one year ago), but there is not sufficient, robust evidence of the NRA's work in this area. ➜ IMPLEMENTED (I): The NRA has policies, mechanisms, and procedures to handle potential conflicts of interest for internal and external experts and committee members, and they are periodically updated and applied consistently over time.
Limitations and remarks:	
Indicator:	**RS07 Financial resources to perform regulatory activities.**
Objective:	The objective of this indicator is to ensure that whether or not a public system operates with cost-recovery, decentralized medical products budgets or other systems, the system should be well-designed and provided with resources sufficient to run properly. Financial planning should match the financial resources with priority needs. The assessor should identify if the NRA has sustainable funding. The assessor should find out if the NRA is funded by the Government, by the fees collected for the services provided or by donor sources. The availability of an adequate budget is essential to provide salaries that will attract personnel with the required training and experience, as well as the facilities and infrastructure needed. The NRA should have the authority to collect and utilize internally the funds that it generates.
Category:	06. Resources (HR, FR, infrastructure and equipment)
Sub Indicator:	**RS07.01: Sources of funding are established for the NRA and affiliated institutions to carry out all regulatory functions.**
Maturity Level:	3
Scope:	1. Medicines 2. Vaccines
Description:	The assessor should verify that sources of funding needed to carry out all functions are available for the NRA and the affiliated institutions. The process or mechanism for obtaining funding should be reviewed. Assessor should evaluate the following when assessing whether the objectives of this indicator have been met: 1. Identify the sources of funding for the NRA (e.g., the government, fees collected for services provided by the NRA, grants, or a combination of these or other sources). 2. Determine whether the NRA has annual budgets. If so, determine whether they cover execution of all regulatory functions. Budgets for at least two years should be reviewed.

Objective:	The objective of this sub-indicator is to confirm that the NRA has sources of funding that allow it to perform its regulatory functions under stable conditions. For an NRA to maintain adequate performance, the agency must have sustainable funding. The budget must allow it to operate satisfactorily and perform all regulatory and oversight duties with sufficient specialized personnel.
Requirement:	Existence of fee system or an equivalent mechanism for stable funding.
Evidence to review:	The assessor should request for and review: 1. Applicable regulations; 2. Annual NRA budget for at least two years; 3. Funding agreements; 4. NRA annual reports on activities and budgets.
References:	1. National drug regulatory legislation: guiding principles for small drug regulatory authorities. In: WHO Expert Committee on Specifications for Pharmaceutical Preparations: thirty-fifth report. Geneva: World Health Organization; 1999: Annex 8 (WHO Technical Report Series, No. 885) (1) (http://apps.who.int/medicinedocs/documents/s21964en/s21964en.pdf) 2. Guidelines for national authorities on quality assurance for biological products. In: WHO Expert Committee on Biological Standardization: forty-second report. World Health Organization; 1992: Annex 2 (WHO Technical Report Series, No. 822), (2), (http://www.who.int/biologicals/publications/trs/areas/biological_products/WHO_TRS_822_A2.pdf) 3. Regulation and licensing of biological products in countries with newly developing regulatory authorities. In: WHO Expert Committee on Biological Standardization: forty-fifth report. Geneva: World Health Organization; 1995: Annex 1 (WHO Technical Report Series, No. 858), (3), (http://www.who.int/bloodproducts/publications/WHO_TRS_858_A1.pdf) 4. How to develop and implement a national drug policy, Second edition. WHO, 2001., (116), (http://apps.who.int/medicinedocs/pdf/s2283e/s2283e.pdf) 5. Quality management systems — Requirements. International Standard ISO 9001:2015. International Organization for Standardization, 2015, (4), (https://www.iso.org/iso-9001-quality-management.html)
Framework:	"Structure/Foundation/Input"
Rating Scale:	➜ NOT IMPLEMENTED (NI): There is no evidence of stable sources of funding, or no budget is established for performing all regulatory functions. ➜ ONGOING IMPLEMENTATION (OI): There is evidence of steps being taken to systematize the sources of funding for the NRA and allocate a budget periodically. ➜ PARTIALLY IMPLEMENTED (PI): There are sources of funding, but they have not been stable during the past three years. The NRA stated that certain functions or indicators (i.e., under this or other modules) cannot be implemented due to budget constraints. ➜ IMPLEMENTED (I): The NRA has defined sources of funding and has been executing a budget for the performance of all its regulatory functions over time.
Limitations and remarks:	Scoring this sub-indicator as "not applicable NA" is excluded (i.e. this sub-indicator will always apply for all benchmarked NRAs).
Sub Indicator:	**RS07.02: The amounts collected for fees, taxes, tariffs or dues payable for the services provided are defined and publicly available.**
Maturity Level:	3
Scope:	1. Medicines 2. Vaccines
Description:	The assessor should verify that the amounts of fees, taxes, tariffs or dues payable for the services provided are defined and that this information is publicly available. Fees, taxes, tariffs or dues are a financial charge imposed upon a taxpayer (an individual or legal entity).

Objective:	The objective of this sub-indicator is to ensure that for purposes of transparency, the NRA or the responsible authority in the country should define the amounts of fees, taxes, tariffs or dues payable for the services provided by the NRA and should make this information available to the public.
Requirement:	Fees, taxes, tariffs
Evidence to review:	The assessor should request for and review: 1. Documentation showing fees, taxes, tariffs or dues payable for the services provided; 2. Documentation demonstrating public availability of this information.
References:	1. National drug regulatory legislation: guiding principles for small drug regulatory authorities. In: WHO Expert Committee on Specifications for Pharmaceutical Preparations: thirty-fifth report. Geneva: World Health Organization; 1999: Annex 8 (WHO Technical Report Series, No. 885) (1) (http://apps.who.int/medicinedocs/documents/s21964en/s21964en.pdf) 2. Guidelines for national authorities on quality assurance for biological products. In: WHO Expert Committee on Biological Standardization: forty-second report. World Health Organization; 1992: Annex 2 (WHO Technical Report Series, No. 822), (2), (http://www.who.int/biologicals/publications/trs/areas/biological_products/WHO_TRS_822_A2.pdf) 3. Regulation and licensing of biological products in countries with newly developing regulatory authorities. In: WHO Expert Committee on Biological Standardization: forty-fifth report. Geneva: World Health Organization; 1995: Annex 1 (WHO Technical Report Series, No. 858), (3), (http://www.who.int/bloodproducts/publications/WHO_TRS_858_A1.pdf) 4. How to develop and implement a national drug policy, Second edition. WHO, 2001., (116), (http://apps.who.int/medicinedocs/pdf/s2283e/s2283e.pdf)
Framework:	"Structure/Foundation/Input"
Rating Scale:	➜ NOT IMPLEMENTED (NI): There is no public list, although fees are charged for services. ➜ ONGOING IMPLEMENTATION (OI): The list is awaiting approval from the governing institutions, and there is evidence that such a proposal has been submitted. ➜ PARTIALLY IMPLEMENTED (PI): The list was recently published (i.e., less than a year ago), or a list was published more than a year ago but it does not include all services. ➜ IMPLEMENTED (I): The NRA has the authority to charge for services, and there is a list with the rates of all NRA services that require payment. This rate list is consistently applied, is updated periodically, and was published digitally or printed less than a year ago.
Limitations and remarks:	Scoring this sub-indicator as "not applicable NA" is excluded (i.e. this sub-indicator will always apply for all benchmarked NRAs).
Sub Indicator:	**RS07.03: There are provisions relating to reduction or exemption of dues, taxes, tariffs or fees in defined situations for public health interest.**
Maturity Level:	4
Scope:	1. Medicines 2. Vaccines
Description:	The assessor should check that there are provisions in the NRA to waive or reduce the fees and taxes in cases of public health interest, for example, to guarantee the availability of medical products. The NRA should define the criteria for specific circumstances, as well as necessary actions.
Objective:	The objective of this sub-indicator is to ensure that provisions exist to facilitate and improve access to medical products and to guarantee the availability of drugs in defined situations (e.g., shortages, emergencies, or outbreaks) through reductions or exemptions in dues, taxes, tariffs or fees. This information should be publicly available.

Requirement:	Reduction or exemption of dues, taxes, tariffs or fees
Evidence to review:	The assessor should request for and review: 1. The provisions in the NRA to waive or reduce the fees and taxes in emergency situations; 2. Examples of tax exemptions or reductions under emergency conditions or other relevant situations.
References:	1. National drug regulatory legislation: guiding principles for small drug regulatory authorities. In: WHO Expert Committee on Specifications for Pharmaceutical Preparations: thirty-fifth report. Geneva: World Health Organization; 1999: Annex 8 (WHO Technical Report Series, No. 885) (1) (http://apps.who.int/medicinedocs/documents/s21964en/s21964en.pdf) 2. Guidelines for national authorities on quality assurance for biological products. In: WHO Expert Committee on Biological Standardization: forty-second report. World Health Organization; 1992: Annex 2 (WHO Technical Report Series, No. 822), (2), (http://www.who.int/biologicals/publications/trs/areas/biological_products/WHO_TRS_822_A2.pdf) 3. Regulation and licensing of biological products in countries with newly developing regulatory authorities. In: WHO Expert Committee on Biological Standardization: forty-fifth report. Geneva: World Health Organization; 1995: Annex 1 (WHO Technical Report Series, No. 858), (3), (http://www.who.int/bloodproducts/publications/WHO_TRS_858_A1.pdf) 4. How to develop and implement a national drug policy, Second edition. WHO, 2001., (116), (http://apps.who.int/medicinedocs/pdf/s2283e/s2283e.pdf)
Framework:	"Structure/Foundation/Input"
Rating Scale:	➜ NOT IMPLEMENTED (NI): There are no provisions relating to reduction or exemption of dues, taxes, tariffs or fees in defined situations for public health interest. ➜ ONGOING IMPLEMENTATION (OI): The provisions are awaiting approval from the governing institutions, and there is evidence that such a proposal has been submitted. ➜ PARTIALLY IMPLEMENTED (PI): The provisions were recently published (i.e., less than a year ago), but there are no examples of tax exemption or reduction to show. ➜ IMPLEMENTED (I): There are provisions relating to reduction or exemption of dues, taxes, tariffs or fees in defined situations for public health interest and there are examples of their application.
Limitations and remarks:	Scoring this sub-indicator as "not applicable NA" is excluded (i.e. this sub-indicator will always apply for all benchmarked NRAs).
Sub Indicator:	**RS07.04: The NRA has authority to manage the funds allocated and/or generated internally.**
Maturity Level:	4
Scope:	1. Medicines 2. Vaccines
Description:	The assessor should verify that the NRA has the authority to manage the funds allocated and/or generated internally. The assessor also should determine the percentage of these funds that are used by the NRA for its functions.
Objective:	The objective of this sub-indicator is to ensure the NRA has the authority to manage allocated or internally-generated funds to finance regulatory activities. This authority plays an important role in enhancing the autonomy and independence of the NRA.
Requirement:	Authority to manage the funds allocated and/or generated internally.
Evidence to review:	The assessor should request for and review 1. Provisions that give authority to NRA to manage allocated funds and to collect and use the funds generated internally; 2. Mechanisms or processes in place to manage these funds; 3. Records of funds that are generated by NRA and the percentage that are used internally.

References:	1. National drug regulatory legislation: guiding principles for small drug regulatory authorities. In: WHO Expert Committee on Specifications for Pharmaceutical Preparations: thirty-fifth report. Geneva: World Health Organization; 1999: Annex 8 (WHO Technical Report Series, No. 885) (1) (http://apps.who.int/medicinedocs/documents/s21964en/s21964en.pdf) 2. Guidelines for national authorities on quality assurance for biological products. In: WHO Expert Committee on Biological Standardization: forty-second report. World Health Organization; 1992: Annex 2 (WHO Technical Report Series, No. 822), (2), (http://www.who.int/biologicals/publications/trs/areas/biological_products/WHO_TRS_822_A2.pdf) 3. Regulation and licensing of biological products in countries with newly developing regulatory authorities. In: WHO Expert Committee on Biological Standardization: forty-fifth report. Geneva: World Health Organization; 1995: Annex 1 (WHO Technical Report Series, No. 858), (3), (http://www.who.int/bloodproducts/publications/WHO_TRS_858_A1.pdf) 4. How to develop and implement a national drug policy, Second edition. WHO, 2001., (116), (http://apps.who.int/medicinedocs/pdf/s2283e/s2283e.pdf)
Framework:	"Structure/Foundation/Input"
Rating Scale:	➜ NOT IMPLEMENTED (NI): The National Regulatory Authority does not have the authority to manage the allocated or internally generated funds. ➜ ONGOING IMPLEMENTATION (OI): There is evidence of steps being taken to enable the NRA to manage the allocated or internally generated budget. ➜ PARTIALLY IMPLEMENTED (PI): The NRA is recently able to manage allocated or internally generated budget or the NRA, with some constraints or limitations, is having the authority to manage allocated or internally generated budget. ➜ IMPLEMENTED (I): The NRA have the full authority to manage the allocated or internally generated funds.
Limitations and remarks:	Scoring this sub-indicator as "not applicable NA" is excluded (i.e. this sub-indicator will always apply for all benchmarked NRAs).
Sub Indicator:	**RS07.05: The NRA periodically publicizes its budget.**
Maturity Level:	4
Scope:	1. Medicines 2. Vaccines
Description:	The assessor should check that the NRA publicizes its budget periodically (i.e., at least once per year). The assessor should review publically available budgets, both an overall budget as well as a budget broken down by regulatory function and/or medical products.
Objective:	The objective of this sub-indicator is to ensure that the NRA periodically publicizes its budget to demonstrate transparency, prevent corruption, and build trust between the public and the NRA.
Requirement:	Periodically publicize its budget
Evidence to review:	The assessor should request for and review: 1. Provisions requiring the NRA to publicize its budget periodically; 2. Records of published budgets.
References:	1. National drug regulatory legislation: guiding principles for small drug regulatory authorities. In: WHO Expert Committee on Specifications for Pharmaceutical Preparations: thirty-fifth report. Geneva: World Health Organization; 1999: Annex 8 (WHO Technical Report Series, No. 885) (1) (http://apps.who.int/medicinedocs/documents/s21964en/s21964en.pdf) 2. Guidelines for national authorities on quality assurance for biological products. In:

	WHO Expert Committee on Biological Standardization: forty-second report. World Health Organization; 1992: Annex 2 (WHO Technical Report Series, No. 822), (2), (http://www.who.int/biologicals/publications/trs/areas/biological_products/WHO_TRS_822_A2.pdf) 3. Regulation and licensing of biological products in countries with newly developing regulatory authorities. In: WHO Expert Committee on Biological Standardization: forty-fifth report. Geneva: World Health Organization; 1995: Annex 1 (WHO Technical Report Series, No. 858), (3), (http://www.who.int/bloodproducts/publications/WHO_TRS_858_A1.pdf) 4. How to develop and implement a national drug policy, Second edition. WHO, 2001., (116), (http://apps.who.int/medicinedocs/pdf/s2283e/s2283e.pdf)
Framework:	"Output".
Rating Scale:	➜ NOT IMPLEMENTED (NI): There is no provision stating the NRA periodically publicizes its budget. ➜ ONGOING IMPLEMENTATION (OI): There is evidence of steps being taken to systematize the publication of the NRA budget. ➜ PARTIALLY IMPLEMENTED (PI): The provisions were recently published (i.e., less than a year ago), but there are no examples of NRA budget publication. ➜ IMPLEMENTED (I): There are provisions stating the NRA periodically publicizes its budget and there are records of published budgets available for two years.
Limitations and remarks:	Scoring this sub-indicator as "not applicable NA" is excluded (i.e. this sub-indicator will always apply for all benchmarked NRAs).
Indicator:	**RS08 Infrastructure and equipment to perform regulatory activities.**
Objective:	The objective of this indicator is to ensure that resources and infrastructure are available to the national regulatory authority in order to perform regulatory activities adequately. A well-resourced authority backed with adequate drug legislation and regulations is needed to ensure the delivery of regulatory activities.
Category:	06. Resources (HR, FR, infrastructure and equipment)
Sub Indicator:	**RS08.01: The workspace and work environment provided for performing the regulatory activities are adequate.**
Maturity Level:	2
Scope:	1. Medicines 2. Vaccines
Description:	The assessor should verify that "work environment" under which work is performed (including physical, environmental and other factors) is adequate to perform regulatory activities. Infrastructure includes, as applicable: 1. buildings, workspaces and associated utilities; 2. lighting and ventilation in the workspaces;
Objective:	The objective of this sub-indicator is to ensure the NRA provides and maintains the minimum infrastructure needed to achieve conformity to service requirements and conduct regulatory activities. The organization should determine and manage the work environment (workspace) and the environmental conditions needed for employees to perform their daily activities.
Requirement:	Workspace and work environment
Evidence to review:	The assessor should request for and review: 1. Number of staff and the number of offices to which they are assigned;

	2. Quality of workspace; 3. Lighting and ventilation in the workspace; 4. Supporting services (e.g., transportation and communication systems).
References:	1. National drug regulatory legislation: guiding principles for small drug regulatory authorities. In: WHO Expert Committee on Specifications for Pharmaceutical Preparations: thirty-fifth report. Geneva: World Health Organization; 1999: Annex 8 (WHO Technical Report Series, No. 885) (1) (http://apps.who.int/medicinedocs/documents/s21964en/s21964en.pdf) 2. Guidelines for national authorities on quality assurance for biological products. In: WHO Expert Committee on Biological Standardization: forty-second report. World Health Organization; 1992: Annex 2 (WHO Technical Report Series, No. 822), (2), (http://www.who.int/biologicals/publications/trs/areas/biological_products/WHO_TRS_822_A2.pdf) 3. Regulation and licensing of biological products in countries with newly developing regulatory authorities. In: WHO Expert Committee on Biological Standardization: forty-fifth report. Geneva: World Health Organization; 1995: Annex 1 (WHO Technical Report Series, No. 858), (3), (http://www.who.int/bloodproducts/publications/WHO_TRS_858_A1.pdf) 4. How to develop and implement a national drug policy, Second edition. WHO, 2001., (116), (http://apps.who.int/medicinedocs/pdf/s2283e/s2283e.pdf) 5. Quality management systems — Requirements. International Standard ISO 9001:2015. International Organization for Standardization, 2015 (4) (https://www.iso.org/iso-9001-quality-management.html)
Framework:	"Structure/Foundation/Input"
Rating Scale:	➜ NOT IMPLEMENTED (NI): There is inadequate work space and work environment to perform regulatory activities. ➜ ONGOING IMPLEMENTATION (OI): There is evidence of steps being taken to ensure adequate work space and work environment to perform all regulatory activities. ➜ PARTIALLY IMPLEMENTED (PI): There is adequate work space and work environment in some areas but not for all regulatory functions. ➜ IMPLEMENTED (I): The NRA provides adequate work space and work environment for all regulatory activities.
Limitations and remarks:	Scoring this sub-indicator as "not applicable NA" is excluded (i.e. this sub-indicator will always apply for all benchmarked NRAs).
Sub Indicator:	**RS08.02: The workspace and work environment provided for performing the regulatory activities includes essential requirements.**
Maturity Level:	3
Scope:	1. Medicines 2. Vaccines
Description:	The assessor should verify the "work environment" including the essential requirements to perform regulatory activities. The assessor should verify that there is enough space for secure storage of documents and an easily accessible archive. In addition, some specific regulatory activities require specific workspace (e.g., laboratory facilities). The archival of the documents should be verified. Infrastructure includes, as applicable: 1. process equipment (both hardware and software); 2. supporting services (servers and information systems); 3. archives; 4. workspace for specific regulatory activities, e.g., laboratories.
Objective:	The objective of this sub-indicator is to ensure the NRA provides the work environment needed to conduct regulatory activities in an efficient manner. The organization should determine and manage the work environment needed to achieve conformity to product requirements.

Requirement:	Workspace and work environment
Evidence to review:	The assessor should request for and review: 1. Workspace and security access for storage of documents (paper and electronic); 2. Archives; 3. List of needed equipment, as well as availability of this equipment (e.g., process equipment and supporting services)
References:	1. National drug regulatory legislation: guiding principles for small drug regulatory authorities. In: WHO Expert Committee on Specifications for Pharmaceutical Preparations: thirty-fifth report. Geneva: World Health Organization; 1999: Annex 8 (WHO Technical Report Series, No. 885) (1) (http://apps.who.int/medicinedocs/documents/s21964en/s21964en.pdf) 2. Guidelines for national authorities on quality assurance for biological products. In: WHO Expert Committee on Biological Standardization: forty-second report. World Health Organization; 1992: Annex 2 (WHO Technical Report Series, No. 822), (2), (http://www.who.int/biologicals/publications/trs/areas/biological_products/WHO_TRS_822_A2.pdf) 3. Regulation and licensing of biological products in countries with newly developing regulatory authorities. In: WHO Expert Committee on Biological Standardization:forty-fifth report. Geneva: World Health Organization; 1995: Annex 1 (WHO Technical Report Series, No. 858), (3), (http://www.who.int/bloodproducts/publications/WHO_TRS_858_A1.pdf) 4. How to develop and implement a national drug policy, Second edition. WHO, 2001., (116), (http://apps.who.int/medicinedocs/pdf/s2283e/s2283e.pdf) 5. Quality management systems — Requirements. International Standard ISO 9001:2015. International Organization for Standardization, 2015 (4) (https://www.iso.org/iso-9001-quality-management.html)
Framework:	"Structure/Foundation/Input"
Rating Scale:	➜ NOT IMPLEMENTED (NI): The workspace or work environment provided for performing the regulatory activities does not include essential requirements as indicated in this fact sheet. ➜ ONGOING IMPLEMENTATION (OI): A plan exists for the the workspace and work environment provided for performing the regulatory activities to meet the essential requirement as indicated in this fact sheet. ➜ PARTIALLY IMPLEMENTED (PI): There is evidence of steps and actions taken for the the workspace and work environment provided for performing the regulatory activities to meet the essential requirement as indicated in this fact sheet. ➜ IMPLEMENTED (I): The workspace and work environment provided for performing the regulatory activities are verified to include essential requirements as indicated in this fact sheet
Limitations and remarks:	Scoring this sub-indicator as "not applicable NA" is excluded (i.e. this sub-indicator will always apply for all benchmarked NRAs).
Sub Indicator:	**RS08.03: The equipment provided for performing the regulatory activities is adequate.**
Maturity Level:	4
Scope:	1. Medicines 2. Vaccines
Description:	The assessor should verify the equipment provided for the performance of regulatory activities is adequate to perform these activities (i.e., taking into consideration the types of activities to be performed and the number of staff allocated).
Objective:	The objective of this sub-indicator is to ensure the NRA provides and maintains adequate equipment as part of the infrastructure needed to achieve conformity to service requirements and to perform regulatory activities.

Requirement:	Equipment provided for performing
Evidence to review:	The assessor should request for and review: 1. List of needed equipment (e.g., computers and printers) and its availability; 2. List of functional equipment and its maintenance.
References:	1. National drug regulatory legislation: guiding principles for small drug regulatory authorities. In: WHO Expert Committee on Specifications for Pharmaceutical Preparations: thirty-fifth report. Geneva: World Health Organization; 1999: Annex 8 (WHO Technical Report Series, No. 885) (1) (http://apps.who.int/medicinedocs/documents/s21964en/s21964en.pdf) 2. Guidelines for national authorities on quality assurance for biological products. In: WHO Expert Committee on Biological Standardization: forty-second report. World Health Organization; 1992: Annex 2 (WHO Technical Report Series, No. 822), (2), (http://www.who.int/biologicals/publications/trs/areas/biological_products/WHO_TRS_822_A2.pdf) 3. Regulation and licensing of biological products in countries with newly developing regulatory authorities. In: WHO Expert Committee on Biological Standardization: forty-fifth report. Geneva: World Health Organization; 1995: Annex 1 (WHO Technical Report Series, No. 858), (3), (http://www.who.int/bloodproducts/publications/WHO_TRS_858_A1.pdf) 4. How to develop and implement a national drug policy, Second edition. WHO, 2001., (116), (http://apps.who.int/medicinedocs/pdf/s2283e/s2283e.pdf) 5. Quality management systems — Requirements. International Standard ISO 9001:2015. International Organization for Standardization, 2015 (4) (https://www.iso.org/iso-9001-quality-management.html)
Framework:	"Structure/Foundation/Input"
Rating Scale:	➜ NOT IMPLEMENTED (NI): There is insufficient equipment to perform regulatory activities. ➜ ONGOING IMPLEMENTATION (OI): There is evidence of steps being taken to ensure adequate equipment to perform all regulatory activities. ➜ PARTIALLY IMPLEMENTED (PI): There is adequate equipment available in some areas but not enough to cover all regulatory functions. ➜ IMPLEMENTED (I): The NRA provides adequate equipment for all regulatory activities.
Limitations and remarks:	Scoring this sub-indicator as "not applicable NA" is excluded (i.e. this sub-indicator will always apply for all benchmarked NRAs).
Indicator:	**RS09 Mechanisms exist to promote transparency, accountability and communication.**
Objective:	The objective of this indicator is to ensure that NRA's general practices and policies dealing with transparency issues are established in procedures and outcomes. On this matter the assessor could undertake interviews outside the NRA, for example, with stakeholders' representatives, to collect information on how the NRA is perceived or operates. Information is a key pre-requisite for communication. Adequate and effective communication plays a fundamental role for exchanging information, informing relevant stakeholders, and preventing misunderstanding. When regularly communicating both internally and externally, organizations remain more transparent. Accountability is the process through which an organization makes a commitment to respond to and balance the needs of stakeholders in its decision-making processes and activities. The assessor should verify that the information and documents are updated for all sub-indicators. Documented evidence to be studied: 1. Reporting and communication policy; 2. Annual or periodic reports; 3. NRA web page or website.

Category:	08. Transparency, accountability and communication
Sub Indicator:	**RS09.01: The NRA participates in regional and/or global networks to promote convergence and harmonization efforts and expand its collaboration in the regulatory field.**
Maturity Level:	4
Scope:	1. Medicines 2. Vaccines
Description:	The assessor should check the global, regional and/or sub-regional networks joined by the relevant NRA. Only those networks which promote convergence, harmonization, collaboration and reliance among the NRAs or related institutions (e.g. pharmacovigilance centers) should be considered. Active participation in meetings, seminars, committees, and adoption of decisions and recommendations by the networks should be verified.
Objective:	The objective of this indicator is to ensure the participation of the NRA in regional or global networks. These networks can serve as a forum for sharing information, exchanging experiences on technical issues and best practices, and facilitating assistance between NRAs. They can contribute to efforts to promote convergence of international regulatory requirements and practices, as well as harmonization efforts.
Requirement:	Regional and/or global networks to promote convergence and harmonization efforts in regulatory requirements and practices
Evidence to review:	The assessor should request for and review: 1. Global, regional and/or sub-regional network memberships and agreements; 2. Minutes of meetings of these networks, documentation of high level decisions (e.g. guidelines adaptation), and records of communications.
References:	1. National drug regulatory legislation: guiding principles for small drug regulatory authorities. In: WHO Expert Committee on Specifications for Pharmaceutical Preparations: thirty-fifth report. Geneva: World Health Organization; 1999: Annex 8 (WHO Technical Report Series, No. 885) (1) (http://apps.who.int/medicinedocs/documents/s21964en/s21964en.pdf) 2. Guidelines for national authorities on quality assurance for biological products. In: WHO Expert Committee on Biological Standardization: forty-second report. World Health Organization; 1992: Annex 2 (WHO Technical Report Series, No. 822), (2), (http://www.who.int/biologicals/publications/trs/areas/biological_products/WHO_TRS_822_A2.pdf) 3. Regulation and licensing of biological products in countries with newly developing regulatory authorities. In: WHO Expert Committee on Biological Standardization: forty-fifth report. Geneva: World Health Organization; 1995: Annex 1 (WHO Technical Report Series, No. 858), (3), (http://www.who.int/bloodproducts/publications/WHO_TRS_858_A1.pdf) 4. How to develop and implement a national drug policy, Second edition. WHO, 2001., (116), (http://apps.who.int/medicinedocs/pdf/s2283e/s2283e.pdf)
Framework:	"Structure/Foundation/Input"
Rating Scale:	➜ NOT IMPLEMENTED (NI): There is no evidence that the NRA participates in a regional and/or global network. ➜ ONGOING IMPLEMENTATION (OI): There is no evidence that the NRA participates in regional and/or global networks but demonstrable steps have been taken towards this. ➜ PARTIALLY IMPLEMENTED (PI): The NRA has participated in some meetings, seminars, or committees but there is no evidence of adoption of decisions or recommendation by the networks. ➜ IMPLEMENTED (I): There is documented evidence of NRA participation in regional and/or global networks.

Limitations and remarks:	Scoring this sub-indicator as "not applicable NA" is excluded (i.e. this sub-indicator will always apply for all benchmarked NRAs).
Sub Indicator:	**RS09.02: The information on laws, regulations guidelines and procedures is publicly available and is kept duly updated.**
Maturity Level:	3
Scope:	1. Medicines 2. Vaccines
Description:	The assessor should verify that all relevant laws, regulations, guidelines and procedures are publicly available and duly updated. Some other information related to internal procedures and decision making may be for internal use only. Assessor should verify the availability of document control mechanisms and procedures for updating the documents at a regular frequency. The assessor should verify that there is public access to non-classified information unless otherwise justified for well-specified reasons as provided by law (such as protection of privacy or ensuring fairness of procurement procedures).
Objective:	The objective of this sub-indicator is to ensure that medical products laws, regulations, guidelines and procedures are available and accessible to stakeholders and the general public. Openness and transparency are key ingredients for building the accountability and trust which are necessary for the functioning of organization and for good governance.
Requirement:	Laws, regulations, guidelines and procedures are publicly available.
Evidence to review:	The assessor should request for and review: 1. Publicly available laws, regulations, guidelines and procedures; 2. Mechanisms in place for information sharing (e.g., website or other public communications); 3. Written procedures describing the process.
References:	1. National drug regulatory legislation: guiding principles for small drug regulatory authorities. In: WHO Expert Committee on Specifications for Pharmaceutical Preparations: thirty-fifth report. Geneva: World Health Organization; 1999: Annex 8 (WHO Technical Report Series, No. 885) (1) (http://apps.who.int/medicinedocs/documents/s21964en/s21964en.pdf) 2. Guidelines for national authorities on quality assurance for biological products. In: WHO Expert Committee on Biological Standardization: forty-second report. World Health Organization; 1992: Annex 2 (WHO Technical Report Series, No. 822), (2), (http://www.who.int/biologicals/publications/trs/areas/biological_products/WHO_TRS_822_A2.pdf) 3. Regulation and licensing of biological products in countries with newly developing regulatory authorities. In: WHO Expert Committee on Biological Standardization: forty-fifth report. Geneva: World Health Organization; 1995: Annex 1 (WHO Technical Report Series, No. 858), (3), (http://www.who.int/bloodproducts/publications/WHO_TRS_858_A1.pdf) 4. How to develop and implement a national drug policy, Second edition. WHO, 2001., (116), (http://apps.who.int/medicinedocs/pdf/s2283e/s2283e.pdf) 5. Good governance for medicines: Model framework. Updated version 2014. WHO, (110), (https://www.who.int/medicines/areas/governance/ggm_modelframe_updated/en/)
Framework:	"Structure/Foundation/Input"
Rating Scale:	➔ NOT IMPLEMENTED (NI): There is no evidence that the information on laws, regulations guidelines and procedures is publicly available and is kept duly updated. ➔ ONGOING IMPLEMENTATION (OI): The information on laws, regulations guidelines and procedures is not publicly available or kept duly updated but demonstrable steps have been taken towards this.

	➔ PARTIALLY IMPLEMENTED (PI): There is some information publicly available but not from all types of documents, or information is not kept duly updated. ➔ IMPLEMENTED (I): The information on laws, regulations guidelines and procedures is publicly available and is kept duly updated.
Limitations and remarks:	Scoring this sub-indicator as "not applicable NA" is excluded (i.e. this sub-indicator will always apply for all benchmarked NRAs).
Sub Indicator:	**RS09.03: Information on decisions related to regulatory activities is available to the public.**
Maturity Level:	4
Scope:	1. Medicines 2. Vaccines
Description:	The assessor should verify that all relevant information and summary reports that serve as the bases for regulatory decisions for different functions are available and that final decisions are communicated to the public.
Objective:	The objective of this sub-indicator is to ensure that relevant documents that support positive or negative NRA decisions are publicly available, and that final decisions are communicated to the public. Evidence-based decisions and honesty regarding the facts and principles considered in the regulatory decision-making process greatly enhance public trust. A basic component of transparency in the work of NRAs is based on whether its decisions are published, and whether the relevant information is quickly and easily accessible to those regulated and to the general public. Regulatory decisions include approvals or denials; unless prohibited by specific legal provisions, decisions to not approve (i.e., denials) should also be published.
Requirement:	Decisions are accessible to the public
Evidence to review:	The assessor should request for and review: 1. Provisions or guidelines describing the public communication process; 2. List of publicly-available final decisions and supporting documents and reports related to different regulatory processes (e.g., marketing authorizations, clinical trials, inspections, market surveillance, pharmacovigilance, and licensing); 3. Relevant documents from website or other mechanisms used to publish the information.
References:	1. National drug regulatory legislation: guiding principles for small drug regulatory authorities. In: WHO Expert Committee on Specifications for Pharmaceutical Preparations: thirty-fifth report. Geneva: World Health Organization; 1999: Annex 8 (WHO Technical Report Series, No. 885) (1) (http://apps.who.int/medicinedocs/documents/s21964en/s21964en.pdf) 2. Guidelines for national authorities on quality assurance for biological products. In: WHO Expert Committee on Biological Standardization: forty-second report. World Health Organization; 1992: Annex 2 (WHO Technical Report Series, No. 822), (2), (http://www.who.int/biologicals/publications/trs/areas/biological_products/WHO_TRS_822_A2.pdf) 3. Regulation and licensing of biological products in countries with newly developing regulatory authorities. In: WHO Expert Committee on Biological Standardization: forty-fifth report. Geneva: World Health Organization; 1995: Annex 1 (WHO Technical Report Series, No. 858), (3), (http://www.who.int/bloodproducts/publications/WHO_TRS_858_A1.pdf) 4. How to develop and implement a national drug policy, Second edition. WHO, 2001., (116), (http://apps.who.int/medicinedocs/pdf/s2283e/s2283e.pdf) 5. Good governance for medicines: Model framework. Updated version 2014. WHO (110) (https://www.who.int/medicines/areas/governance/ggm_modelframe_updated/en/)
Framework:	"Output"

Rating Scale:	➜ NOT IMPLEMENTED (NI): No regulatory decisions are published. ➜ ONGOING IMPLEMENTATION (OI): There is evidence that a process is underway for the publication of regulatory decisions. ➜ PARTIALLY IMPLEMENTED (PI): Regulatory decisions began to be published recently (i.e., less than a year ago). ➜ IMPLEMENTED (I): The NRA systematically publishes the positive and negative regulatory decisions.
Limitations and remarks:	In some countries, legislation may not allow the publication of negative regulatory decisions. In this case, the assessment of this sub-indicator should be limited to the publication of positive regulatory decisions (e.g. marketing authorizations granted or Good Manufacturing Practice compliance assessments). Scoring this sub-indicator as "not applicable NA" is excluded (i.e. this sub-indicator will always apply for all benchmarked NRAs).
Sub Indicator:	**RS09.04: Information on marketed medical products, authorized companies and licensed facilities is publicly available.**
Maturity Level:	3
Scope:	1. Medicines 2. Vaccines
Description:	The assessor should verify that lists identifying all authorized products and all licenses issued to manufacturers, importers, wholesalers and other institutions engaged in manufacture, control, distribution, or marketing of medical products are published and publicly available. Experience in countries has demonstrated that informing consumers and public interest groups on regulation of medicines enhances political support for the regulatory process, promotes NRA transparency and accountability, and shields them from negative external influence.
Objective:	The objective of this sub-indicator is to ensure that information on NRA decisions is available to the public. Such transparency can help to reduce conflicts of interest and corruption. In addition, public availability of a list of approved products may prevent use of any unregistered products.
Requirement:	Transparency
Evidence to review:	The assessor should request for and review: 1. Guidelines which describe the information that should be publicly available; 2. Publicly available information on marketed products and authorized companies and facilities.
References:	1. National drug regulatory legislation: guiding principles for small drug regulatory authorities. In: WHO Expert Committee on Specifications for Pharmaceutical Preparations: thirty-fifth report. Geneva: World Health Organization; 1999: Annex 8 (WHO Technical Report Series, No. 885) (1) (http://apps.who.int/medicinedocs/documents/s21964en/s21964en.pdf) 2. Guidelines for national authorities on quality assurance for biological products. In: WHO Expert Committee on Biological Standardization: forty-second report. World Health Organization; 1992: Annex 2 (WHO Technical Report Series, No. 822), (2), (http://www.who.int/biologicals/publications/trs/areas/biological_products/WHO_TRS_822_A2.pdf) 3. Regulation and licensing of biological products in countries with newly developing regulatory authorities. In: WHO Expert Committee on Biological Standardization: forty-fifth report. Geneva: World Health Organization; 1995: Annex 1 (WHO Technical Report Series, No. 858), (3), (http://www.who.int/bloodproducts/publications/WHO_TRS_858_A1.pdf) 4. How to develop and implement a national drug policy, Second edition. WHO, 2001., (116), (http://apps.who.int/medicinedocs/pdf/s2283e/s2283e.pdf)

Framework:	"Output".
Rating Scale:	➔ NOT IMPLEMENTED (NI): No information on marketed medical products, authorized companies and licensed facilities is published. ➔ ONGOING IMPLEMENTATION (OI): There is evidence that a process is underway for the publication of some regulatory decisions on marketed medical products, authorized companies and licensed facilities. ➔ PARTIALLY IMPLEMENTED (PI): Regulatory decisions on marketed medical products, authorized companies and licensed facilities began to be published recently (i.e., less than a year ago). ➔ IMPLEMENTED (I): The NRA systematically publishes the positive and negative regulatory decisions on marketed medical products, authorized companies and licensed facilities and there is evidence available for more than 2 years.
Limitations and remarks:	Scoring this sub-indicator as "not applicable NA" is excluded (i.e. this sub-indicator will always apply for all benchmarked NRAs).
Sub Indicator:	**RS09.05: All publicly available information is periodically reviewed and maintained.**
Maturity Level:	4
Scope:	1. Medicines 2. Vaccines
Description:	The assessor should verify that public information is reviewed on regular basis so that the latest updates are currently available to the public.
Objective:	The objective of this sub-indicator is to ensure the NRA considers and defines specific intervals for reviewing and maintaining the publicly available information. As part of this process, the NRA should consider the risks linked to different categories of information.
Requirement:	Publicly available information is reviewed and maintained.
Evidence to review:	The assessor should request for and review: 1. A guideline for publication of information that describes the types of information to be published, specifies the format for publication, identifies the persons responsible, and defines the frequency for updating; 2. Records documenting that these procedures are followed.
References:	1. National drug regulatory legislation: guiding principles for small drug regulatory authorities. In: WHO Expert Committee on Specifications for Pharmaceutical Preparations: thirty-fifth report. Geneva: World Health Organization; 1999: Annex 8 (WHO Technical Report Series, No. 885) (1) (http://apps.who.int/medicinedocs/documents/s21964en/s21964en.pdf) 2. Guidelines for national authorities on quality assurance for biological products. In: WHO Expert Committee on Biological Standardization: forty-second report. World Health Organization; 1992: Annex 2 (WHO Technical Report Series, No. 822), (2), (http://www.who.int/biologicals/publications/trs/areas/biological_products/WHO_TRS_822_A2.pdf) 3. Regulation and licensing of biological products in countries with newly developing regulatory authorities. In: WHO Expert Committee on Biological Standardization: forty-fifth report. Geneva: World Health Organization; 1995: Annex 1 (WHO Technical Report Series, No. 858), (3), (http://www.who.int/bloodproducts/publications/WHO_TRS_858_A1.pdf) 4. How to develop and implement a national drug policy, Second edition. WHO, 2001., (116), (http://apps.who.int/medicinedocs/pdf/s2283e/s2283e.pdf)
Framework:	"Output".

Rating Scale:	➜ NOT IMPLEMENTED (NI): There is no evidence that publicly available information is periodically reviewed and maintained. ➜ ONGOING IMPLEMENTATION (OI): The publicly available information is not periodically reviewed and maintained but demonstrable steps have been taken towards this. ➜ PARTIALLY IMPLEMENTED (PI): There is some information publicly available but not from all types of documents or information is not kept duly updated. ➜ IMPLEMENTED (I): The publicly available information is periodically reviewed and maintained.
Limitations and remarks:	Scoring this sub-indicator as "not applicable NA" is excluded (i.e. this sub-indicator will always apply for all benchmarked NRAs).
Sub Indicator:	**RS09.06: Appropriate mechanisms exist for management of confidential information.**
Maturity Level:	3
Scope:	1. Medicines 2. Vaccines
Description:	The assessor should identify the written procedures for the management of confidential information for internal staff, external experts and members of advisory committees. A written document and established mechanisms should explain which information should be kept confidential and how this should be done. The mechanisms should be explicit regarding the means used by the NRA to keep confidentiality, including administrative, physical and technical controls. It is very important to define how information can be shared within and outside the NRA.
Objective:	The objective of this sub-indicator is to ensure that the NRA has appropriate mechanisms and procedures for management of confidential information. Confidential Information refers to any documents, materials or information (whether in written, oral, electronic or any other format) which are of a confidential, proprietary, personal or non-public nature. Such confidential information may belong to either (i) the NRA or (ii) any third party collaborating with the NRA or to whom the NRA owes a duty of confidentiality (including, but not limited to, manufacturers, marketing authorization holders and clinical investigators). Confidential information must be protected from unauthorized access to safeguard the privacy or security of an individual or organization.
Requirement:	Management of confidential information
Evidence to review:	The assessor should request for and review: 1. Written documents that describe management of confidential information; 2. Documentation that there is adequate infrastructure to keep the confidential information, e.g., locked rooms or secure computerized systems.
References:	1. National drug regulatory legislation: guiding principles for small drug regulatory authorities. In: WHO Expert Committee on Specifications for Pharmaceutical Preparations: thirty-fifth report. Geneva: World Health Organization; 1999: Annex 8 (WHO Technical Report Series, No. 885) (1) (http://apps.who.int/medicinedocs/documents/s21964en/s21964en.pdf) 2. Guidelines for national authorities on quality assurance for biological products. In: WHO Expert Committee on Biological Standardization: forty-second report. World Health Organization; 1992: Annex 2 (WHO Technical Report Series, No. 822), (2), (http://www.who.int/biologicals/publications/trs/areas/biological_products/WHO_TRS_822_A2.pdf) 3. Regulation and licensing of biological products in countries with newly developing regulatory authorities. In: WHO Expert Committee on Biological Standardization: forty-fifth report. Geneva: World Health Organization; 1995: Annex 1 (WHO Technical

	Report Series, No. 858), (3), (http://www.who.int/bloodproducts/publications/WHO_TRS_858_A1.pdf) 4. How to develop and implement a national drug policy, Second edition. WHO, 2001., (116), (http://apps.who.int/medicinedocs/pdf/s2283e/s2283e.pdf) 5. Good governance for medicines: Model framework. Updated version 2014. WHO (110) (https://www.who.int/medicines/areas/governance/ggm_modelframe_updated/en/)
Framework:	"Structure/Foundation/Input"
Rating Scale:	➔ NOT IMPLEMENTED (NI): There is no evidence that the NRA has an appropriate mechanism to manage confidential information. ➔ ONGOING IMPLEMENTATION (OI): There is no evidence that the NRA has an appropriate mechanism to manage confidential information but demonstrable steps have been taken towards this. ➔ PARTIALLY IMPLEMENTED (PI): The NRA has developed a draft document to manage confidential information but it has not yet been implemented. ➔ IMPLEMENTED (I): There is documented evidence that the NRA has an appropriate mechanism to manage confidential information.
Limitations and remarks:	▪ Confidential information means any documents, materials or information (whether in written, oral, electronic or any other format) which are of a confidential, proprietary, personal or non-public nature. Such confidential information may belong to either (i) the NRA or (ii) any third party collaborating with the NRA or to whom the NRA owes a duty of confidentiality (including, but not limited to, manufacturers). ▪ Scoring this sub-indicator as "not applicable NA" is excluded (i.e. this sub-indicator will always apply for all benchmarked NRAs).
Sub Indicator:	**RS09.07: A code of conduct, which includes management of conflicts of interest, is published and enforced for internal and external staff, including members of the advisory committees.**
Maturity Level:	3
Scope:	1. Medicines 2. Vaccines
Description:	The assessor should verify the existence of a written, published and enforced code of conduct for internal staff and for external experts and members of advisory committees. The main issues are related to the independence of all experts involved in the regulatory processes and to the management and prevention of potential conflicts of interests.
Objective:	The objective of this sub-indicator is to ensure the NRA has established codes of conduct based on professionalism, institutional values, and ethical principles. This is a mechanism to prevent unethical behavior by public servants and external staff (including members of the advisory committees) in the performance of their duties. Studies by Transparency International indicate that governments which have established a framework for good governance, based on codes of conduct, ethical principles and other key components of an integrity system, are listed among the countries with very low levels of corruption. There is a logical and consistent link between values, principles and a code of conduct. A code of conduct attempts to articulate in concrete terms the application of ethical principles. The normative base for the code of conduct is the framework of institutional values.
Requirement:	Code of conduct
Evidence to review:	The assessor should request for and review: 1. A guideline describing the code of conduct for the NRA; 2. Records of signed conflict of interest forms.

References:	1. National drug regulatory legislation: guiding principles for small drug regulatory authorities. In: WHO Expert Committee on Specifications for Pharmaceutical Preparations: thirty-fifth report. Geneva: World Health Organization; 1999: Annex 8 (WHO Technical Report Series, No. 885) (1) (http://apps.who.int/medicinedocs/documents/s21964en/s21964en.pdf) 2. Guidelines for national authorities on quality assurance for biological products. In: WHO Expert Committee on Biological Standardization: forty-second report. World Health Organization; 1992: Annex 2 (WHO Technical Report Series, No. 822), (2), (http://www.who.int/biologicals/publications/trs/areas/biological_products/WHO_TRS_822_A2.pdf) 3. Regulation and licensing of biological products in countries with newly developing regulatory authorities. In: WHO Expert Committee on Biological Standardization: forty-fifth report. Geneva: World Health Organization; 1995: Annex 1 (WHO Technical Report Series, No. 858), (3), (http://www.who.int/bloodproducts/publications/WHO_TRS_858_A1.pdf) 4. How to develop and implement a national drug policy, Second edition. WHO, 2001., (116), (http://apps.who.int/medicinedocs/pdf/s2283e/s2283e.pdf) 5. Good governance for medicines: Model framework. Updated version 2014. WHO (110) (https://www.who.int/medicines/areas/governance/ggm_modelframe_updated/en/)
Framework:	"Structure/Foundation/Input"
Rating Scale:	➔ NOT IMPLEMENTED (NI): There is no evidence that a code of conduct, including management of conflicts of interest, is published and enforced for internal and external staff, including members of the advisory committees. ➔ ONGOING IMPLEMENTATION (OI): There is no evidence that a code of conduct, including management of conflicts of interest, is published and enforced; however, demonstrable steps have been taken towards this. ➔ PARTIALLY IMPLEMENTED (PI): The NRA has developed a draft document but it has not yet been implemented. ➔ IMPLEMENTED (I): There is documented evidence that a code of conduct, including management of conflicts of interest, is published and enforced.
Limitations and remarks:	Scoring this sub-indicator as "not applicable NA" is excluded (i.e. this sub-indicator will always apply for all benchmarked NRAs).
Sub Indicator:	**RS09.08: The NRA uses computerized systems to process information, manage records, and analyze data.**
Maturity Level:	4
Scope:	1. Medicines 2. Vaccines
Description:	The assessor should verify that the NRA makes appropriate use of automation and effectively manages its databases to process information and generate good quality and readily accessible reports. "E-government" refers to the use of information and communication technologies to promote more efficient and effective government, facilitate more accessible government services, allow greater public access to information, and make government more accountable to citizens. The assessor should verify the utilization of electronic systems and workstations by the NRA to handle these activities, which may be repetitive in nature. In general, e-governance would be required to be checked.
Objective:	The objective of this sub-indicator is to ensure the NRA manages computerized systems for information processing, records management, and data analysis. This sub-indicator measures the NRA's handling of automated data management systems, use of safeguards to protect data integrity, and development of integrated networks. Under this indicator, the degree to which these objectives are achieved is also assessed. E-governance can play a facilitating role.

Requirement:	Computerized systems to automate repetitive activities
Evidence to review:	The assessor should request for and review: 1. Evidence for availability of electronic systems and workstations; 2. Evidence for availability of required software for conducting regulatory activities; 3. List of processes that use computerized systems; 4. Databases in use or under in development within the NRA; 5. Databases and systems in use that can be consulted by those regulated and the general public.
References:	1. National drug regulatory legislation: guiding principles for small drug regulatory authorities. In: WHO Expert Committee on Specifications for Pharmaceutical Preparations: thirty-fifth report. Geneva: World Health Organization; 1999: Annex 8 (WHO Technical Report Series, No. 885) (1) (http://apps.who.int/medicinedocs/documents/s21964en/s21964en.pdf) 2. Guidelines for national authorities on quality assurance for biological products. In: WHO Expert Committee on Biological Standardization: forty-second report. World Health Organization; 1992: Annex 2 (WHO Technical Report Series, No. 822), (2), (http://www.who.int/biologicals/publications/trs/areas/biological_products/WHO_TRS_822_A2.pdf) 3. Regulation and licensing of biological products in countries with newly developing regulatory authorities. In: WHO Expert Committee on Biological Standardization: forty-fifth report. Geneva: World Health Organization; 1995: Annex 1 (WHO Technical Report Series, No. 858), (3), (http://www.who.int/bloodproducts/publications/WHO_TRS_858_A1.pdf) 4. How to develop and implement a national drug policy, Second edition. WHO, 2001., (116), (http://apps.who.int/medicinedocs/pdf/s2283e/s2283e.pdf)
Framework:	"Structure/Foundation/Input"
Rating Scale:	➜ NOT IMPLEMENTED (NI): There is no evidence that the NRA uses computerized systems for information processing, records management, and data analysis. ➜ ONGOING IMPLEMENTATION (OI): There is no evidence that the NRA uses computerized systems for information processing, records management, and data analysis, but demonstrable steps have been taken towards this. ➜ PARTIALLY IMPLEMENTED (PI): The NRA has started to use computerized systems for information processing, records management, and data analysis but this has not been applied in all regulatory processes. ➜ IMPLEMENTED (I): There is documented evidence that the NRA uses computerized systems for information processing, records management, and data analysis.
Limitations and remarks:	Scoring this sub-indicator as "not applicable NA" is excluded (i.e. this sub-indicator will always apply for all benchmarked NRAs).
Sub Indicator:	**RS09.09: The NRA has its own web page with timely information that gives public access to related legal provisions, guidelines and decisions.**
Maturity Level:	3
Scope:	1. Medicines 2. Vaccines
Description:	The assessor should check that the NRA web page serves as a platform for sharing timely information and for providing public access to legal provisions, guidelines and decisions.
Objective:	The objective of this sub-indicator is to ensure the NRA's website plays an active role in effective and timely communication of information required to be publicized.
Requirement:	Website

Evidence to review:	The assessor should request for and review: 1. NRA website and information available on it; 2. NRA communication policy; 3. Written documents describing how frequently information provided in the website should be reviewed and updated.
References:	1. National drug regulatory legislation: guiding principles for small drug regulatory authorities. In: WHO Expert Committee on Specifications for Pharmaceutical Preparations: thirty-fifth report. Geneva: World Health Organization; 1999: Annex 8 (WHO Technical Report Series, No. 885) (1) (http://apps.who.int/medicinedocs/documents/s21964en/s21964en.pdf) 2. Guidelines for national authorities on quality assurance for biological products. In: WHO Expert Committee on Biological Standardization: forty-second report. World Health Organization; 1992: Annex 2 (WHO Technical Report Series, No. 822), (2), (http://www.who.int/biologicals/publications/trs/areas/biological_products/WHO_TRS_822_A2.pdf) 3. Regulation and licensing of biological products in countries with newly developing regulatory authorities. In: WHO Expert Committee on Biological Standardization: forty-fifth report. Geneva: World Health Organization; 1995: Annex 1 (WHO Technical Report Series, No. 858), (3), (http://www.who.int/bloodproducts/publications/WHO_TRS_858_A1.pdf) 4. How to develop and implement a national drug policy, Second edition. WHO, 2001., (116), (http://apps.who.int/medicinedocs/pdf/s2283e/s2283e.pdf)
Framework:	"Structure/Foundation/Input"
Rating Scale:	➜ NOT IMPLEMENTED (NI): The NRA does not have a website with timely information that gives public access to related legal provisions, guidelines and decisions. ➜ ONGOING IMPLEMENTATION (OI):The NRA does not have a website but demonstrable steps have been taken towards this. ➜ PARTIALLY IMPLEMENTED (PI): The NRA has started to use its website but the information posted is not up to date. ➜ IMPLEMENTED (I): The NRA has a website with timely information that gives public access to related legal provisions, guidelines and decisions.
Limitations and remarks:	Scoring this sub-indicator as "not applicable NA" is excluded (i.e. this sub-indicator will always apply for all benchmarked NRAs).
Indicator:	**RS10 Mechanism in place to monitor regulatory performance and output.**
Objective:	The objective of this indicator is to ensure monitoring of regulatory performance through the establishment of key performance indicators. Monitoring of regulatory performance plays an important role when taking the appropriate actions and when adjusting the process to ensure that the regulatory activity conforms to its specifications. In addition, the NRA should monitor and review the performance of the contracted entities (in the case of outsourced activities) including the implementation and effectiveness of any needed improvements.
Category:	09. Monitoring progress and assessing outcomes and impact
Sub Indicator:	**RS10.01: Requirements established to monitor, supervise and review the performance of the NRA and affiliated institutions using key performance indicators (KPIs).**
Maturity Level:	4
Scope:	1. Medicines 2. Vaccines
Description:	The assessor should verify the existence and implementation of requirements and procedures for monitoring, supervising, and reviewing the performance of the NRA and affiliated institutions. Monitoring and evaluating NRA performance are essential

	components of a regulatory framework, and the provisions necessary to achieve this need to be included in the regulatory oversight of medical products. Key issues include: explicit government commitment to the principles of monitoring and evaluation; monitoring of the pharmaceutical sector through regular indicator-based surveys; and independent external evaluation of the impact of the regulatory oversight. The assessor should confirm the establishment of a set of KPIs for monitoring progress in meeting the objectives of the strategic plan (or equivalent) and the institutional development plan. The assessor should check whether the outcome of monitoring and measuring regulatory performance has resulted in corrective actions, preventive actions, and/or improvements in the regulatory activities.
Objective:	The objective of this sub-indicator is to ensure the NRA and affiliated institutions have established requirements to monitor, supervise and review its performance. Establishment of KPIs is a very effective approach for measuring and monitoring progress. A KPI is a measurable value that evaluates how effectively the NRA is achieving the strategic plan and the institutional development plan. Organizations use KPIs to evaluate their success at reaching targets. In the case of outsourced activities, the NRA should monitor and review the performance of the contract acceptor including the implementation of any needed improvements and the assessment of their effectiveness.
Requirement:	Monitor, supervise and review the key regulatory performance indicators used for monitoring progress
Evidence to review:	The assessor should request for and review: 1. Written documents that describe the monitoring, supervision and review of different regulatory activities; 2. Supporting records, including corrective actions and preventive actions, when applicable; 3. Documentation of KPIs; 4. Records of surveys conducted, and indicators reported; 5. KPI evaluation reports, including statistical data and trend analyses in regard to KPIs, where applicable.
References:	1. National drug regulatory legislation: guiding principles for small drug regulatory authorities. In: WHO Expert Committee on Specifications for Pharmaceutical Preparations: thirty-fifth report. Geneva: World Health Organization; 1999: Annex 8 (WHO Technical Report Series, No. 885) (1) (http://apps.who.int/medicinedocs/documents/s21964en/s21964en.pdf) 2. Guidelines for national authorities on quality assurance for biological products. In: WHO Expert Committee on Biological Standardization: forty-second report. World Health Organization; 1992: Annex 2 (WHO Technical Report Series, No. 822), (2), (http://www.who.int/biologicals/publications/trs/areas/biological_products/WHO_TRS_822_A2.pdf) 3. Regulation and licensing of biological products in countries with newly developing regulatory authorities. In: WHO Expert Committee on Biological Standardization: forty-fifth report. Geneva: World Health Organization; 1995: Annex 1 (WHO Technical Report Series, No. 858), (3), (http://www.who.int/bloodproducts/publications/WHO_TRS_858_A1.pdf) 4. How to develop and implement a national drug policy, Second edition. WHO, 2001., (116), (http://apps.who.int/medicinedocs/pdf/s2283e/s2283e.pdf)
Framework:	"Process"
Rating Scale:	➜ NOT IMPLEMENTED (NI): There are no established requirements to monitor, supervise and review the performance of the NRA and affiliated institutions using KPIs. ➜ ONGOING IMPLEMENTATION (OI): There are no established requirements to monitor, supervise and review the performance of the NRA and affiliated institutions using KPIs, but demonstrable steps have been taken towards this. ➜ PARTIALLY IMPLEMENTED (PI): There are some established requirements to monitor, supervise and review the performance of the NRA and affiliated institutions but KPIs have not been established.

	➔ IMPLEMENTED (I): There are established requirements to monitor, supervise and review the performance of the NRA and affiliated institutions using KPIs.
Limitations and remarks:	▪ A regulatory impact analysis is a valuable tool for systematic assessment of the expected effects of regulatory proposals. It is aimed mainly at assisting decision makers in their consideration of the recommended proposal. ▪ Scoring this sub-indicator as "not applicable NA" is excluded (i.e. this sub-indicator will always apply for all benchmarked NRAs).
Sub Indicator:	**RS10.02: Reports on the regulatory activities and on the progression and status of resources are available at regular intervals.**
Maturity Level:	4
Scope:	1. Medicines 2. Vaccines
Description:	The assessor should verify that reviews are planned and carried out at regular intervals, and that these reviews take into consideration: 1. NRA performance and effectiveness of medical products regulatory oversight; 2. opportunities for improvement; 3. adequacy of resources. The organization should retain documented evidence of results of management reviews.
Objective:	The objective of this sub-indicator is to ensure that top management reviews the NRA performance, the areas for improvement, and the status of resources at planned intervals. The purpose is to ensure continued effectiveness of medical products regulatory oversight and alignment with the organization's strategic direction. In addition, the review should evaluate whether required resources are available for conducting the regulatory activities.
Requirement:	Reports at regular intervals on the regulatory activities
Evidence to review:	The assessor should request for and review: 1. Management review procedures (i.e., SOPs or other written documents); 2. Records documenting the conduct of management reviews, including periodicity; 3. Annual reports; 4. Documentation of the inputs to (e.g., audit results and customer satisfaction surveys) and outputs from (e.g., decisions, corrective actions, and preventive actions) these periodic reviews.
References:	1. National drug regulatory legislation: guiding principles for small drug regulatory authorities. In: WHO Expert Committee on Specifications for Pharmaceutical Preparations: thirty-fifth report. Geneva: World Health Organization; 1999: Annex 8 (WHO Technical Report Series, No. 885) (1) (http://apps.who.int/medicinedocs/documents/s21964en/s21964en.pdf) 2. Guidelines for national authorities on quality assurance for biological products. In: WHO Expert Committee on Biological Standardization: forty-second report. World Health Organization; 1992: Annex 2 (WHO Technical Report Series, No. 822), (2), (http://www.who.int/biologicals/publications/trs/areas/biological_products/WHO_TRS_822_A2.pdf) 3. Regulation and licensing of biological products in countries with newly developing regulatory authorities. In: WHO Expert Committee on Biological Standardization: forty-fifth report. Geneva: World Health Organization; 1995: Annex 1 (WHO Technical Report Series, No. 858), (3), (http://www.who.int/bloodproducts/publications/WHO_TRS_858_A1.pdf) 4. How to develop and implement a national drug policy, Second edition. WHO, 2001., (116), (http://apps.who.int/medicinedocs/pdf/s2283e/s2283e.pdf)
Framework:	"Output".
Rating Scale:	➔ NOT IMPLEMENTED (NI): The NRA does not have reports at regular intervals on the NRA performance, areas for improvement and status of resources.

- ONGOING IMPLEMENTATION (OI): The NRA does not have reports of such activities but demonstrable steps have been taken towards this.
- PARTIALLY IMPLEMENTED (PI): The NRA has started to report on the NRA performance, areas for improvement and status of resources, but the activity is not conducted regularly.
- IMPLEMENTED (I): Reports at regular intervals on the regulatory activities, progression and status of resources are available.

Limitations and remarks:	Scoring this sub-indicator as "not applicable NA" is excluded (i.e. this sub-indicator will always apply for all benchmarked NRAs).

02

Registration and Marketing Authorization (MA): Indicators and Fact Sheets

WHO Global Benchmarking Tool (GBT) for Evaluation of National Regulatory System of Medical Products

02. Registration and Marketing Authorization (MA): Indicators and Fact Sheets

Function:	02 — REGISTRATION AND MARKETING AUTHORIZATION (MA)
Description:	The issuance of marketing authorizations (also referred as product licensing or registration) is critical to any National Regulatory Authority (NRA). Marketing authorization (MA) refers to a procedure for approval of a medical product for marketing after it has undergone a process of evaluation to determine the safety, efficacy and quality of the product and the appropriateness of the product information. The objective of this regulatory function is to provide a system which ensures that only medical products which have been duly authorized by the NRA are allowed to be manufactured, imported, distributed, sold or supplied to end-users. The process of assessment for MA includes the review of data on quality, safety and efficacy submitted by the applicant. The same standards should be applied to imported and locally manufactured medical products. Nevertheless, the evaluation of the complex data used to support market authorization of new or novel medical products may require specialized resources and experience not available in the NRA; therefore, countries with limited resources may wish to give priority to well-established products. In the evaluation of well-established products, the NRA may elect to prepare its own report, rely on evaluation reports prepared by other national authorities, rely on decisions made by another NRA, or use a combination of these approaches. Good Manufacturing Practices (GMP) inspections or certifications should be part of the MA requirements. A legal provision should exist that allows the NRA to grant MA of either unlimited or limited duration. In the earlier case, measures should be in place to ensure continued adherence of the medical product to quality, safety, and efficacy standards (e.g. through a vigilance system). In the latter case, MA should be renewed at a predefined time interval. Mechanisms should exist to ensure that information on MA applications, including authorized, suspended, rejected or completed applications, is published to promote transparency and information sharing among stakeholders. Regular publication of MA decisions is helpful to procurement and distribution networks and to other NRAs. Mechanisms and procedures should be in place to monitor and ensure that all activities within the MA function are checked to reduce errors and to reasonably ensure that the processes are consistent and will provide assurance of high quality outputs. Such approaches would lead to consistency in the performance of the MA regulatory function and to reliability of the regulatory outputs.
Indicator:	**MA01 Legal provisions, regulations and guidelines required to define regulatory framework of registration and/or marketing authorization.**
Objective:	The objective of this indicator is to ensure the existence of the legal provisions, regulations and guidelines which form the backbone of the regulatory framework. Such mandates will support the MA function by ensuring that medical products for human use in a particular jurisdiction have been assessed by an NRA and found to be of adequate quality, safety and efficacy (or effectiveness) before being registered or granted MA and placed in the market. The legal provisions empower the NRA with the legal mandate to register and grant MA and also to penalize those who market medical products without the proper health registration or MA.
Category:	Legal provisions, regulations and guidelines

Sub Indicator:	**MA01.01: There are legal provisions that require the receipt of a registration or marketing authorization (MA) before placing the product on the market.**
Maturity Level:	1
Scope:	1. Medicines 2. Vaccines
Description:	The assessor should verify that legal provisions requiring registration or MA before placing a medical product on the market exist and are enacted and implemented. The legal provisions should clearly mandate that all medical products require registration or MA before they are placed on the market. These provisions should provide a list of medical product classes (e.g. drugs, vaccines, or medical devices) that require registration or MA before they are marketed or sold. The legal provisions should specify the applicable fines, charges, penalties, or sanctions in the event of non-compliance. The assessor should note that some medical products may be imported and marketed before registration or MA in special circumstances such as during an emergency or in response to an urgent public health concern. The National Regulatory Authority (NRA) should have systems in place for the active monitoring of such medical products. The assessor may refer to the legal provisions related to emergency situations before applying the scoring
Objective:	The objective of this sub-indicator is to ensure legal provisions are in place that require that a medical product must have been registered or granted MA by the NRA before it is marketed or placed on the market
Requirement:	Legal provisions for medical product registration or MA
Evidence to review:	The assessor should ask for and review: 1) Legal provisions that mandate that all medical products require registration or MA before they are placed on the market. The legal provisions should also specify the applicable fines, charges, penalties, and sanctions in the event of non-compliance. 2) Evidence that the legal provisions have been published and implemented; 3) Evidence that the legal provisions are applicable to all medical products. 4) Evidence that registrations or MAs have been issued. Note that this evidence may be the registration or MA numbers or the registration or MA certificates
References:	1. Guiding principles for small national drug regulatory authorities. In: WHO Expert Committee on Specifications for Pharmaceutical Preparations: thirty-first report. Geneva: World Health Organization; 1990: Annex 6 (WHO Technical Report Series, No. 790), (5), (http://apps.who.int/medicinedocs/documents/s21964en/s21964en.pdf) 2. Regulation and licensing of biological products in countries with newly developing regulatory authorities. In: WHO Expert Committee on Biological Standardization: forty-fifth report. Geneva: World Health Organization; 1995: Annex 1 (WHO Technical Report Series, No. 858), (3), (http://www.who.int/bloodproducts/publications/WHO_TRS_858_A1.pdf)
Framework:	Structure/Foundation/Input
Rating Scale:	➜ NOT IMPLEMENTED (NI): There is no evidence of legal provisions to hold a registration or MA before placing the product on the market. ➜ ONGOING IMPLEMENTATION (OI): The NRA has recently drafted legal provisions to hold a registration or MA but it has not yet been followed. ➜ PARTIALLY IMPLEMENTED (PI): The NRA has legal provisions to hold a registration or MA and has been applying it for less than two years. ➜ IMPLEMENTED (I): The NRA has legal provisions to hold a registration or MA before placing a product on the market and can demonstrate a proven track record of applying them.
Limitations and remarks:	Scoring this sub-indicator as "not applicable NA" is excluded (i.e. this sub-indicator will always apply for all benchmarked NRAs).

Sub Indicator:	**MA01.02: There are legal provisions that require the NRA to withhold, suspend, withdraw or cancel an MA if there are concerns regarding quality, safety or efficacy issues.**
ML	1
Scope:	1. Medicines 2. Vaccines
Description:	The assessor should verify that legal provisions are in place that address the withholding, suspending, withdrawing or cancelling of a registration or MA in the event that quality, safety or efficacy issues are uncovered. Such legal provisions should be enacted and implemented. The legal provisions also should specify requirements on when and how to withhold, suspend, withdraw or cancel a registration or MA.
Objective:	The objective of this sub-indicator is to ensure that legal provisions exist mandating the NRA to withhold, suspend, withdraw or cancel registration or MA in the event of adverse findings related to the quality, safety or efficacy of medical products. The NRA is empowered by legal provisions to withhold, suspend, withdraw or cancel a registration or MA if the requirements set forth for registration or MA are no longer being met. Details on reasons for these decisions should be notified to MA holders. These legal provisions should provide for the sanctioning of those who market medical products without the proper registration or MA.
Requirement:	Legal provisions on withholding, suspending, withdrawing or cancelling an MA
Evidence to review:	The assessor should ask for and review: 1. Legal provisions that mandate the NRA to withhold, suspend, withdraw or cancel a registration or MA in the event of adverse findings related to the quality, safety and efficacy of the medical products. 2. Regulations and guidelines presenting details on when and how to withhold, suspend, withdraw or cancel registration or MA, 3. Evidence that the legal provisions have been implemented, and if possible, examples of implementation. 4. Evidence that stakeholders (e.g., applicants, wholesalers, and retailers) are aware of the legal provisions.
References:	1. Guidelines for national authorities on quality assurance for biological products. In: WHO Expert Committee on Biological Standardization: forty-second report. Geneva. World Health Organization; 1992: Annex 2 (WHO Technical Report Series, No. 822) (2) (http://www.who.int/biologicals/publications/trs/areas/biological_products/WHO_TRS_822_A2.pdf) 2. Guiding principles for small national drug regulatory authorities. In: WHO Expert Committee on Specifications for Pharmaceutical Preparations: thirty-first report. Geneva: World Health Organization; 1990: Annex 6 (WHO Technical Report Series, No. 790), (5), (http://apps.who.int/medicinedocs/documents/s21964en/s21964en.pdf)
Framework:	Structure/Foundation/Input
Rating Scale:	➜ NOT IMPLEMENTED (NI): There is no evidence of legal provisions to withhold, suspend, withdraw or cancel a MA in case there are concerns on quality, safety or efficacy issues. ➜ ONGOING IMPLEMENTATION (OI): The NRA has recently drafted the legal provisions but they have not yet been followed. ➜ PARTIALLY IMPLEMENTED (PI): The NRA has legal provisions and has been applying them for less than two years. ➜ IMPLEMENTED (I): The NRA has legal provisions to withhold, suspend, withdraw or cancel a MA in case there are concerns on quality, safety or efficacy issues and can demonstrate proven track record of applying them
Limitations and remarks:	Scoring this sub-indicator as "not applicable NA" is excluded (i.e. this sub-indicator will always apply for all benchmarked NRAs).

Sub Indicator:	**MA01.03: There are legal provisions that require demonstration of the product quality, safety and efficacy prior to registration or MA.**
Maturity Level:	1
Scope:	1. Medicines 2. Vaccines
Description:	The assessor should verify that legal provisions are in place that stipulate that the demonstration of acceptable quality, safety and efficacy profiles, including demonstration of bioequivalence/bioavailability (BE/BA) when deemed necessary for multisource generic medicines, is a pre-requisite to registration or MA. These legal provisions should be enacted and implemented. Assessors should note that in the case of multisource generic medicines, BE/BA studies would be required based on type of dosage form, method of administration, and health risk criteria determined by the NRA. The legal provisions should empower the NRA to request satisfactory information on the quality, safety and efficacy of medical products seeking registration or MA. The submission should follow the either the common technical document format or another internationally-accepted format. The provisions should be supported by regulations and guidelines that provide guidance to applicants on the required quality, safety and efficacy documentation. All the necessary legal documents should be published, easily accessible, and enforceable.
Objective:	The objective of this sub-indicator is to ensure that legal provisions exist mandating the NRA to request a demonstration (technically and scientifically) that the medical product meets all quality, safety and efficacy regulatory requirements prior to MA. The NRA should require that applicants comply fully with the legal requirements for product registration or MA.
Requirement:	Quality, safety and efficacy prerequisites for registration or MA
Evidence to review:	The assessor should ask for and review: 1. Legal provisions that empower the NRA to request satisfactory information on the quality, safety and efficacy of medical products seeking registration or MA. This information would include the demonstration of BE/BA when it is deemed necessary for multisource generic medicines. 2. Evidence that legal provisions are published and easily accessible to applicants and other stakeholders. 3. Evidence that systems and structures are in place to enforce implementation of the legal provision. 4. Evidence that the legal provisions have been implemented. 5) Evidence that MA application guidance documents provide direction on the quality, safety and efficacy aspects of the legal provisions.
References:	1. Guidelines for national authorities on quality assurance for biological products. In: WHO Expert Committee on Biological Standardization: forty-second report. Geneva. World Health Organization; 1992: Annex 2 (WHO Technical Report Series, No. 822) (2) (http://www.who.int/biologicals/publications/trs/areas/biological_products/WHO_TRS_822_A2.pdf) 2. Guiding principles for small national drug regulatory authorities. In: WHO Expert Committee on Specifications for Pharmaceutical Preparations: thirty-first report. Geneva: World Health Organization; 1990: Annex 6 (WHO Technical Report Series, No. 790), (5), (http://apps.who.int/medicinedocs/documents/s21964en/s21964en.pdf)
Framework:	Structure/Foundation/Input
Rating Scale:	➔ NOT IMPLEMENTED (NI): There is no evidence of existence of legal provisions that require demonstration of the product quality, safety and efficacy prior to registration or MA.

	➔ ONGOING IMPLEMENTATION (OI): The NRA has recently established these legal provisions, but they have not yet been implemented. ➔ PARTIALLY IMPLEMENTED (PI): The NRA has legal provisions and has been applying them for less than two years. ➔ IMPLEMENTED (I): The NRA has legal provisions that require demonstration of the product quality, safety and efficacy prior to registration or MA and can demonstrate a proven track record of applying them.
Limitations and remarks:	Scoring this sub-indicator as "not applicable NA" is excluded (i.e. this sub-indicator will always apply for all benchmarked NRAs).
Sub Indicator:	**MA01.04: There are legal provisions or regulations limiting the duration of the validity of the MA and requiring periodic reviews of MAs (i.e. renewals).**
Maturity Level:	2
Scope:	1. Medicines 2. Vaccines
Description:	The assessor should verify that the legal provisions or regulations specifying the validity period for registrations or MAs (and their renewals) should exist and be enacted and implemented. The legal provisions or regulations should mandate the NRA to register or grant MA with limited validity and also require that the registration or MA be renewed before the medical product is re-introduced onto the market. The legal provisions and regulations should specify the appropriate validity periods of the initial registration or MA and subsequent renewals of registration or MA. The legal provisions also should provide information on the requirements for renewing the registrations or MAs. Ideally, the validity period for MA should not be more than five years.
Objective:	The objective of this sub-indicator is to ensure that legal provisions or regulations exist that mandate the NRA to register or grant MA with limited validity and that require the registration or MA to be renewed before the medical product is re-introduced onto the market.
Requirement:	Registration or MA validity period and registration or MA renewal
Evidence to review:	The assessor should ask for and review: 1. Legal provisions or regulations that mandate the NRA to register or grant MA with limited validity and that require the registration or MA to be renewed before the medical product is re-introduced onto the market 2. Legal provisions or regulations that specify the validity periods for the initial registration or MA and subsequent registration or MA renewals. 3. Regulations and guidelines that provide the requirements for renewing registrations or MAs.
References:	1. Guiding principles for small national drug regulatory authorities. In: WHO Expert Committee on Specifications for Pharmaceutical Preparations: thirty-first report. Geneva: World Health Organization; 1990: Annex 6 (WHO Technical Report Series, No. 790), (5), (http://apps.who.int/medicinedocs/documents/s21964en/s21964en.pdf)
Framework:	Structure/Foundation/Input
Rating Scale:	➔ NOT IMPLEMENTED (NI): There are no legal provisions or regulations regarding the limited duration of the validity of the MA and for periodic reviews to MAs ➔ ONGOING IMPLEMENTATION (OI): The NRA has recently drafted these legal provisions, but they have not yet been implemented. ➔ PARTIALLY IMPLEMENTED (PI): The NRA has legal provisions and has been applying them for less than two years. ➔ IMPLEMENTED (I): The NRA has legal provisions or regulations regarding the limited duration of the validity of the MA and for periodic reviews to MAs and can demonstrate a proven track record of applying them.

Limitations and remarks:	▪ The assessor should note that some NRAs have regulations that mandate them to grant a "One Time" registration to a medical product due to active post-market surveillance ▪ (PMS) (i.e., market surveillance and vigilance) activities. The assessor may review the PMS portfolio of the NRA for more information; if this applies, the scoring should be "Not Applicable".
Sub Indicator:	**MA01.05: There are regulations or guidelines for the definitions, types and the scope of variations along with the required documentation for these variations.**
Maturity Level:	3
Scope:	1. Medicines 2. Vaccines
Description:	The assessor should verify that the regulations or guidelines with respect to the definitions, types and the scope of variations as well as the documentation requirements for these variations should exist and be enacted and implemented. The regulations or guidelines should provide details of the corresponding documentation requirements for each type or class of variation as well as guidance on the scope of evaluation required. Ideally, these guidelines should follow international best practices such as those from World Health Organization (WHO) or International Council on Harmonization (ICH).
Objective:	The objective of this sub-indicator is to ensure that regulations or guidelines exist to provide definitions, types and the scope of variations, as well as documentation requirements for each variation. Scientific and technological advancements or new developments and approaches that may affect the requirements that permitted the original product registration or MA should be communicated to the NRA in support to the variation or post-approval changes application.
Requirement:	Regulations/ guidelines on variations
Evidence to review:	The assessor should ask for and review: 1. Regulations or guidelines that document the definitions, types and scope of variations, as well as the corresponding documentation requirements. 2. Evidence that the regulations or guidelines are published, easily accessible, implemented and known to the applicant, and that these regulations and guidelines effectively communicate requirements. 3. Examples of the types of variations documented and the scope of evaluations required. 4. Documentation supporting the appropriateness of the corresponding fees (if any). 5. Processes, procedures and applicable timelines for submitting variations to the NRA for review and for receiving feedback
References:	1. Procedure for Assessing the Acceptability, in Principle, of Vaccines for Purchase by United Nations Agencies, (77), (http://apps.who.int/medicinedocs/en/q/ and http://digicollection.org/whoqapharm/) 2. Collaborative procedure between the World Health Organization (WHO) Prequalification Team and interested national regulatory authorities in the assessment and accelerated national registration of WHO-prequalified pharmaceutical products and vaccines, (56), (http://apps.who.int/medicinedocs/en/q/ and http://digicollection.org/whoqapharm/) 3. Guidelines on procedures and data requirements for changes to approved vaccines, (50), (http://apps.who.int/medicinedocs/en and https://www.who.int/biologicals/vaccines/en/) 4. Multisource (generic) pharmaceutical products: guidelines on registration requirements to establish interchangeability, (12), (http://digicollection.org/whoqapharm/p/about and http://apps.who.int/medicinedocs/en)
Framework:	Structure/Foundation/Input

Rating Scale:	➔ NOT IMPLEMENTED (NI): There are no regulations or guidelines for the definitions, types and the scope of variations along with the required documentation. ➔ ONGOING IMPLEMENTATION (OI): The NRA has recently drafted these regulations or guidelines but they have not yet been implemented. ➔ PARTIALLY IMPLEMENTED (PI): The NRA has regulations or guidelines and has been applying them for less than two years. ➔ IMPLEMENTED (I): The NRA has regulations or guidelines for the definitions, types and the scope of variations along with the required documentation and required evidence of implementation.
Limitations and remarks:	Scoring this sub-indicator as "not applicable NA" is excluded (i.e. this sub-indicator will always apply for all benchmarked NRAs).
Sub Indicator:	**MA01.06: There are legal provisions to cover circumstances under which the routine MA procedures may not be followed (e.g., for public health interest).**
Maturity Level:	1
Scope:	1. Medicines 2. Vaccines
Description:	The assessor should verify that legal provisions, which describe the circumstances under which the routine medical product registration or MA procedures may not be followed, should exist and be enacted and implemented. The legal provisions should clearly describe the instances or situations when the normal or routine procedures should not be applied. The legal provisions also should provide guidance on the scope of evaluation and on the documentation required in the event that the non- routine approach is used for registration or MA. In addition, if the conditional authorization is time limited, the assessor should verify that the duration of validity is defined in this regulation.
Objective:	The objective of this sub-indicator is to ensure that legal provisions exist to allow the NRA to use a non-routine approach or procedure for registration or MA of medical products under exceptional circumstances in the interest of public health (e.g., emergencies or epidemics).
Requirement:	Exemptions to routine MA procedures
Evidence to review:	The assessor should ask for and review: 1. Legal provisions that define circumstances or instances under which the routine MA procedures may not be followed. 2. Regulations or guidelines that give clarity on the regulatory requirements for granting MA to medical products through a route other than the routine MA procedure. 3. Records of medical products, if any, that have been authorized by this route.
References:	1. Guiding principles for small national drug regulatory authorities. In: WHO Expert Committee on Specifications for Pharmaceutical Preparations: thirty-first report. Geneva: World Health Organization; 1990: Annex 6 (WHO Technical Report Series, No. 790), (5), (http://apps.who.int/medicinedocs/documents/s21964en/s21964en.pdf) 2. WHO Emergency response framework, second edition. Geneva. World Health Organization, 2017 (140) (http://apps.who.int/iris/bitstream/handle/10665/258604/9789241512299-eng.pdf?sequence=1) 3. Emergency Use Assessment and Listing Procedure (EUAL) for Candidate Medicines for Use in the Context of a Public Health Emergency, (121), (http://apps.who.int/medicinedocs/en/) 4. Emergency Use Assessment and Listing Procedure (EUAL) for Candidate Vaccines for Use in the Context of a Public Health Emergency, (122), (http://apps.who.int/medicinedocs/en/)
Framework:	Structure/Foundation/Input

Rating Scale:	➜ NOT IMPLEMENTED (NI): There is no evidence of existence of legal provisions to cover circumstances in which the routine MA procedures may not be followed. ➜ ONGOING IMPLEMENTATION (OI): The NRA has recently drafted these legal provisions but they have not yet been followed. ➜ PARTIALLY IMPLEMENTED (PI): The NRA has legal provisions and has been applying them for less than two years. ➜ IMPLEMENTED (I): The NRA has legal provisions to cover circumstances in which the routine MA procedures may not be followed and has applied them for all medical products that are used under this condition.
Limitations and remarks:	▪ It is proposed that the NRA should establish a provision to clarify the role and responsibilities of all involved stakeholders who are involved in the emergency. The establishment of an advisory committee is suggested to make decisions and to share the responsibilities during an emergency situation. ▪ Non-routine MA procedures are those applicable only under specific circumstances (e.g., emergencies with public health impact) and aimed at reducing the time needed for registration or granting MA. The terminology may vary according the national legislation. Examples of such procedures include different types of collaborative and facilitated registration and MA procedures (e.g., WHO collaborative procedure or stringent regulatory authority facilitated registration procedure). The collaborative procedure is a procedure for collaboration between the WHO Prequalification Team and interested national regulatory authorities for the assessment and accelerated national registration of WHO-prequalified pharmaceutical products and vaccines.
Sub Indicator:	**MA01.07: There are legal provisions or regulations that define regulatory requirements to approve donation of medical products.**
Maturity Level:	1
Scope:	1. Medicines 2. Vaccines
Description:	The assessor should verify that legal provisions or regulations, which define the circumstances under which medical products can be received through donation, exist and are implemented. The legal provisions should provide guidance regarding required information and documentation that should be reviewed before approval of donated medical products. The provisions should also provide guidance on the scope of evaluation as well as the documentation required to show quality, safety and efficacy of donated medical products.
Objective:	The objective of this sub-indicator is to ensure that legal provisions or regulations exist and are implemented to mandate the NRA to have adequate regulatory oversight on medical products received through donation.
Requirement:	MA procedures for approval of donated medical products
Evidence to review:	The assessor should ask for and review: 1. Legal provisions that mandate the NRA to have adequate regulatory oversight on medical products received through donation. 2. Regulations or guidelines giving clarity on the regulatory requirements for use of medical products that are received through donation. 3. Supporting records for any application of these provisions.
References:	1. GPV Policy statement. Vaccine donations. Geneva. World Health Organization (WHO/VSQ/97.03), (111), (https://www.who.int/immunization/hpv/plan/who_unicef_joint_statement_on_vaccine_donations_who_unicef_2011.pdf) 2. Guidelines for Medicine Donations - Revised 2010. (First Edition 1996, Second Edition 1999, Third Edition 2011), (141), (http://apps.who.int/medicinedocs/en/)

	3. Improvements for International Medicine Donations: a Review of the World Health Organization Guidelines for Medicine Donations, 3rd Edition, (142), (http://apps.who.int/medicinedocs/en/)
Framework:	Structure/Foundation/Input
Rating Scale:	➜ NOT IMPLEMENTED (NI): There is no evidence for existence of legal provisions or regulations that define regulatory requirements for use of donated medical products ➜ ONGOING IMPLEMENTATION (OI): The NRA has recently drafted these legal provisions or regulations but they have not yet been followed. ➜ PARTIALLY IMPLEMENTED (PI): The NRA has these legal provisions and has been applying them for less than two years. ➜ IMPLEMENTED (I): The NRA has legal provisions or regulations that define the regulatory requirements for use of donated medical products and these have been applied for all medical products received through donation.
Limitations and remarks:	In exceptional cases in the interest of public health (e.g., emergencies or epidemics), use of a non-routine approach or procedure should be considered to permit use of a donated medical product or to grant MA to a donated medical product. If the NRA use the same regulatory approach for review of donated products as it uses for review of other medical products, this sub indicator can score as not applicable.
Sub Indicator:	**MA01.08: Legal provisions or regulations allow the NRA to recognize and/or rely on MA-relevant decisions, reports or information from other NRAs or regional and international bodies.**
Maturity Level:	1
Scope:	1. Medicines 2. Vaccines
Description:	The assessor should verify that the legal provisions or regulations allowing the NRAs to recognize and/or use relevant MA decisions, reports or information from other NRAs or regional and international bodies should exist and be enacted and implemented. The legal provisions or regulations should provide clarity on the modalities, processes and procedures to employ to recognize and/or use relevant MA decisions, reports or information from other NRAs or regional and international bodies. The legal provisions also should provide clarity on the conditions (i.e., when and how) under which it is acceptable to recognize and/or use relevant MA decisions, reports or information from other NRAs, or regional and international bodies. The legal provisions or regulations should also provide clear directives on the scope or extent of recognition and/or use of MA decisions, reports or information from other NRAs, or regional and international bodies (e.g., WHO prequalification).
Objective:	The objective of this sub-indicator is to verify that legal provisions or regulations exist to allow the NRA to establish a systematic framework to recognize and/or use relevant MA decisions, reports or information from other NRAs, or regional and international bodies.
Requirement:	Recognition and/or reliance of MA application decisions and information
Evidence to review:	The assessor should ask for and review: 1. Legal provisions including guidelines that permit the NRA to recognize and/or use relevant MA decisions, reports or information from other NRAs or regional and international bodies 2. Documentation defining the scope and extent of recognition and /or use of relevant MA decisions, reports or information from other NRAs, or regional and international bodies. 3. Documentation providing examples of instances or situations that have permitted recognition and/or use of relevant MA decisions, reports or information from other NRAs or regional and international bodies

	4. List of NRAs or regional and international bodies whose relevant decisions, reports or information may be used to influence a MA application decision. 5. Evidence that the listed NRAs or regional and international bodies are aware that their relevant MA decisions, reports or information may be used (i.e., aware of the legal provision).
References:	1. Good regulatory practices: guidelines for national regulatory authorities for medical products, (112), (http://digicollection.org/whoqapharm/p/about and http://apps.who.int/medicinedocs/en) 2. WHO general guidance on variations to multisource pharmaceutical products, (143), (http://digicollection.org/whoqapharm/p/about and http://apps.who.int/medicinedocs/en) 3. Guidelines on procedures and data requirements for changes to approved vaccines, (50), (http://apps.who.int/medicinedocs/en and https://www.who.int/biologicals/vaccines/en/) 4. Guidelines on procedures and data requirements for changes to approved biotherapeutic products, (144), (http://apps.who.int/medicinedocs/en/)
Framework:	Structure/Foundation/Input
Rating Scale:	➜ NOT IMPLEMENTED (NI): There is no evidence for existence of legal provisions or regulations that allow the NRA to recognize and/or use MA-relevant decisions, reports or information from other NRAs or regional and international bodies ➜ ONGOING IMPLEMENTATION (OI): The NRA has recently drafted these legal provisions or regulations but they have not yet been followed. ➜ PARTIALLY IMPLEMENTED (PI): The NRA has these legal provisions or regulations and has been applying them to some supported resources for less than two years. ➜ IMPLEMENTED (I): The NRA has legal provisions or regulations allowing the NRA to recognize and/or use MA-relevant decisions, reports or information from other NRAs or regional and international bodies and is able to provide evidence supporting implementation for a list of NRAs or regional and international bodies.
Limitations and remarks:	If the NRA has adequate resources, this sub indicator can be considered not applicable; however, the NRA should have the legal bases for any reliance that does exist.
Sub Indicator:	**MA01.09: Specific guidelines on the quality, nonclinical and clinical aspects are established and implemented.**
Maturity Level:	3
Scope:	1. Medicines 2. Vaccines
Description:	The assessor should verify that specific guidelines on quality, nonclinical, and clinical requirements (as well as guidelines for BE/BA studies in the case of multisource generic medicines) for registering or granting MA should be established and implemented. The guidelines should be detailed and should provide the specific regulatory requirementsfor each section of the quality, nonclinical, and clinical dossier. The guidelines should be specific for the type of application and the medical product. In some cases, the specific guidelines may consist of documents that were not prepared by the NRA but instead were adopted in accordance with proper process.
Objective:	The objective of this sub-indicator is to verify that specific guidelines exist on the quality, nonclinical and clinical requirements for registering or granting MA, and to verify that they have been implemented.
Requirement:	Requirement on quality, nonclinical and clinical aspects
Evidence to review:	The assessor should ask for and review: 1. Guidelines detailing the specific regulatory requirements for the quality, nonclinical and clinical aspects (as well as guidelines for BE/BA studies in the case of multisource generic medicines) of the MA dossier. The requirements, including the content and format, should

	comply with updated international best practices such as those from WHO or ICH. 2. Evidence that the guidelines are specific for the quality, nonclinical, and clinical aspects of the MA application dossier and for the type of application and pharmaceutical product. 3. Evidence that the guidelines are published and implemented. 4. Examples of MA application submissions that are in compliance with the published guidelines. 5. Evidence that documents submitted were appropriate for the type of product and type of application (e.g., new drug application, multisource drug, or product of biological origin or chemical synthesis). 6. Specific guidelines related to a. product labelling and packaging, b. package inserts, c. summary of product characteristics (SPC) information pamphlet for professionals or equivalent d. information pamphlet for patients. 7. Copies of all quality, safety, efficacy reports for recently approved MA applications to determine whether reviews were done thoroughly and based on guidelines requirements.
References:	1. Quality assurance of pharmaceuticals WHO guidelines, good practices, related regulatory guidance and GXP training materials, (79), (http://digicollection.org/whoqapharm/) 2. Guidelines on the quality, safety and efficacy of biotherapeutic protein products prepared by recombinant DNA technology, (54), (https://www.who.int/biologicals/WHO_ECBS/en/ and https://www.who.int/biologicals/vaccines/en/) 3. WHO good manufacturing practices for pharmaceutical products: main principles, (51), (http://digicollection.org/whoqapharm/p/about and http://apps.who.int/medicinedocs/en) 4. Multisource (generic) pharmaceutical products: guidelines on registration requirements to establish interchangeability, (12), (http://digicollection.org/whoqapharm/p/about and http://apps.who.int/medicinedocs/en) 5. Guidelines for national authorities on quality assurance for biological products. In: WHO Expert Committee on Biological Standardization: forty-second report. Geneva. World Health Organization; 1992: Annex 2 (WHO Technical Report Series, No. 822), (2), (http://www.who.int/biologicals/publications/trs/areas/biological_products/WHO_TRS_822_A2.pdf)
Framework:	Structure/Foundation/Input
Rating Scale:	➜ NOT IMPLEMENTED (NI): There is no evidence for the existence of specific guidelines on the quality, nonclinical, and clinical aspects. ➜ ONGOING IMPLEMENTATION (OI): The NRA has recently drafted these guidelines but they have not yet been followed. ➜ PARTIALLY IMPLEMENTED (PI): The NRA has these guidelines and has been applying them for less than two years. ➜ IMPLEMENTED (I): The NRA has established and implemented specific guidelines on the quality, nonclinical, and clinical aspects.
Limitations and remarks:	Scoring this sub-indicator as “not applicable NA” is excluded (i.e. this sub-indicator will always apply for all benchmarked NRAs).
Sub Indicator:	**MA01.10: There are guidelines on the format and content for submission of MA applications that are consistent with the WHO or other internationally accepted standards.**
Maturity Level:	3
Scope:	1. Medicines 2. Vaccines
Description:	The assessor should verify that guidelines on the format and content of a MA submission exist and that they are consistent with international best practices, such as those

	proposed or recommended by WHO or other internationally established agencies such as ICH. The guidelines should provide clarity on the format and content on all sections of the MA application submission and should provide specific guidance for each medical product stream. The guideline also should describe the processes and procedures for submitting the application to the NRA. Additionally, the guidelines should be established and implemented.
Objective:	The objective of this sub-indicator is to verify that guidelines exist for the format and content of a MA application submitted to the NRA; these guidelines should consider the nature of products and the different medical product streams. The content and format of submitted applications should be consistent with the recommendations from the WHO or other internationally accepted agencies.
Requirement:	Format and content for MA application
Evidence to review:	The assessor should ask for and review: 1. Guidelines providing clarity on the format and content of the MA application submission, as well as the processes and procedures for submitting the application to the NRA. 2. Evidence that the guidelines are consistent with international best practices, such as those proposed by the WHO or other internationally accepted agencies. 3. Copies of the checklist used to ensure that MA submissions actually comply with the content of the guidelines before a MA application is acknowledged by the NRA.
References:	1. Multisource (generic) pharmaceutical products: guidelines on registration requirements to establish interchangeability, (12), (http://digicollection.org/whoqapharm/p/about and http://apps.who.int/medicinedocs/en) 2. WHO good manufacturing practices for pharmaceutical products: main principles, (51), (http://digicollection.org/whoqapharm/p/about and http://apps.who.int/medicinedocs/en) 3. Guidelines on the quality, safety and efficacy of biotherapeutic protein products prepared by recombinant DNA technology, (54), (https://www.who.int/biologicals/WHO_ECBS/en/ and https://www.who.int/biologicals/vaccines/en/) 4. Open this document and view its content Guidelines on Submission of Documentation for a Multisource (Generic) Finished Product. General Format: Preparation of Product Dossiers in Common Technical Document Format, (65), (http://apps.who.int/medicinedocs/en/q/ and http://digicollection.org/whoqapharm/) 5. Guidelines on submission of documentation for a multisource (generic) finished pharmaceutical product: quality part, (52), (http://digicollection.org/whoqapharm/p/about and http://apps.who.int/medicinedocs/en) 6. International Conference on Harmonization, ICH tripartite guidelines. The Common Technical document for registration of pharmaceuticals for human use: quality. M4Q (R1). Quality overall summary of Module 2. Module 3: Quality; September 2002, (118), (https://www.ich.org/products/ctd/ctdsingle/article/m4qr1-quality.html)
Framework:	Structure/Foundation/Input
Rating Scale:	➜ NOT IMPLEMENTED (NI): There are no guidelines for the format and content of submitted MA applications. ➜ ONGOING IMPLEMENTATION (OI): The NRA has recently developed or drafted these guidelines, but they have not yet been followed. ➜ PARTIALLY IMPLEMENTED (PI): The NRA has developed or adopted these guidelines and has been applying them for less than two years, or these guidelines have not been applied for all marketed medical products. ➜ IMPLEMENTED (I): The NRA has guidelines for the format and content of submitted MA applications that are consistent with WHO or other internationally accepted standards and that specify required documentation. This process is implemented and followed for all marketed medical products.
Limitations and remarks:	▪ In case of benchmarking for more than one medical product stream, the assessor should consider and review different guidelines, as applicable. In some cases, instructions for dossier compilation may be part of the main (technical) guideline.

- Scoring this sub-indicator as "not applicable NA" is excluded (i.e. this sub-indicator will always apply for all benchmarked NRAs).

Sub Indicator:	**MA01.11: There are guidelines for MA holders that define the types and scope of variations, the format and content to be used for documenting the variations, and the identification of those variations that require prior approval or notification.**
Maturity Level:	3
Scope:	1. Medicines 2. Vaccines
Description:	The assessor should verify the existence, enactment and implementation of guidelines for MA holders that provide guidance on the types and scope of variations, the format and content to be used for documenting the variations, and the identification of the variations that require prior approval or notification. The guidelines should include directives on changes made to leaflets, package inserts, labelling (i.e., container and package), and SPCs. They should also clearly communicate to the MA holder the variations that require NRA approval before implementation, those that require only notifying the NRA before or during implementation, and those that do not require notifying the NRA.
Objective:	The objective of this sub-indicator is to ensure that guidelines exist that provide guidance to MA holders on the types and scope of variations, the format and the content to be used for documenting the variations, and the identification of those variations that require prior approval or notification.
Requirement:	Variation documents for MA holders
Evidence to review:	The assessor should ask for and review: 1. Guidelines that provide guidance to MA holders on the types and scope of variations, the format and content to be used for documenting the variations, and the identification of those variations that require prior approval or notification. The assessor should note that the guidelines should include changes to information contained in leaflets, package inserts, labelling (i.e., package and containers), and SPCs that have been previously approved. 2. Guidelines that communicate to the MA holder the variations that require approval before implementation, those that require only notifying the NRA before or during implementation, and those that do not require notifying the NRA. The assessor should review examples of submitted and processed variation applications and evaluate them for conformance to the guidelines.
References:	1. Guiding principles for small national drug regulatory authorities. In: WHO Expert Committee on Specifications for Pharmaceutical Preparations: thirty-first report. Geneva: World Health Organization; 1990: Annex 6 (WHO Technical Report Series, No. 790), (5), (http://apps.who.int/medicinedocs/documents/s21964en/s21964en.pdf) 2. Regulation and licensing of biological products in countries with newly developing regulatory authorities. In: WHO Expert Committee on Biological Standardization: forty-fifth report. Geneva: World Health Organization; 1995: Annex 1 (WHO Technical Report Series, No. 858), (3), (http://www.who.int/bloodproducts/publications/WHO_TRS_858_A1.pdf) 3. Guidelines on procedures and data requirements for changes to approved biotherapeutic products, (144), (http://apps.who.int/medicinedocs/en/) 4. WHO guidelines on variations to a prequalified product, (145), (http://apps.who.int/medicinedocs/en/q/ and http://digicollection.org/whoqapharm/) 5. Guidelines on procedures and data requirements for changes to approved vaccines, (50), (http://apps.who.int/medicinedocs/en and https://www.who.int/biologicals/vaccines/en/)
Framework:	Structure/Foundation/Input

Rating Scale:	➔ NOT IMPLEMENTED (NI): There is no evidence for existence and implementation of guidelines for MA holders that define the types and scope of variations, the format and the documentation required for each variation, and the identification of the variations that require prior approval. ➔ ONGOING IMPLEMENTATION (OI): The NRA has recently developed or drafted these guidelines, but they have not yet been followed. ➔ PARTIALLY IMPLEMENTED (PI): The NRA has developed or adopted these guidelines and has been applying them for less than two years or they have not been applied to all marketed medical products. ➔ IMPLEMENTED (I): The NRA has guidelines for MA holders that define the types and scope of variations, the format and the documentation required for each variation, and the identification of the variations that require prior approval, and they have been implemented and documented for all marketed medical products
Limitations and remarks:	▪ In case of benchmarking of more than one medical product stream, the assessor should consider and review different guidelines as applicable. ▪ Scoring this sub-indicator as "not applicable NA" is excluded (i.e. this sub-indicator will always apply for all benchmarked NRAs).
Sub Indicator:	**MA01.12: There are established guidelines that cover circumstances under which the routine MA procedures may not be followed (e.g., for public- health interest).**
Maturity Level:	3
Scope:	1. Medicines 2. Vaccines
Description:	The assessor should verify that guidelines that provide guidance to the NRA on how to manage MA applications using a non-routine MA application procedure during public health emergencies are established and implemented. The guidelines should provide guidance on the critical requirements that need to be reviewed by the NRA (e.g. label indication, mode of usage or application, storage conditions, and Good Manufacturing Practice (GMP) certificates and reports), and on the information that should be documented and monitored (e.g., location of deployment, quantities to be deployed, and identity of persons to receive and manage deployment) by the NRA before registration of the medical products. The guidelines should be supported with Standard Operating Procedures (SOPs) that provide guidance on the assessment and evaluation process and on the scope of evaluation needed. The assessor should verify that the NRA will have access to experts (e.g., advisory committees) to support the NRA during the decision-making process. Guidance on the application processing flow and corresponding timelines should be available.
Objective:	The objective of this sub-indicator is to ensure that guidelines exist to provide guidance to the NRA on how to process MA applications using a non-routine MA approach or procedure in exceptional cases and in the interest of public health (e.g. emergencies or epidemics).
Requirement:	Guidance on non-routine MA procedures
Evidence to review:	The assessor should ask for and review: 1. Guidelines that provide guidance to the NRA on the application of a non-routine MA procedure in emergency situations, as well as the corresponding SOPs or supporting documents. 2. A sample application that was processed using the guidelines. The assessor should verify that the information required by the guidelines was submitted and duly evaluated, and that the evaluation process flow and timelines were respected. 3. Evidence of access to experts or advisory committee in case of emergency
References:	1. Guidance on development and implementation of a national deployment and vaccination plan for pandemic influenza vaccines. Geneva: World Health Organization;

	2012, (76), (http://apps.who.int/iris/bitstream/handle/10665/75246/9789241503990_eng.pdf?sequence=1) 2. WHO Emergency response framework, second edition. Geneva. World Health Organization, 2017, (140), (http://apps.who.int/iris/bitstream/handle/10665/258604/9789241512299-eng.pdf?sequence=1)
Framework:	Structure/Foundation/Input
Rating Scale:	➜ NOT IMPLEMENTED (NI): There are no guidelines that cover circumstances under which the routine MA procedures may not be followed. ➜ ONGOING IMPLEMENTATION (OI): The NRA has recently developed or drafted these guidelines but they have not yet been followed. ➜ PARTIALLY IMPLEMENTED (PI): The NRA has developed or officially adopted these guidelines but has not been applied them to all medical products that were approved by non-routine regulatory procedures. ➜ IMPLEMENTED (I): The NRA has guidelines that cover circumstances under which the routine MA procedures may not be followed and has applied them for all medical products that have been approved under this condition.
Limitations and remarks:	There is need to verify that these guidelines have been applied in emergency situations and that all relevant records are available. If there were not any emergency situations after development of the guidelines, the assessor should verify that all required resources are available.
Sub Indicator:	**MA01.13: There are guidelines on the content of product information leaflets, SPC-like information, and product packaging and labelling.**
Maturity Level:	3
Scope:	1. Medicines 2. Vaccines
Description:	The assessor should verify the existence and implementation of guidelines that provide guidance on the MA application requirements with respect to the content of the product information leaflets, SPC-like information, and product packaging and labelling. These guidelines should also provide clarity on the information to be included in the package inserts (i.e., inserts and patient information leaflets), SPC-like information (i.e., information leaflets for professionals or equivalent) and labelling of container-packaging.
Objective:	The objective of this sub-indicator is to ensure that guidelines exist that provide guidance on the MA application requirements with respect to the content of the product information leaflets, SPC-like information, and product packaging and labelling.
Requirement:	Guidance on content of product information leaflets, SPC-like information, and product packaging and labelling
Evidence to review:	The assessor should ask for and review: 1. Guidelines that provide guidance on the MA application requirements with respect to the content of the product information leaflets, SPC-like information, and product packaging and labelling. 2. Relevant supporting documentation including forms and records (e.g., samples of mock-ups and published product information).
References:	1. Guidelines on packaging for pharmaceutical products, World Health Organization (WHO), (80), (http://apps.who.int/medicinedocs/en/q/ and http://digicollection.org/whoqapharm/)
Framework:	Structure/Foundation/Input

Rating Scale:	➔ NOT IMPLEMENTED (NI): There are no guidelines on the content of product information leaflets, SPC-like information, and product packaging and labelling ➔ ONGOING IMPLEMENTATION (OI): The NRA has recently drafted these guidelines but they have not yet been followed ➔ PARTIALLY IMPLEMENTED (PI): The NRA has developed or adopted these guidelines and has been applying them for less than two years or has not fully followed them for all marketed medical products. ➔ IMPLEMENTED (I): The NRA has guidelines on the content of product information leaflets, SPC-like information, and product packaging and labelling and they are followed for all marketed medical products.
Limitations and remarks:	Scoring this sub-indicator as "not applicable NA" is excluded (i.e. this sub-indicator will always apply for all benchmarked NRAs).
Indicator:	**MA02 Arrangement for effective organization and good governance.**
Objective:	The objective of this indicator is to ensure that there is a legal basis and relevant administrative process supporting the organization and governance of the authority that is responsible for registration and MA. These provisions should be documented and should provide for the smooth coordination, collaboration and exchange of information inside and outside the regulatory authority. The arrangement should establish and define the roles and responsibilities inside and outside the NRA for registration and MA activities. Provisions should ensure that the NRA responsible for registration and MA has complete control or access to all relevant submitted information related to produced, procured or received medical products. Relevant information includes, for example, GMP inspection reports, analyses of laborat ory data, collected vigilance data, applications for registration and MA, the number and identity of medical products registered and granted MA, activities of ongoing registrations and MAs, new directives, registrations for newly registered products, withdrawn or suspended registrations and MAs, and rejected applications. The objective of this indicator is to establish that structures are in place at the organizational and governance levels to promote effective intra- and inter-NRA relationships and efficient management of information traffic.
Category:	Organization and governance
Sub Indicator:	**MA02.01: There is a defined structure with clear responsibilities to conduct registration or MA activities.**
Maturity Level:	2
Scope:	1. Medicines 2. Vaccines
Description:	The assessor should verify that defined structures with clear responsibilities to conduct registration or MA activities have been established and implemented. The organizational structure should identify the entities within the NRA that have the mandate for registration or MA activities. The structure should be supported with regulations or guidelines mandating such entities to conduct registration or MA activities and defining the scope and extent of their roles and responsibilities within the NRA in relation to registration or MA activities. The guidance should also clarify lines of reporting in these structures. The organizational structure of the entities should be defined with respect to relationships and ranks, as well as information exchange and flow both inside and outside (e.g., officers at the port of entry or officers in the PMS unit) of the entities.
Objective:	The objective of this sub-indicator is to ensure that there are structures in place, with clearly defined roles and responsibilities for each structural and governance level, to carry out registration or MA activities that ensure effectiveness, efficiency and consistency.

Requirement:	Structure and responsibilities
Evidence to review:	The assessor should ask for and review: 1. Documents that define the roles and responsibilities of the entities responsible for registration or MA activities, and that describe the placement of the entities on the organizational chart in relation to other entities involved in registration or MA–related activities. 2. Regulations or guidelines empowering such entities or authorities with the responsibility to conduct registration or MA activities. 3. Documentation of the organizational structure of the entities
References:	1. National drug regulatory legislation: guiding principles for small drug regulatory authorities. In: WHO Expert Committee on Specifications for Pharmaceutical Preparations: thirty-fifth report. Geneva: World Health Organization; 1999: Annex 8 (WHO Technical Report Series, No. 885), (1), (http://apps.who.int/medicinedocs/documents/s21964en/s21964en.pdf) 2. Multisource (generic) pharmaceutical products: guidelines on registration requirements to establish interchangeability, (12), (http://digicollection.org/whoqapharm/p/about and http://apps.who.int/medicinedocs/en)
Framework:	Structure/Foundation/Input
Rating Scale:	➜ NOT IMPLEMENTED (NI): There is no evidence for a defined structure with clear responsibilities to conduct registration or MA activities. ➜ ONGOING IMPLEMENTATION (OI): The NRA has recently drafted a defined structure with clear responsibilities to conduct registration or MA activities, but it has not yet been implemented. ➜ PARTIALLY IMPLEMENTED (PI): The NRA has a defined and established structure with clear responsibilities to conduct registration or MA activities; however there is the need to improve this function by providing the additional resources and support needed for effective implementation and coordination with other entities. ➜ IMPLEMENTED (I): The NRA has a defined structure with clear responsibilities to conduct registration or MA activities that is fully supported with the required resources.
Limitations and remarks:	Scoring this sub-indicator as “not applicable NA” is excluded (i.e. this sub-indicator will always apply for all benchmarked NRAs).
Sub Indicator:	**MA02.02: Documented and implemented procedures exist to ensure involvement and communication with all relevant regulatory entities as necessary.**
Maturity Level:	3
Scope:	1. Medicines 2. Vaccines
Description:	The assessor should verify the existence and implementation of documented procedures promoting involvement and communication between all relevant entities inside the NRA. These procedures should be supported with adequate documentation. The procedures should provide clear directives on the regulatory divisions and provide guidance on how to implement the operational procedures to ensure the involvement and communication between relevant entities within the NRA (e.g., the dossier assessment entity, quality control laboratory, vigilance and PMS entities, and inspectorate). The procedures should be clear on the scope and extent of the roles and responsibilities of each relevant entity. In addition, the procedures should be supported by an information and documentation transfer policy that ensures that directives, information, and other documentation reach the intended recipients and that feedback is received. The procedures should be captured in the form of SOPs and guidelines which are approved and authorized to be implemented. In case of exchange of confidential information, appropriate measures should be considered; such measures may include confidentiality agreements.

Objective:	The objective of this sub-indicator is to ensure there are documented procedures, mechanisms, and structures in place to ensure proper relationships between and within entities within the NRA (e.g., dossier assessment entity, quality control laboratory, vigilance and PMS entities and inspectorate) and to ensure effective and efficient exchange of information among these entities.
Requirement:	Procedures for effective communication
Evidence to review:	The assessor should ask for and review: 1. The registration or marketing application guidelines that capture the duties, roles and responsibilities of those entities inside the NRA that are involved in registration or marketing activities. 2. Evidence that the guidelines and related documents are known to the relevant organizations, divisions, institutions, and/or departments. 3. Evidence that the documented procedures have been implemented, and that the impact of the implementation has been evaluated. 4. SOPs that guide and inform effective communication and collaboration within and among relevant entities inside the NRA (e.g., dossier assessment entity, quality control laboratory, vigilance entity, and inspectorate). 5. Documentation for the feedback mechanism in the information and documentation transfer policy that covers information exchange among all relevant regulatory divisions.
References:	1. Quality systems requirements for national good manufacturing practice inspectorates. In: WHO Expert Committee on Specifications for Pharmaceutical Preparations: thirty-sixth report. Geneva: World Health Organization; 2002: Annex 8 (WHO Technical Report Series, No. 902), (8), (http://apps.who.int/medicinedocs/documents/s22112en/s22112en.pdf) 2. WHO good practices for pharmaceutical quality control laboratories, (35), (http://digicollection.org/whoqapharm/p/about and http://apps.who.int/medicinedocs/en)
Framework:	Process
Rating Scale:	➜ NOT IMPLEMENTED (NI): There is no evidence of documented procedures to ensure involvement and communication with all relevant regulatory entities as necessary. ➜ ONGOING IMPLEMENTATION (OI): The NRA has recently drafted procedures to ensure involvement and communication, but they have not yet been followed. ➜ PARTIALLY IMPLEMENTED (PI): The relevant entities inside the NRA established the procedures to ensure involvement and communication, but these either have not been fully incorporated or they are not consistent with relevant SOPs. ➜ IMPLEMENTED (I): The NRA has procedures to ensure involvement and communication with all relevant regulatory entities as necessary, including required documentation and records.
Limitations and remarks:	Scoring this sub-indicator as "not applicable NA" is excluded (i.e. this sub-indicator will always apply for all benchmarked NRAs).
Indicator:	**MA03 Human resources to perform registration and marketing authorization activities.**
Objective:	The objective of this indicator is to ensure that all entities within an NRA are adequately resourced with a trained, experienced and skilled workforce, and are empowered to fully perform the function of registering and granting MA for medical products. This will ensure that medical products registration and MA processes or activities are performed in accordance with international best practices. The objective of this indicator is to evaluate the human resource capacity of the entities with respect to the number of personnel, the skills and experience of the personnel, and the overall composition of the workforce, with the goal of evaluating whether the workforce possesses the specific expertise required to perform the registration and MA function.
Category:	Resources (HR, FR, infrastructure and equipment)

Sub Indicator:	**MA03.01: Sufficient competent staff (i.e., education, training, skills and experience) are assigned to perform MA or registration activities.**
Maturity Level:	3
Scope:	1. Medicines 2. Vaccines
Description:	The assessor should verify that the human resources assigned to perform MA or registration activities should be sufficient with respect to numbers and competent with respect to the requisite skills, education, experience and training. There should be technical documents and SOPs that provide guidance on the required background for MA or registration activities and that consider the requirements for educational background, competencies, skills, experience, and training. The assessor should verify that the NRA estimated the number of staff required to effectively and efficiently perform the MA or registration function and that the NRA actually recruited that number. In addition, the assessor should verify that these competency requirements are well-established and maintained by the NRA. Metrics and statistics on the different activities performed as well as performance indicators can be used for estimating the adequacy of the number of the assigned staff. The assessor should also verify that the competency of the assigned staff is built, maintained and improved through recruitment as well as continuous on-the-job training.
Objective:	The objective of this sub-indicator is to ensure the existing human resources for MA or registration is sufficient, in terms of numbers, experience, and specific competencies, to perform all the activities along the entire MA or registration chain.
Requirement:	Sufficient number of competent human resources in charge of MA or registration activities.
Evidence to review:	The assessor should ask for and review: 1. Evidence that the number of staff members involved in each of the documented activities along the entire MA or registration process flow is adequate. 2. Evidence that the systems and structures are in place to ensure appropriate placement of staff with respect to competence and skills. 3. Evidence that the system and structures have been implemented. The documentation should include the records to verify that the staff competence is appropriate for the job requirements. 4. Evidence that the professional profiles of the human resources engaged in MA or registration activities are appropriate with respect to education, skills, and expertise, to perform a particular function along the MA or registration chain. Documentation should include a list of the requisite skills and training for each position. 5. Recruitment plan.
References:	1. National drug regulatory legislation: guiding principles for small drug regulatory authorities. In: WHO Expert Committee on Specifications for Pharmaceutical Preparations: thirty-fifth report. Geneva: World Health Organization; 1999: Annex 8 (WHO Technical Report Series, No. 885), (1), (http://apps.who.int/medicinedocs/documents/s21964en/s21964en.pdf) 2. WHO good manufacturing practices for pharmaceutical products: main principles, (51), (http://digicollection.org/whoqapharm/p/about and http://apps.who.int/medicinedocs/en)
Framework:	Structure/Foundation/Input
Rating Scale:	➔ NOT IMPLEMENTED (NI): The NRA does not have enough competent staff (i.e., education, training, skills and experience) to perform MA or registration activities ➔ ONGOING IMPLEMENTATION (OI): The NRA has recently developed a plan to recruit adequate competent staff; however, the plan has not been implemented. ➔ PARTIALLY IMPLEMENTED (PI): The NRA has initiated the implementation of the human resources development plan; however, there is need to complete the competency profile.

	➔ IMPLEMENTED (I): The NRA has a sustained number of competent staff (i.e., education, training, skills and experience) assigned to perform MA or registration activities.
Limitations and remarks:	▪ Assessment of the adequacy and appropriateness of the number of staff members is quite subjective and should be linked to some process or output indicators. When estimating staff adequacy, the assessor should consider the workload, backlog, and delays in delivery based on established timeframes. ▪ Scoring this sub-indicator as "not applicable NA" is excluded (i.e. this sub-indicator will always apply for all benchmarked NRAs).
Sub Indicator:	**MA03.02: Duties, functions, and responsibilities of the staff in charge of MA or registration activities are established and updated in the respective job descriptions.**
Maturity Level:	3
Scope:	1. Medicines 2. Vaccines
Description:	The assessor should verify that procedures are in place to maintain a current and updated structure for managing job descriptions for personnel participating in MA or registration activities. In addition, job descriptions should address current staff duties, responsibilities and the requisite competencies. A job description with this format and content should be established and implemented for all staff. The management of job descriptions should be supported by a guidance document that provides direction on when and how to update the information, and where the information should be kept for easy access. The guidance document should present the appropriate duties and responsibilities that are assigned to each member of the organization involved in MA or registration activities. Thus, the professional profiles of staff are reflected in their respective roles and responsibilities within the NRA. There should be procedures to guide responsible persons to document that duties, functions and responsibilities are revised and kept up to date. In addition, procedures should be available to guide the keeping and documenting of up to date work schedules and enforcing the implementation of the documented guidelines and procedures.
Objective:	The objective of this sub-indicator is to ensure that duties and responsibilities of the staff are clear and well defined, that job descriptions are kept up to date with current duties, functions and responsibilities, and that these activities are adequately documented.
Requirement:	Duties, roles and responsibilities of the staff relevant to MA or registration activities.
Evidence to review:	The assessor should ask for and review: 1. Procedure and guidelines that guide placement of staff members within the NRA; 2. The professional profiles of staff (i.e., job descriptions) and documentation that they are related to their current roles and duties; 3. The professional profiles of the external experts and documentation that the profiles provide a composition that is complete and consistent with that prescribed in the legal provisions; 4. Procedures to guide the documentation of up to date duties and work schedules, and to enforce the implementation of the documented guidelines and procedures; 5. Job descriptions for designated staff.
References:	1. National drug regulatory legislation: guiding principles for small drug regulatory authorities. In: WHO Expert Committee on Specifications for Pharmaceutical Preparations: thirty-fifth report. Geneva: World Health Organization; 1999: Annex 8 (WHO Technical Report Series, No. 885), (1), (http://apps.who.int/medicinedocs/documents/s21964en/s21964en.pdf) 2. Quality management systems — Requirements. International Standard ISO 9001:2015. Geneva. International Organization for Standardization, 2015, (4), (https://www.iso.org/iso-9001-quality-management.html)

	3. Guiding principles for small national drug regulatory authorities. In: WHO Expert Committee on Specifications for Pharmaceutical Preparations: thirty-first report. Geneva: World Health Organization; 1990: Annex 6 (WHO Technical Report Series, No. 790), (5), (http://apps.who.int/medicinedocs/documents/s21964en/s21964en.pdf) 4. Effective drug regulation: A multicounty study. Geneva: World Health Organization; 2002, (7), (http://apps.who.int/medicinedocs/pdf/s2300e/s2300e.pdf)
Framework:	Structure/Foundation/Input
Rating Scale:	➔ NOT IMPLEMENTED (NI): There is no evidence of defined or established duties, functions, responsibilities, respective job descriptions and necessary required competencies. ➔ ONGOING IMPLEMENTATION (OI): The NRA has recently drafted or developed the role and responsibilities document but it has not yet been implemented. ➔ PARTIALLY IMPLEMENTED (PI): The NRA has initiated implementation of this requirement but it has not been defined or followed for all staff or the roles and responsibilities documents, including staff job descriptions, are not up to date. ➔ IMPLEMENTED (I): The NRA has defined and established all required duties, functions, and responsibilities, and respective job descriptions are up-to-date.
Limitations and remarks:	▪ The issue of overlapping responsibilities among members of the MA assessment teams is very common in some NRAs. Assessor should recognize the arrangement and assess on the basis of the adequacy of competencies of the official for each of the different functions to which they have been assigned. ▪ Scoring this sub-indicator as "not applicable NA" is excluded (i.e. this sub-indicator will always apply for all benchmarked NRAs).
Sub Indicator:	**MA03.03: Training plan developed, implemented and updated at least once a year for staff in charge of MA or registration activities.**
Maturity Level:	3
Scope:	1. Medicines 2. Vaccines
Description:	The assessor should verify that training plans are developed, implemented and updated at least once every year to reflect the current situation by considering education and experience of the staff. The training plan should be complemented with guidelines or similar documents that guide the development and implementation of training plans. The assessor should ensure that induction training for new staff as well as continued on- the-job for staff is planned and implemented. There should be procedures to approve the training plan and the budget allocated for implementing and updating the training plan. The plans should present clearly defined training goals and should include training in certain topics and skills to address identified deficiencies. Learning objectives, training methods and activities, evidence of learning, and evaluation and assessment of training should be documented. This documentation should confirm that the learning objectives were achieved and were designed to address weaknesses within the entities. Procedures should be in place to ensure that a training plan is developed, implemented and updated at least once every year. The assessor should verify that there is a system in place for monitoring the implementation and effectiveness of the training plan and for documenting the skills acquired in training activities for internal and external experts.
Objective:	The objective of this sub-indicator is to ensure that a training plan for staff exists, and that it is implemented and updated annually. Through the training plan, NRA can be sure that competency of staff in charge of MA or registration activities is maintained and enhanced.
Requirement:	Implementation of training plan

Evidence to review:	The assessor should ask for and review: 1. Guidelines for development, implementation and annual update (i.e., at least once per year) of the training plan. Guidelines should also provide for a mechanism to measure effectiveness of training. 2. Documentation for the system or structures used to approve the training plan and to evaluate the adequacy of the budget allocated to the training activities. 3. The current or existing staff training plan (or matrix) for staff. The assessor should assess this in in relation to the respective individual job descriptions. 4. SOP for developing and maintaining the training plan. 5. Evidence that the NRA has investigated and identified training needs. 6. List of trainings performed. 7. Example records for training activities.
References:	1. Effective drug regulation: A multicounty study. Geneva: World Health Organization; 2002, (7), (http://apps.who.int/medicinedocs/pdf/s2300e/s2300e.pdf) 2. Guidelines for national authorities on quality assurance for biological products. In: WHO Expert Committee on Biological Standardization: forty-second report. Geneva. World Health Organization; 1992: Annex 2 (WHO Technical Report Series, No. 822), (2), (http://www.who.int/biologicals/publications/trs/areas/biological_products/WHO_TRS_822_A2.pdf)
Framework:	Process
Rating Scale:	➜ NOT IMPLEMENTED (NI): There is no systematic training program including training plan (or matrix). ➜ ONGOING IMPLEMENTATION (OI): The NRA has recently drafted or developed the training plan but there is no evidence of implementation. ➜ PARTIALLY IMPLEMENTED (PI): The NRA has developed and initiated the training plan implementation. However, the NRA has not fulfilled all required planned training or has been applying the plan for less than two years. ➜ IMPLEMENTED (I): The NRA has an updated training plan developed that is supported by adequate records to demonstrate effective plan implementation, including induction training for new staff and routine on-the-job training for recruited staff.
Limitations and remarks:	▪ Training plans must be updated regularly; ideally on an annual basis, but not less frequently that once every two years. ▪ Some regulatory functions may include many training activities that are not incorporated in the institutional training programme. Such training normally is offered by invitation. In this case, the assessor should recognize reports from non-routine MA-relevant training not included in the NRA training plan. ▪ Scoring this sub-indicator as "not applicable NA" is excluded (i.e. this sub-indicator will always apply for all benchmarked NRAs).
Sub Indicator:	**MA03.04: The NRA generates and maintains records of staff training activities and training effectiveness verification.**
Maturity Level:	3
Scope:	1. Medicines 2. Vaccines
Description:	The assessor should verify that records of staff training that is performed or organized by the NRA are generated, maintained, regularly updated. This activity should be supported by guidelines that direct the NRA to generate and maintain records of staff training activities. Procedures should be in place to document and propose staff training needs and to allocate a budget for continuous staff capacity building and development. The assessor should check that there is an evaluation or assessment mechanism to verify the quality of learning, and to confirm that learning objectives are achieved. Documentation should include an inventory (i.e., soft and/or hard) system that records all impactful and non-impactful trainings and identifies all staff members who participated. A system to measure or estimate impact of trainings should be established.

Objective:	The objective of this sub-indicator is to ensure that training organized by the NRA or responsible regulatory authority is adequately documented and that the training records are adequately maintained and kept. Staff training records are considered an integral part of staff file and are a tool for measuring and tracking staff competency, development and adequacy.
Requirement:	Training records
Evidence to review:	The assessor should ask for and review: 1. Guidelines or similar documents that guide the NRA to generate and maintain records of staff training activities; 2. Evaluations of training effectiveness; 3. The training inventory, and procedures for completing the inventory; 4. Examples of archived records of staff training, and procedures for the archiving system.
References:	1. Guiding principles for small national drug regulatory authorities. In: WHO Expert Committee on Specifications for Pharmaceutical Preparations: thirty-first report. Geneva: World Health Organization; 1990: Annex 6 (WHO Technical Report Series, No. 790), (5), (http://apps.who.int/medicinedocs/documents/s21964en/s21964en.pdf) 2. 4Effective drug regulation: A multicounty study. Geneva: World Health Organization; 2002, (7), (http://apps.who.int/medicinedocs/pdf/s2300e/s2300e.pdf)
Framework:	Output
Rating Scale:	➜ NOT IMPLEMENTED (NI): There is no evidence that the NRA generates and maintains records of staff training activities. ➜ ONGOING IMPLEMENTATION (OI): The NRA has recently initiated plans to generate, document and keep records of staff training activities, however they are not yet followed. ➜ PARTIALLY IMPLEMENTED (PI): The NRA has recently initiated plans to generate, document and keep records of staff training activities but they are not fully followed for all training activities or they have been established for less than two years. ➜ IMPLEMENTED (I): The NRA generates and maintains records of staff training activities.
Limitations and remarks:	▪ The assessor should note that some NRAs out-source training including staff capacity development activities. In this case the assessor should request the identity of the provider, as well as evaluations of the provider. The assessor may request the professional profiles of tutors or resource persons used to offer training. The assessor may also request records covering the archiving systems in place. ▪ Scoring this sub-indicator as "not applicable NA" is excluded (i.e. this sub-indicator will always apply for all benchmarked NRAs).
Indicator:	**MA04 Procedures established and implemented to perform registration and/or marketing authorization.**
Objective:	The objective of this indicator is to ensure that procedures have been established and implemented to effectively perform registration and MA activities. The NRA should have documented procedures for registration and MA activities and these procedures should be implemented. The documented procedures should be efficiently designed to assist in the preparation of the registration and MA application dossier and in the documentation of the receipt and evaluation of the dossier. The procedures should present an overview of the activities to be carried out, the steps to be followed, the resources required, and the processes to be implemented. These activities include, but are not limited to, receipt of registration applications, acknowledgement of registration applications, assessment of the various components of the applications, generation of recommendations following the assessment process, issuance of a decision (i.e., approval, deferral, or rejection) for registration applications, issuance of registration and MA numbers or certificates, and publication and public sharing of Summary of Product Characteristics-like information

	and technical evaluation summary reports. The established procedures will give guidance on how registration and MA applications should be handled to ensure efficiency and effectiveness of the process.
Category:	Regulatory process
Sub Indicator:	**MA04.01: Documented procedures and tools are implemented for the assessment of the different parts of the application (i.e., quality, and efficacy) and for the assessment of specific requirements applicable to specific classes of medical products.**
Maturity Level:	3
Scope:	1. Medicines 2. Vaccines
Description:	The assessor should verify that documented procedures and tools are developed, made available and implemented for the assessment of the different parts of the registration or MA applications and for assessment of particular requirements applicable to a specific class of medical products. The benefit-risk balance of the medical product under review for registration or MA is the core consideration for regulatory authorities. The assessment procedures should be designed to be adaptable to all applications regardless of the source and product class. The procedures should provide guidance on the different parts of the MA application processing flow, including receipt, screening, review, and decision-making. The procedures for the assessment of registration or MA should be supported by adequate SOPs or similar documents. The scope and extent of the screening and review processes should be clearly documented for routine and non- routine MA applications. The assessor should note that there may be other registration or MA routes in special cases, e.g., for prequalified products or during emergencies when the normal procedures and tools may not apply.
Objective:	The objective of this sub-indicator is to ensure that documented procedures and tools exist for the assessment of the different parts of the registration or MA application and for the assessment of particular requirements applicable to a specific class of medical products. These procedures and tools should be implemented during the assessment process to avoid discrimination or bias.
Requirement:	Documented procedures and tool implemented
Evidence to review:	The assessor should ask for and review: 1. Documented procedures and tools, including SOPs, that are developed and used in the assessment of different parts of registration or MA applications or in the assessment of particular requirements applicable to a specific class of medical products 2. SOPs used for different parts of MA applications, such as receipt, screening, review and decision-making. 3. Evidence of use these SOPs, for example, by checking whether major milestones and decision points are recorded for a selected recent MA. 4. Documents addressing the scope and extent of the assessment process with respect to MA applications received and processed through the routine and non-routine routes. 5. Documents addressing the registration application backlog and that relate the backlog to the timelines for the review process and to the number of competent officers involved in the review process
References:	1. Regulation of vaccines: building on existing drug regulatory authorities. Geneva: World Health Organization; 1999 (WHO/V&B/99.10), (6), (http://apps.who.int/iris/bitstream/handle/10665/65968/WHO_V-B_99.10_eng.pdf?sequence=1) 2. Regulation and licensing of biological products in countries with newly developing regulatory authorities. In: WHO Expert Committee on Biological Standardization: forty-fifth report. Geneva: World Health Organization; 1995: Annex 1 (WHO Technical Report Series, No. 858), (3), (http://www.who.int/bloodproducts/publications/WHO_TRS_858_A1.pdf) 3. Quality assurance of pharmaceuticals WHO guidelines, good practices, related regulatory guidance and GXP training materials, (79), (http://digicollection.org/whoqapharm/)

Framework:	Process
Rating Scale:	➔ NOT IMPLEMENTED (NI): There are no documented procedures or tools for the assessment of the different parts of the application (i.e., quality, safety & efficacy) and for the assessment of particular requirements applicable to specific classes of medical products. ➔ ONGOING IMPLEMENTATION (OI): The NRA has recently drafted or adopted the documented procedures and tools for the assessment of MA but they has not yet been followed. ➔ PARTIALLY IMPLEMENTED (PI): The NRA has developed or adopted documented procedures and tools for the assessment of MA and has been applying it for less than two years, or has not considered them for all marketed products. ➔ IMPLEMENTED (I): The NRA has documented procedures and tools for the assessment of different parts of the application (i.e., quality, safety & efficacy) and for the assessment of particular requirements applicable to specific classes of medical products and has applied them for all reviewed and marketed medical products.
Limitations and remarks:	▪ There may not be adequate time during the on-site assessment to review and compare the scope, extent, and consistency of the assessment processes for two or more MAs. This may be done off site though review of point 4 (scope and extent of the assessment process) and will likely require expert assessors (e.g., dossier reviewers) from stringent regulatory authority or pre-qualification assigned reviewers. ▪ Scoring this sub-indicator as "not applicable NA" is excluded (i.e. this sub-indicator will always apply for all benchmarked NRAs).
Sub Indicator:	**MA04.02: Documented procedures have been implemented to renew and/or to periodically review the MAs granted.**
Maturity Level:	3
Scope:	1. Medicines 2. Vaccines
Description:	The assessor should verify that documented procedures and tools to renew and / or periodic review medical product registrations or MAs have been established and implemented. Similar to the initial registration and MA, the benefit-risk balance of the medical product is the core consideration for marketing re-authorization by regulatory authorities. The procedures should be supported with guidance on the requirements to be reviewed, and on the SOPs to be implemented at the various stages of the renewal or periodic review process. Guidance should be available for each stage of the renewal process, including, for example, receipt of application, screening, reviewing, and decision-making. The process flow should be a documented and implemented.
Objective:	The objective of this sub-indicator is to ensure that documented procedures and tools exist and are implemented for the renewal and /or periodical review of registrations or MAs previously granted. These procedures will ensure consistency and effectiveness of the renewal process.
Requirement:	Registration or MA renewal
Evidence to review:	The assessor should ask for and review: 1. Document listing legally-approved validity periods for authorized products. 2. Documented procedures and tools, including SOPs and other technical documents covering the stages of the renewal process, e.g., receiving, screening, reviewing, decision-making, and issuing of registration numbers or certificates. 3. Procedures describing process flow with responsible divisions and timelines
References:	1. Quality assurance of pharmaceuticals WHO guidelines, good practices, related regulatory guidance and GXP training materials, (79), (http://digicollection.org/whoqapharm/)

Framework:	Process
Rating Scale:	➔ NOT IMPLEMENTED (NI): There is no evidence of documented procedures to renew and/or to periodically review the MAs granted. ➔ ONGOING IMPLEMENTATION (OI): The NRA has recently drafted or adopted documented procedures to renew and/or to periodically review the MAs granted, but they have not yet been applied. ➔ PARTIALLY IMPLEMENTED (PI): The NRA has developed or adopted documented procedures to renew and/or to periodically review the MAs granted and has been applying them for less than five years or has not developed them yet for all marketed medical products. ➔ IMPLEMENTED (I): The NRA has documented procedures to renew and/or periodically review the MAs granted and has applied them for all marketed products.
Limitations and remarks:	The assessor should note that not all NRAs apply the registration and/ or MA renewal or periodic review system. Some NRA's maintain a stringent and functional vigilance and market surveillance system or structure with a demonstrated ability to perform its functions. In this case, the assessor should score this sub indicator as not applicable.
Sub Indicator:	**MA04.03: Documented procedures are implemented for assessing applications for variations of MAs.**
Maturity Level:	3
Scope:	1. Medicines 2. Vaccines
Description:	The assessor should verify that documented procedures and SOPs that will guide the assessment of the various classes and types of variations for the various product classes are established and implemented. These documents should contain procedures for receiving and processing the various classes and types of variation applications.
Objective:	The objective of this sub-indicator is to ensure that documented procedures to assess variations to registrations or MAs exist and are implemented.
Requirement:	Documented and implemented variations assessment procedures
Evidence to review:	The assessor should ask for and review. 1. Procedures and SOPs that guide the assessment of the various classes of variations. The documented procedures should be medical product class specific. 2. Procedures for receiving and processing variation applications, and evidence that the prescribed procedures been implemented. 3. A sample application that was received and reviewed by the NRA. The assessor should review for compliance with documented procedures.
References:	1. Quality assurance of pharmaceuticals WHO guidelines, good practices, related regulatory guidance and GXP training materials, (79), (http://digicollection.org/whoqapharm/)
Framework:	Process
Rating Scale:	➔ NOT IMPLEMENTED (NI): There is no evidence of documented procedures for assessing the applications for variations of MAs. ➔ ONGOING IMPLEMENTATION (OI): The NRA has recently drafted or adopted documented procedures for assessing the applications for variations of Mas, but they have not yet been followed. ➔ PARTIALLY IMPLEMENTED (PI): The NRA has developed or adopted documented procedures for assessing the applications for variations of MAs and has been applying them for less than two years or all submitted variations were not reviewed based on these procedures.

	➔ IMPLEMENTED (I): The NRA has documented procedures for assessing the applications for variations of MAs and has implemented them for all marketed medical products.
Limitations and remarks:	▪ This review may also require an expert dossier reviewer. The assessor should note that NRA may have different requirements and guidelines for different medical product streams. ▪ Scoring this sub-indicator as "not applicable NA" is excluded (i.e. this sub-indicator will always apply for all benchmarked NRAs).
Sub Indicator:	**MA04.04: The same criteria apply for assessing applications regardless of the origin of or destination for the medical products (e.g., domestic, foreign, public sector, or private sector).**
Maturity Level:	3
Scope:	1. Medicines 2. Vaccines
Description:	The assessor should verify that the criteria applied to assess registration or MA applications are the same regardless of the origin or source of the medical product and the product application, and regardless of the location where the product will be used. A set of criteria for assessment should be documented and implemented for the various classes of medical product applications. The criteria should be documented in the form of SOPs. Guidance in the form of SOPs should be documented and implemented.
Objective:	The objective of this sub-indicator is to ensure the criteria used for assessing registration or MA applications for medical products is the same, regardless of the source or origin of the product or the destination for use of the product.
Requirement:	Same criteria for assessing registration or MA applications regardless of applicant
Evidence to review:	The assessor should ask for and review: 1. Evidence that SOPs or similar documents are in place to ensure that the same set of criteria is used to assess registration or MA applications regardless of source, origin or destination of the medical product. 2. Evidence that the staff members are aware of the single set of criteria and know how to apply the criteria in their assessment activities. 3. Evidence that the criteria are documented, published and implemented. 4. Sample registration or MA applications from different sources. The assessor should review these for the purpose of verifying consistent compliance with specified procedures. The assessor also should compare the procedures and determine whether there are any discrepancies in terms of scientific review and assessment. Sample MA applications of medical products coming from different sources (e.g. domestic, imported, public, or private,) along with their assessment reports, should be checked by the assessor.
References:	1. Multisource (generic) pharmaceutical products: guidelines on registration requirements to establish interchangeability, (12), (http://digicollection.org/whoqapharm/p/about and http://apps.who.int/medicinedocs/en) 2. WHO good manufacturing practices for pharmaceutical products: main principles, (51), (http://digicollection.org/whoqapharm/p/about and http://apps.who.int/medicinedocs/en) 3. Effective drug regulation: A multicounty study. Geneva: World Health Organization; 2002, (7), (http://apps.who.int/medicinedocs/pdf/s2300e/s2300e.pdf)
Framework:	Process
Rating Scale:	➔ NOT IMPLEMENTED (NI): The NRA does not apply the same criteria for assessing all applications (e.g., domestic, foreign, public sector, or private sector)

	➔ ONGOING IMPLEMENTATION (OI): The NRA has recently defined or drafted the same criteria or policy for assessing all applications but they have not yet been applied. ➔ PARTIALLY IMPLEMENTED (PI): The NRA has defined the same criteria or policy for assessing all applications and has been applying them for assessing applications for less than two years or has not applied them for all currently market medical products. ➔ IMPLEMENTED (I): The NRA has the same criteria or policy for assessing applications regardless of the origin or destination of the medical products (e.g. domestic, foreign, public sector, or private sector) and has applied them for all marketed medical products.
Limitations and remarks:	There may not be adequate time during the on-site assessment to review and compare the scope, extent, and consistency of the assessment processes for two or more MAs. This may be done off site though review of the evidence gathered for this sub-indicator. The assessor should consider that in non-producing countries, there would be no records for a domestic product that could be used when evaluating the implementation of this requirement. Scoring this sub-indicator as "not applicable NA" is excluded (i.e. this sub-indicator will always apply for all benchmarked NRAs).
Sub Indicator:	**MA04.05: An advisory or scientific committee, including external experts is involved in the review of MA applications (as needed).**
Maturity Level:	4
Scope:	1. Medicines 2. Vaccines
Description:	The assessor should verify that the use of advisory or scientific committees, including external experts, in the review of registration or MA applications is documented and supported by adequate regulations. The objectives and functions of the committee, as well as the professional profile of the committee members, should be available. The composition of the committee should be guided by appropriate regulations. For each member of the committee, there should be clearly defined roles and responsibilities in the review of registrations or MAs. Terms of reference for each member of the committee and each external expert should be prepared and documented.
Objective:	The objective of this sub-indicator is to ensure that an advisory or scientific committee, including external experts, is involved in the review of the registration or MA applications.
Requirement:	Advisory or scientific committee, including external experts
Evidence to review:	The assessor should ask for and review: 1. Documents defining the composition of the advisory or scientific committee, and evidence that the composition is in line with the directives prescribed in the regulations. 2. Documents defining the objectives and functions of the committee and its individual members, as well as that of the external experts. 3. The terms of reference for committee and its members as well as that of the external experts. 4. Documents defining the scope and extent of the advisory or scientific contributions to the registration or MA activities of the NRA 5. SOPs defining the review activities of the advisory or scientific committee and its programme of work. 6. Meeting minutes and related documents that provide evidence for the activities that result in registration or granting MA.
References:	
Framework:	Process

Rating Scale:	➔ NOT IMPLEMENTED (NI): The NRA does not have access to an advisory or scientific committee, including external experts, for assisting in review of MA applications or providing scientific advice as necessary.. ➔ ONGOING IMPLEMENTATION (OI): The NRA has recently defined the criteria and composition of the advisory or scientific committee, but the advisory or scientific committee has not yet been established. ➔ PARTIALLY IMPLEMENTED (PI): The NRA has established the advisory or scientific committee, but less than two years ago. ➔ IMPLEMENTED (I): The NRA has access to an advisory or scientific committee, including external experts, in the review of MA applications; this is supported by adequate documentation and records
Limitations and remarks:	The assessor should note that some NRAs may not involve an advisory or scientific committee, including external experts, in the review of the submitted registration or MA applications, due to the availability of internal experts with the requisite competencies. Some NRAs may refer to the committee or external experts only certain applications that require their specialist attention and expert advice. In this case the scoring is not applicable.
Sub Indicator:	**MA04.06: Timelines for the assessment of the applications are defined and an internal tracking system has been established to monitor adherence to the targeted time frames.**
Maturity Level:	3
Scope:	1. Medicines 2. Vaccines
Description:	The assessor should verify that documented timelines and internal timeline tracking systems that guide the registration or MA application process exist and are implemented. These should be supported by guidelines that stipulate that MA applications should be processed and assessed per a published timeline and that the published timeline should be monitored internally for compliance. The guidelines should be supported with SOPs that provide guidance on how to establish the timelines and how to monitor the established timelines. The guidelines should be designed to adapt to the various classes of medical products registration or MA applications (e.g., innovative medicines, generic medicines, new molecular entities, in vitro devices, and vaccines). Timelines should be designed to address each stage of the registration or MA application process flow. The system should be developed to monitor the various timelines for the various registration or MA application assessment procedures (i.e., the routine and non-routine procedures). The assessor should note that some NRAs will have varied timelines for the different registration or MA assessment routes, as well as varied internal tracking systems to ensure adherence to the timelines. In this case, the assessor should review the timelines for each route and their corresponding tracking systems.
Objective:	The objective of this sub-indicator is to ensure that timelines for the assessment of registration or MA applications exist, and that the timelines are monitored by internal tracking systems to ensure compliance.
Requirement:	Timelines and internal control mechanisms
Evidence to review:	The assessor to ask for and review: 1. The documented registration application process flow and corresponding timelines for the various registration or MA application routes and product classes. 2. Documentation for the internal tracking systems used for monitoring adherence to the assessment timelines. 3. Evidence that the timelines are published, easily accessible and known to all stakeholders, including the applicants and reviewers. 4. Evidence that these timelines have been implemented and are being adhered to during the assessment process.

	5. Evidence that a dedicated unit or office is responsible for instituting, implementing and monitoring the assessment timelines tracking system for the purposes for compliance. 6. Evidence that corrective measures are available in the event of non-compliance.
References:	1. National drug regulatory legislation: guiding principles for small drug regulatory authorities. In: WHO Expert Committee on Specifications for Pharmaceutical Preparations: thirty-fifth report. Geneva: World Health Organization; 1999: Annex 8 (WHO Technical Report Series, No. 885), (1), (http://apps.who.int/medicinedocs/documents/s21964en/s21964en.pdf)
Framework:	Structure/Foundation/Input & Process
Rating Scale:	➜ NOT IMPLEMENTED (NI): There are no timelines for the assessment of the applications and no internal tracking system to monitor the targeted time frames ➜ ONGOING IMPLEMENTATION (OI): The NRA has recently defined timelines for the assessment of the applications but an internal tracking system to monitor the targeted time frames has not been implemented. ➜ PARTIALLY IMPLEMENTED (PI): The NRA has defined the timelines for the assessment of the applications and it has been applying an internal tracking system to monitor the targeted time frames for less than two years. ➜ IMPLEMENTED (I): The NRA has timelines for the assessment of the applications and an internal tracking system to monitor the targeted time frames has been implemented
Limitations and remarks:	Scoring this sub-indicator as "not applicable NA" is excluded (i.e. this sub-indicator will always apply for all benchmarked NRAs).
Sub Indicator:	**MA04.07: There are documented mechanisms to handle non-routine registration or MA requirements in special situations (e.g., public-health interest).**
Maturity Level:	3
Scope:	1. Medicines 2. Vaccines
Description:	The assessor should verify the existence and implementation of regulations and guidelines allowing the use of a non-routine mechanism that is supported with specific registration requirements. The regulation also should be supported with guidelines and SOPs that clearly specify the registration requirements and the instances (e.g., products for use in public health emergencies, or orphan medicinal products) in which an application would be considered for a specific pathway in the interest of public health. In addition, the registration or MA application process flow and their corresponding specific timelines should be provided, published and implemented. SOPs for the assessment process should be developed to reflect the process flow and the specific requirements.
Objective:	The objective of this sub-indicator is to ensure that documented mechanisms for specific registration requirements exist and are implemented when necessary in special situations (e.g., public-health interest).
Requirement:	Non-routine registration or MA applications
Evidence to review:	The assessor should ask for and review: 1. Regulations related to the establishment and implementation of a mechanism, with specific registration requirements, that can be used, in special situations, for assessing MA applications and for granting MA. 2. Guidelines on the instances and special situations in which this system applies, and guidelines on the specific registration requirements that should be applied. These requirements should be based on the nature of the products (e.g., new, biological, or generic products).

	3. An example of an application that was processed through this route. The documents should be reviewed to determine if content and format is consistent with the prescribed requirements and if the process adhered to published timelines. 4. Documents describing the registration or MA application process flow and the corresponding timelines. The timelines should demonstrate timely review relative to the normal route or process. 5. SOPs that provide guidance for the assessment process.
References:	1. Regulation of vaccines: building on existing drug regulatory authorities. Geneva: World Health Organization; 1999 (WHO/V&B/99.10), (6), (http://apps.who.int/iris/bitstream/handle/10665/65968/WHO_V-B_99.10_eng.pdf?sequence=1). 2. Regulation and licensing of biological products in countries with newly developing regulatory authorities. In: WHO Expert Committee on Biological Standardization: forty-fifth report. Geneva: World Health Organization; 1995: Annex 1 (WHO Technical Report Series, No. 858), (3), (http://www.who.int/bloodproducts/publications/WHO_TRS_858_A1.pdf) 3. Guidelines on evaluation of similar biotherapeutic products (SBPs), (70), (http://apps.who.int/medicinedocs/en/q/)
Framework:	Process
Rating Scale:	➜ NOT IMPLEMENTED (NI): There is no documented mechanism, with specific registration requirements, for special situations (e.g., public-health interest) ➜ ONGOING IMPLEMENTATION (OI): The NRA has recently drafted or adopted a documented mechanism, with specific registration requirements, for special situations (e.g. public-health interest) but it has not yet been applied. ➜ PARTIALLY IMPLEMENTED (PI): The NRA has developed or adopted a documented mechanism, with specific registration requirements, for special situations (e.g. public-health interest), and has been applying this for less than two years or in fewer than three cases. ➜ IMPLEMENTED (I): The NRA has a documented and implemented non-routine mechanism, with specific registration requirements, for special situations (e.g. public-health interest)
Limitations and remarks:	In case that there has been no emergency that required the application of this mechanism, the assessor should verify the implementation of this sub-indicator by considering the availability of adequate resources and procedures for implementation of the non-routine mechanism.
Sub Indicator:	**MA04.08: SPC-like, labelling and packaging information are approved by the NRA as part of the MA procedure.**
Maturity Level:	3
Scope:	1. Medicines 2. Vaccines
Description:	The assessor should verify the existence of regulations or guidelines that state that product information (i.e., SPC-like, packaging and labelling information) should comply with the regulations that cover product information for medical products. The information should be assessed as part of the registration or MA application package assessment process. During this review process, the product information must be found to be appropriate and satisfactory. The regulation should be supported by specific guidelines or SOPs that guide the assessment of product information (i.e., SPC-like information, packaging information, and product labels). The product information should be updated periodically.
Objective:	The objective of this sub-indicator is to ensure that product information, including SPC-like, packing and labelling information, are approved by the NRA as part of the registration or MA application process. The NRA should have clear requirements regarding medical products information that should be provided in the SPC-like, packaging and labelling information.

Requirement:	SPC-like, packaging, and labelling information
Evidence to review:	The assessor should ask for and review: 1. Regulations or guidelines stating that product information (i.e., SPC-like, packaging, and labelling information) should comply with the regulations provided to cover product information on medical products. 2. Guidelines or SOPs for assessing product information on SPC-like information, packaging, and product labels. 3. Medical products registration or MA application assessment reports. 4. Documents describing the registration or MA application processing flow for the stage or phase of the process in which review of the product information (i.e., SPC-like, packaging and labelling information) is conducted. .
References:	1. Guidelines on packaging for pharmaceutical products, World Health Organization (WHO), (80), (http://apps.who.int/medicinedocs/en/q/ and http://digicollection.org/whoqapharm/) 2. 13-Ethical criteria for medicinal drug promotion. WHO, 1998, (13), (http://apps.who.int/medicinedocs/documents/whozip08e/whozip08e.pdf)
Framework:	Process
Rating Scale:	➔ NOT IMPLEMENTED (NI): There are no requirements for approving SPC-like, labelling and packaging information by the NRA as part of the MA procedure. ➔ ONGOING IMPLEMENTATION (OI): The NRA has recently drafted or adopted the requirements to comply with the regulations provided to cover product information on medical products, such as SPC-like, labelling and packaging information, but they have not yet been followed. ➔ PARTIALLY IMPLEMENTED (PI): The NRA has defined the requirements to comply with the regulations provided to cover product information on medical products, such as SPC-like, labelling and packaging information, and has been applying them for less than two year or they have not been considered for all marketed medical products. ➔ IMPLEMENTED (I): The NRA is approving SPC-like, labelling and packaging information as part of the MA procedure for all reviewed medical products.
Limitations and remarks:	Scoring this sub-indicator as "not applicable NA" is excluded (i.e. this sub-indicator will always apply for all benchmarked NRAs).
Sub Indicator:	**MA04.09: GMP inspection report and/or certification is considered as part of the MA process.**
Maturity Level:	3
Scope:	1. Medicines 2. Vaccines
Description:	The assessor should verify that regulations or guidelines are established and implemented that specify the type, content and format of GMP documentation that should be submitted to the NRA by another NRA (i.e., in case of imported medical products), or that describes the processes and procedures through which an on-site inspection or verification will be conducted by the NRA. The guidelines should be supported by supplementary guidelines or SOPs that provide guidance for use during the on-site inspection or verification visits or during assessment of the submitted GMP documentation. The assessor should verify the existence and implementation of procedures and SOPs that ensure that the GMP inspections or GMP documentation verifications are part of the medical products registration or MA process and that ensure that GMP requirements are established, implemented, published, and easily accessible as part of the registration or MA application process. The assessor should note that, in some NRAs, the GMP on-site visits and inspections may be carried out by consultants hired by the NRA to perform the task rather that by NRA staff. In such instances, if the competencies of the hired consultants are appropriate, the scoring will apply.

Objective:	The objective of this sub-indicator is to ensure that GMP inspections or certifications are part of the registration or MA requirements, and that the NRA has a legal provision to request the manufacturer to demonstrate adherence to GMP in the manufacture of the medical products. This can be done either through on-site verification or inspection by the NRA or through a satisfactory assessment of GMP documentation issued by other NRAs.
Requirement:	GMP inspection report or certificate as part of MA process
Evidence to review:	The assessor should ask for and review: 1. Legal provisions that clearly state that compliance with the principles of GMP is part of the medical products registration or MA application requirements. 2. Legal provisions that clearly describe the format and content of the GMP requirements, i.e., either through a satisfactory on-site verification or inspection by the NRA or through a satisfactory assessment of GMP documentation issued by another NRA. 3. Guidelines and SOPs that provide guidance to be used during the on-site inspection or verification visits or during assessment of the submitted GMP documentation. These should be reviewed for completeness. 4. Guidelines or regulations that specify the type, content and format of GMP documentation that should be submitted to the NRA by another NRA (i.e., for the purpose of GMP verification), or that describes the processes and procedure through which an on-site inspection or verification will be conducted by the NRA. 5. Procedures that ensure that the GMP inspections or the verifications of submitted GMP documentation are part of the authorization process, as well as procedures that ensure that GMP requirements are implemented as part of the MA application process. 6. Evidence that a GMP report or certification is a requirement for all registration or MA applications and that a risk-based routine inspection is required periodically. 7. A record of registration and MA application submissions. The should be evaluated for the purposes of verification and compliance with the guidelines.
References:	1. Guidance on Good Manufacturing Practices (GMP): inspection report, (32), (http://digicollection.org/whoqapharm/p/about and http://apps.who.int/medicinedocs/en) 2. WHO good manufacturing practices for pharmaceutical products: main principles, (51), (http://digicollection.org/whoqapharm/p/about and http://apps.who.int/medicinedocs/en)
Framework:	Structure/Foundation/Input & Process
Rating Scale:	➜ NOT IMPLEMENTED (NI): A GMP inspection report or certification is not required as part of the MA process ➜ ONGOING IMPLEMENTATION (OI): The NRA has recently defined GMP inspection report or certification as a requirement for MA authorization, but it has not yet been followed. ➜ PARTIALLY IMPLEMENTED (PI): The NRA has required a GMP inspection report or certification as a requirement for MA authorization and has been applying this for less than two years. ➜ IMPLEMENTED (I): GMP inspection report or certification is required by the NRA as part of the MA process, and has been considered in all received MA applications.
Limitations and remarks:	▪ The assessor should verify that all requirements are same regardless of the source of products. ▪ Scoring this sub-indicator as "not applicable NA" is excluded (i.e. this sub-indicator will always apply for all benchmarked NRAs).
Sub Indicator:	**MA04.10: The regulations and guidelines for good review practices (GRevPs) are developed or recognized and implemented.**
Maturity Level:	3
Scope:	1. Medicines 2. Vaccines

Description:	The assessor should verify that procedures and documentation on GRevPs are established and implemented. The procedures should be supported by an operation manual (i.e., with documented and approved SOPs for the screening and review of the various classes of medical products and their corresponding routine or non-routine application routes) that guides the screening and review of registration or MA applications. The procedures should include quality control and quality assurance systems or structures that ensure that actual application assessment and review is conducted in accordance with approved SOPs. The procedures should provide guidance on how to handle medical product application non-conformities.
Objective:	The objective of this indicator is to ensure that regulations and guidelines exist for the NRA to review and evaluate the different components of registration or MA applications; to review and evaluate the specific requirements of each product class; and to register or grant MAs or to reject registrations following documented procedures for the different parts of the application. These procedures will provide consistency in the approval or rejection of applications through the application of defined requirements and criteria such that the resultant decision would be seen to be based on submitted documentation irrespective of the reviewer.
Requirement:	Guidelines and SOP for GRevPs
Evidence to review:	The assessor should ask for and review: 1. Regulations and guidelines that provide guidance on principles of GRevP. 2. SOPs for assessment of registration or MA applications that guide the reviewer during the screening and review of the different components of the various classes of medical products. 3. Evidence that the same set of principles is applied during the screening and review of MA applications submitted through the non-routine procedure. The assessor should request SOPs that provide guidance on how to handle actual review of applications through the non-routine procedure. 4. Evidence that procedures are in place to ensure that actual application assessments and reviews are conducted in accordance with the principles of GRevP and that the assessment reports are peer-reviewed. 5. An example of an assessment report for a particular product class. The assessor should evaluate this for compliance to the corresponding GRevP SOPs and related documents.
References:	1. Good review practices: guidelines for national and regional regulatory authorities, (49), (http://digicollection.org/whoqapharm/p/about and http://apps.who.int/medicinedocs/en)
Framework:	Process
Rating Scale:	➜ NOT IMPLEMENTED (NI): There are no regulations or guidelines for GRevPs ➜ ONGOING IMPLEMENTATION (OI): The NRA has recently drafted or adopted GRevPs but they have not yet been followed. ➜ PARTIALLY IMPLEMENTED (PI): The NRA has developed or adopted GRevPs and has been applying them for less than two years or the principles are not yet reflected in other relevant SOPs and guideline for MA activities. ➜ IMPLEMENTED (I): The NRA has regulations or guidelines for GRevPs and is following them in all relevant activities.
Limitations and remarks:	Scoring this sub-indicator as "not applicable NA" is excluded (i.e. this sub-indicator will always apply for all benchmarked NRAs).
Indicator:	**MA05 Mechanism exists to promote transparency, accountability and communication.**
Objective:	The objective of this indicator is to ensure that mechanisms are in place to ensure that information on registration and MA applications, including authorized, suspended, rejected and completed applications, are published to promote transparency and information

	sharing among stakeholders and potential stakeholder (e.g., retailers and patients). This approach will build trust among stakeholders. A mechanism for appeal of MA should be described.
Category:	Transparency, accountability and communication
Sub Indicator:	**MA05.01: Web site or other official publication with SPC-like information is available and regularly updated.**
Maturity Level:	3
Scope:	1. Medicines 2. Vaccines
Description:	The assessor should verify that a website or other official publication where SPC-like information is published is in existence and regularly updated. Guidelines and SOPs should be documented and implemented to provide guidance on preparation, content and format of the SPC-like information that is to be published, as well as guidance on the procedures and processes to be used for the regular updates (i.e., frequency and processes). The website to host the information should be clearly documented.
Objective:	The objective of this sub-indicator is to ensure the NRA has the legal provisions or regulations to generate and publish SPC-like information, and to ensure that the practice is implemented.
Requirement:	SPC-like information available
Evidence to review:	The assessor should ask for and review: 1. Evidence that the SPC-like information document is published, and if published, that the publication is in the appropriate format per the published guidelines. 2. Evidence that the website is regularly updated to reflect the current situation. The assessor should review the SOP for updating the website. 3. Evidence that the publications are easily accessible, regardless of where the information is hosted (i.e., NRA website, Ministry of Health (MoH) website, or another website). If on another website, the assessor should request SOPs that provide guidance on how to remotely upload new information onto the website and to update existing information.
References:	1. National drug regulatory legislation: guiding principles for small drug regulatory authorities. In: WHO Expert Committee on Specifications for Pharmaceutical Preparations: thirty-fifth report. Geneva: World Health Organization; 1999: Annex 8 (WHO Technical Report Series, No. 885), (1), (http://apps.who.int/medicinedocs/documents/s21964en/s21964en.pdf)
Framework:	Output
Rating Scale:	➜ NOT IMPLEMENTED (NI): There is no evidence of official SPC-like information publication on website or in another place. ➜ ONGOING IMPLEMENTATION (OI): The NRA has recently defined official SPC-like information publication, but it has not yet been published. ➜ PARTIALLY IMPLEMENTED (PI): The NRA has developed and initiated official SPC-like information publication but the information is not updated regularly or all information is not yet reflected. ➜ IMPLEMENTED (I): The NRA has official SPC-like information publication on website or in another place for all marketed medical products.
Limitations and remarks:	▪ The assessor should note that in some instances, the NRA may not physically host the website. The website may be hosted by the MoH, a professional body, a standards authority, or another entity. In all instances the NRA has the responsibility to ensure that SPC-like information is published, and that the website is regularly updated. The scoring is applicable.

- Scoring this sub-indicator as "not applicable NA" is excluded (i.e. this sub-indicator will always apply for all benchmarked NRAs).

Sub Indicator:	**MA05.02: Updated list of all medical products granted MA is regularly published and publicly available.**
Maturity Level:	3
Scope:	1. Medicines 2. Vaccines
Description:	The assessor should verify that a list of medical products registered or granted MA is in existence. This list should be regularly updated and published. The published information should be supported by SOPs that provide guidance on the procedure to enter information, the procedure to translate the information into the appropriate format, and the type of information to enter (e.g., may include, but is not limited to, the product brand name, International Nonproprietary Name, the registration or MA number, the registration or MA certificate number, the validity period of the registration or MA, the active ingredients, manufacturer, and potency or concentration). The host or website where the list is published should be documented and should be easily accessible to the general public.
Objective:	The objective of this sub-indicator is to ensure that guidelines and regulations exist to guide and advise the NRA to regularly update and publish the list of medical products that are registered or granted MA
Requirement:	List of all medical products registered or granted MA
Evidence to review:	The assessor should ask for and review: 1. The published list of medical products registered or granted MA. 2. Evidence that the information published for the registered medical products is in compliance with guidelines and SOPs. 3. Evidence that the list is regularly updated. The assessor should verify that the list is current. 4. SOPs or similar documents for updating the list. 5. Evidence that an internal register (i.e., paper or electronic version) for entering registered medical products exists. If the internal register exists, the assessor should review the guidelines and SOPs for completing and regularly updating the register. 6. Evidence that the published list is accessible. The assessor should also identify the host organization, e.g., NRA, MoH, or other organization.
References:	1. National drug regulatory legislation: guiding principles for small drug regulatory authorities. In: WHO Expert Committee on Specifications for Pharmaceutical Preparations: thirty-fifth report. Geneva: World Health Organization; 1999: Annex 8 (WHO Technical Report Series, No. 885), (1), (http://apps.who.int/medicinedocs/documents/s21964en/s21964en.pdf)
Framework:	Output
Rating Scale:	➜ NOT IMPLEMENTED (NI): The updated list of all medical products granted MA is not regularly published or publicly available. ➜ ONGOING IMPLEMENTATION (OI): The NRA has recently committed to publish the list of all medical products granted MA, but it has not yet been followed. ➜ PARTIALLY IMPLEMENTED (PI): The NRA has initiated publication of the list of all medical products granted MA; however it is not updated regularly, or the list does not reflect of all medical products granted MA. ➜ IMPLEMENTED (I): The NRA has publicly published the list of all medical products granted MA and it is regularly updated.
Limitations and remarks:	▪ For different products medical streams, some NRAs publish different lists. If so, each list should be easy to access.

	The assessor should consider that existence of the database of all granted MA medical products is not adequate to fulfill this requirement (unless the database is publicly available), since the purpose is transparency. ▪ Scoring this sub-indicator as "not applicable NA" is excluded (i.e. this sub-indicator will always apply for all benchmarked NRAs).
Sub Indicator:	**MA05.03: A summary technical evaluation report for approved registration MA applications is published and available to the public.**
Maturity Level:	4
Scope:	1. Medicines 2. Vaccines
Description:	The assessor should verify that the summary technical evaluation reports of those medical products registration applications that have been approved, are published and made available to the public, and these actions are supported by a regulation or a guideline. The content and format of the report should be guided by an SOP to ensure uniformity. Procedures should be in place to monitor the generation of the reports to ensure that the content and format conforms to the approved standards, and that the reports are regularly published and made available to the public.
Objective:	The objective of this sub-indicator is to ensure that guidelines or regulations exist to allow the NRA to publish and make available to the public the summary technical evaluation reports of approved MA applications. The NRA should actually publish and make available to the public the summary technical evaluation reports.
Requirement:	Summary technical evaluation report (Public assessment report) available to stakeholders
Evidence to review:	The assessor should ask for and review: 1. Procedures in place to support and monitor the generation of the reports, to ensure that the content and format conforms to the approved standards, and to ensure that the reports are regularly published and made available to the public. 2. A sample of the report for the purpose of evaluating conformance to the published guidelines and or SOPs. The assessor should verify that the report is generated, published and made available to the public. 3. The website for hosting the reports, and the SOPs that provide guidance to staff on procedures for uploading new reports and updating existing reports.
References:	1. Regulation of vaccines: building on existing drug regulatory authorities. Geneva: World Health Organization; 1999 (WHO/V&B/99.10), (6), (http://apps.who.int/iris/bitstream/handle/10665/65968/WHO_V-B_99.10_eng.pdf?sequence=1). 2. Regulation and licensing of biological products in countries with newly developing regulatory authorities. In: WHO Expert Committee on Biological Standardization: forty-fifth report. Geneva: World Health Organization; 1995: Annex 1 (WHO Technical Report Series, No. 858), (3), (http://www.who.int/bloodproducts/publications/WHO_TRS_858_A1.pdf)
Framework:	Output
Rating Scale:	➜ NOT IMPLEMENTED (NI): There is no evidence for publication and public availability of a summary technical evaluation report for approved registration or MA applications. ➜ ONGOING IMPLEMENTATION (OI): The NRA has recently defined this requirement, but it has not yet been implemented. ➜ PARTIALLY IMPLEMENTED (PI): The NRA has initiated publication of summary technical evaluation reports for approved registration or MA applications, but this has not been applied for all evaluated medical product applications. ➜ IMPLEMENTED (I): The NRA has published and made available to the public summary technical evaluation reports for approved registration or MA applications.

Limitations and remarks:	The assessor should note that some NRAs will not publish the summary of the technical evaluation report for medical product applications processed under special circumstances, for example, emergencies, WHO collaborative registration procedures, WHO prequalified products, Article 58 reviews, or reviews by orphan drug route (i.e., abridged registration application processing route or pathway).
Sub Indicator:	**MA05.04: A summary technical evaluation report for deferred or rejected registration or MA applications is published and available to the public.**
Maturity Level:	4
Scope:	1. Medicines 2. Vaccines
Description:	The assessor should verify that the summary technical evaluation reports of those medical products registration applications that have been deferred or rejected is published and made available to the public, and these actions are supported by a regulation or guideline. The content and format of the report should be guided by an SOP to ensure uniformity. Procedures should be in place to monitor the generation of the reports to ensure that the content and format conforms to the approved standards, and that the reports are regularly published and made available to the public.
Objective:	The objective of this sub-indicator is to ensure that guidelines or regulations exist to allow the NRA to publish and make available to the public the summary technical evaluation reports of deferred or rejected MA applications. The NRA should actually publish and make the summary technical evaluation reports available to the public.
Requirement:	Summary technical evaluation report (Public assessment report) available to stakeholders
Evidence to review:	The assessor should ask for and review: 1. Procedures in place to support and monitor the generation of the reports, to ensure that the content and format conforms to the approved standards, and to ensure that the reports are regularly published and made available to the public. 2. A sample of the report for the purposes of evaluating conformance to the published guidelines and or SOPs. The assessor should verify that the report is generated, published and made available to the public. 3. The website for hosting the reports, and the SOPs that provide guidance to staff on procedures for uploading new reports and updating existing reports.
References:	1. Regulation of vaccines: building on existing drug regulatory authorities. Geneva: World Health Organization; 1999 (WHO/V&B/99.10), (6), (http://apps.who.int/iris/bitstream/handle/10665/65968/WHO_V-B_99.10_eng.pdf?sequence=1). 2. Regulation and licensing of biological products in countries with newly developing regulatory authorities. In: WHO Expert Committee on Biological Standardization: forty-fifth report. Geneva: World Health Organization; 1995: Annex 1 (WHO Technical Report Series, No. 858), (3), (http://www.who.int/bloodproducts/publications/WHO_TRS_858_A1.pdf)
Framework:	Output
Rating Scale:	➜ NOT IMPLEMENTED (NI): There is no evidence for publication and public availability of a summary technical evaluation report for deferred or rejected registration or MA applications. ➜ ONGOING IMPLEMENTATION (OI): The NRA has recently defined this requirement, but it has not yet been implemented. ➜ PARTIALLY IMPLEMENTED (PI): The NRA has initiated publication of summary technical evaluation reports for deferred or rejected registration or MA applications, but this has not been applied for all evaluated medical products applications. ➜ IMPLEMENTED (I): The NRA has published and made available to the public summary technical evaluation reports for deferred or rejected registration or MA applications.

Limitations and remarks:	Some NRAs may not publish the report of registrations applications that were rejected or deferred based on the NRA's legal provisions. In either case, the scoring will not apply. However, it is recommended that summary technical evaluation reports for all medical product applications regardless of the evaluation outcome should be published and made available to the public. In this case, the scoring should be yes.
Indicator:	**MA06 Mechanism in place to monitor regulatory performance and output.**
Objective:	The objective of this indicator is to ensure that mechanisms and procedures are in place to monitor and ensure that all activities within the MA functionality are subjected to quality control and other checks to reduce errors and to ensure that the processes and results of the registration application assessment are consistent and able to generate a reliable output. These monitoring mechanisms lead to consistency in the regulatory performance of the registration and MA function and to reliability of outputs.
Category:	Monitoring progress and assessing outcomes & impact
Sub Indicator:	**MA06.01: There is a database of all product applications received, approved, rejected, suspended or withdrawn along with their supporting documentation.**
Maturity Level:	3
Scope:	1. Medicines 2. Vaccines
Description:	The assessor should verify that a database to keep all medical product registration applications received, approved, rejected, suspended or withdrawn, as well as their supporting documentation exists, and that the database is continually updated to reflect the current situation. The operation and management of the database should be supported by guidelines and SOPs that specify the types of information and documentation to keep and the format and duration of storage. Personnel with authorization to access information should be documented and the procedure to access the information should be defined. The location of the actual database should be documented. Information on the back-up database should be provided. Plans or efforts to secure a back-up system should be reviewed if a back-up system is not currently available.
Objective:	The objective of this sub-indicator is to ensure that regulations or guidelines exist to require the NRA to keep and manage a database of the supporting documentation for all medical products registration or MA applications received, approved, rejected, suspended or withdrawn. This database should continually be kept up to date. This database would significantly contribute to consistency in regulatory approach and to expansion of institutional memory.
Requirement:	Database of all medical products application
Evidence to review:	The assessor should ask for and review: 1. Evidence that a database exists for keeping an up to date list of supporting documentation and information (e.g., legal information and requirements, communications, application files, and bases of decision) for all medical products registration or MA applications received, approved, rejected, suspended or withdrawn. 2. Guidelines and SOPs that define the essential information to keep in the database and the timelines for retaining this information. 3. Evidence that the database is up to date and current and that it is supported by a back-up data base. 4. Documents defining the authorization needed to access or to update the information in the database. Procedures for monitoring, maintaining, and updating the database should also be reviewed.
References:	

Framework:	Output
Rating Scale:	➔ NOT IMPLEMENTED (NI): There is no database of all product applications received, approved, rejected, suspended or withdrawn, along with their supporting documentation. ➔ ONGOING IMPLEMENTATION (OI): The NRA has recently initiated and drafted the requirement to create the database but it has not yet been established. ➔ PARTIALLY IMPLEMENTED (PI): The NRA has established a database of all product applications received, approved, rejected, suspended or withdrawn along with their supporting documentation but not all applications have been included in the database or the database is not regularly updated or fully integrated. ➔ IMPLEMENTED (I): The NRA has a database of all product applications received, approved, rejected, suspended or withdrawn along with their supporting documentation, and the database is kept up-to-date.
Limitations and remarks:	Scoring this sub-indicator as "not applicable NA" is excluded (i.e. this sub-indicator will always apply for all benchmarked NRAs).
Sub Indicator:	**MA06.02: Performance indicators for registration and MA activities are established and implemented.**
Maturity Level:	4
Scope:	1. Medicines 2. Vaccines
Description:	The assessor should verify the existence and implementation of performance indicators for different activities included under the registration and MA functions. Specifically, the system should define key performance indicators (KPIs) along the entire registration and MA activity chain and all indicators should be adequately justified. For the purpose of clarity and consistency, established KPIs should be supported with guidelines for monitoring and maintenance of the KPIs. The guidelines in turn should be supported by SOPs and tools that define the procedures to be used for monitoring and evaluating theperformance indicators and that define procedures and timelines for reviewing and revising the indicators. Established KPIs might be qualitative, quantitative or combination of both. In general, quantitative indicators are preferred to avoid bias or misinterpretation. However, qualitative indicators are also accepted. Qualitative indicators may or may not include scoring or scaling to render them semi-quantitative and thus more informative. The assessor should ensure that indicators are measured on a regular basis to monitor progress and advancement. In addition, the assessor should verify measured indicators are analyzed to identify trends or abnormalities. Justifications for any identified abnormalities should be provided; when necessary, process optimizations should be introduced to avoid recurrence.
Objective:	The objective of this sub-indicator is to ensure that a system, mechanism, or procedure exists to require the NRA to establish performance indicators along the entire registration and MA chain. Additionally, the objective is to ensure that KPIs are actually contributing to monitoring of regulatory performance, to measuring effectiveness of registration and MA regulatory activities, and to making any necessary adjustments or optimizations.
Requirement:	KPIs for registration and MA activities
Evidence to review:	The assessor should ask for and review: 1. Documents supporting the system, mechanism, or procedure compelling the NRA to establish and implement performance indicators along the entire registration and MA activity chain. 2. Evidence that the performance indicators have been established and implemented, and that the members of staff involved in the registration and MA function are aware of the indicators and the guidelines and SOPs used for monitoring and evaluating their performance.

	3. The current performance indicators for registration and MA activities 4. Analyses of the measured indicators along with the investigations done to identify trends or abnormalities. 5. Documentation for follow-up of any observed abnormalities, including justifications for any identified abnormalities as well as any process optimizations introduced to avoid recurrence.
References:	1. Quality management -- Quality of an organization -- Guidance to achieve sustained success, ISO 9004:2018, International Organization for Standardization (ISO), (115), (https://www.iso.org/standard/70397.html)
Framework:	Structure/Foundation/Input
Rating Scale:	➔ NOT IMPLEMENTED (NI): There are no KPIs for registration and MA activities. ➔ ONGOING IMPLEMENTATION (OI): The NRA has recently drafted KPIs for registration and MA activities but they have not yet been reported. ➔ PARTIALLY IMPLEMENTED (PI): The NRA has developed KPIs for registration and MA activities and has been applying them for less than two year or they have not covered all critical steps. ➔ IMPLEMENTED (I): The NRA has established and implemented KPIs for registration and MA activities. The indicators are reviewed regularly, and appropriate actions are taken, and decisions made.
Limitations and remarks:	▪ When they refer to outcomes, indicators may be ambiguous and difficult to interpret, as outcomes are the result of many factors that are difficult to disentangle. When they refer to processes, indicators are often too specific, as they may focus on a particular intervention or condition or they may quickly become outdated as business models develop. ▪ Different methodologies are used to measure the NRAs performance on registration and MA activities. In this case, the assessor should verify that adequate supporting documents are available. The assessor should consider that developed performance indicators should be Specific, Measurable, Achievable, Realistic, and Time- bound (i.e., “SMART”). ▪ Scoring this sub-indicator as “not applicable NA” is excluded (i.e. this sub-indicator will always apply for all benchmarked NRAs).

03

Vigilance (VL): Indicators and Fact Sheets

WHO Global Benchmarking Tool (GBT) for Evaluation of National Regulatory System of Medical Products

03. Vigilance (VL): Indicators and Fact Sheets

Function:	03 — VIGILANCE (VL)
Description:	Medical products vigilance, defined as the science and activities relating to the detection, assessment, understanding and prevention of adverse effects or any other medical product-related problems, is extremely important for guaranteeing that safe and effective medical products of high quality are used within the country. Vigilance activities should be established in the countries based on a risk management approach. A reporting system should be established to monitor the safety of medical products. One important activity within that function is to monitor and assess side effects and other product-related safety issues (e.g., adverse drug reactions (ADRs) for medicines, and adverse events following immunization (AEFI) for vaccines). While common side effects are likely to be detected during pre-approval clinical trials (phases I. II and III), rare events are more likely to be observed after the marketing of medical products. Other unexpected events may also be due to errors and thus could occur at any time during product development and marketing. Side effects may differ with respect to severity, causes and public health consequences. Hence, it is advised that each country establish its own vigilance system. A vigilance system, in general, monitors all kinds of patient harm potentially related to medical products, be it due to inadequate product quality, inappropriate use (e.g., medication errors) or intrinsic adverse effects. Serious effects (e.g., AEFI) often lead to public concerns and could erode the confidence in medical products and the overall regulatory and health systems. If not dealt with adequately, such concerns could have significant negative implications on the public health. A post-marketing vigilance system of medical products is therefore essential. Networking with other international bodies and regulators is a logical method for acquiring, sharing, and exchanging the relevant information on medical products safety. This information, in turn, contributes to informed science-based decisions. To facilitate networking and exchange of information with other international bodies and regulators, harmonization across countries of the vigilance systems and safety reporting requirements in accordance with internationally agreed standards, is expected.
Indicator:	**VL01 Legal provisions, regulations and guidelines required to define regulatory framework of vigilance.**
Objective:	The objective of this indicator is to ensure that vigilance is supported by a comprehensive set of legal provisions, regulations and guidelines which provide the necessary mandate to implement all activities related to this regulatory function. The scope and extent of the vigilance system should be clearly defined in relevant legislation, regulations and guidelines. There should be a legal basis to establish a reporting system for ADRs and AEFIs and to provide the authority for the responsible entity to take actions if needed. The legislation should also provide for adequate and proportional sanctions, penalties and prosecution of violations of the applicable legislation. (Please refer to regulatory inspection function for further information on the regulatory enforcement and compliance activities).
Category:	01. Legal provisions, regulations and guidelines
Sub Indicator:	**VL01.01: Legal provisions for a national vigilance system exist.**
Maturity Level:	1

Scope:	1. Medicines 2. Vaccines
Description:	The assessor should identify and review the applicable legal provisions establishing the national vigilance system and assess whether these provisions have been enacted. The assessor should verify that legal provisions mandating vigilance activities in both public as well as private sectors exist and are actually implemented. In addition, legislation should support activities related to the vigilance function. This legislation should define the duties, powers, and responsibilities of the regulatory authority to manage risks associated with the use of medical products, including collection of data on the safety of the medical products, analysis and investigation of this data, and adoption of regulatory measures by the health authority. In general, legal provisions should designate the entities responsible for undertaking different activities pertinent to vigilance functions. Such entities may or may not lie within the National Regulatory Authority (NRA). However, in all cases, the entities responsible for vigilance functions should be independent from all interested parties (e.g., manufacturers, marketing authorization holders (MAHs), purchasers and supply divisions, including the expanded programme on immunization (EPI), distributors, and health care professionals).
Objective:	The objective of this sub-indicator is to ensure that legal provisions exist for establishing the national vigilance system. These legal provisions provide the mandate for the responsible entities to actually implement their activities. Without such a mandate, the relevant regulatory activities would be too fragile and could be easily challenged.
Requirement:	Legal provisions establishing the national vigilance system
Evidence to review:	The assessor should ask for and review: 1. Legal provisions establishing the national medical products vigilance system (e.g., defining the responsible entities as well as the roles, responsibilities, accountability, and obligations of these entities).
References:	1. Safety Monitoring of Medicinal Products: Guidelines for Setting Up and Running a Pharmacovigilance Centre. UMC, WHO, 2000, (26), (http://apps.who.int/medicinedocs/en/d/Jh2934e/)
Framework:	Structure/Foundation/Input
Rating Scale:	➜ NOT IMPLEMENTED: There are no legal provisions or regulations to satisfy the requirement of the sub- indicator. ➜ ONGOING IMPLEMENTATION (OI): The NRA is taking steps towards establishment of legal provisions and regulations to satisfy the requirement of the sub-indicator; however no results yet exist. ➜ PARTIALLY IMPLEMENTED (PI): Legal provisions and regulations to satisfy the requirement of the sub- indicator were recently established and are in early implementation phase so no consolidated results exist yet. ➜ IMPLEMENTED (I): There are legal provisions and regulations which satisfy the requirement of the sub-indicator and which are actually implemented and enforced.
Limitations and remarks:	Scoring this sub-indicator as "not applicable NA" is excluded (i.e. this sub-indicator will always apply for all benchmarked NRAs).
Sub Indicator:	**VL01.02: Legal provisions and regulations require the manufacturers and/or MAHs to set up a vigilance system of their medical products and periodically report vigilance data to the NRA.**
Maturity Level:	1
Scope:	1. Medicines 2. Vaccines

Description:	The assessor should verify that legal provisions stipulate that manufacturers and/or MAHs have an organized vigilance system to collect, record, store, maintain, evaluate and analyze adverse events (AEs) of their medical products in order to monitor their safety profile. In addition, the legal provisions should require manufacturers and/or MAHs to set up a vigilance system during the life cycle of their medical products and periodically report such events In addition, the assessor should also confirm that the legal provisions allow the NRA to conduct inspections in order to check the existence of vigilance systems as well as the implementation of the Good Vigilance Practices at the manufacturer's and/or MAH's site. and these data, including "zero" events (i.e., situations where no events are reported), to the NRA. Reporting of these events should be done according to established requirements and in alignment with international standards. Examples include periodic safety update reports, and periodic benefit risk evaluation reports. The assessor should verify that the "zero" events have been included systematically in routine periodic reports (i.e., include a confirmation that no reports had been received). The assessor should also verify that legislation includes the obligation that manufacturers and/or MAHs inform the NRA of any safety signal of a product as well as any marketing or regulatory decisions taken in the country of origin or other countries where the product is marketed. In line with these legal provisions, the assessor should verify that relevant guidelines include provisions that endorse this obligation and that explain how, when and what safety issues have to be reported (e.g. recall notifications, reporting of study results from ongoing or previous studies, and information on supervision of clinical trials). A similar obligation should also be in force for the MAH for all products marketed in the country.
Objective:	The objective of this sub-indicator is to ensure the existence of legal provisions mandating that the responsible entities require the MAH to establish a vigilance system for their medical products.
Requirement:	Legal provisions mandating vigilance system establishment by the MAH
Evidence to review:	The assessor should ask for and review: 1. Legal provisions mandating the manufacturers and/or MAHs to establish vigilance systems for their medical products. 2. Legal provisions obligating the manufacturers and/or MAHs to report safety data to the NRA. 3. Legal provisions authorizing the NRA to conduct vigilance inspections. 4. Regulations and guidelines explaining the obligations of the manufacturers and MAHs for safety data reporting.
References:	1. Safety Monitoring of Medicinal Products: Guidelines for Setting Up and Running a Pharmacovigilance Centre. UMC, WHO, 2000, (26), (http://apps.who.int/medicinedocs/en/d/Jh2934e/) 2. The importance of Pharmacovigilance: safety monitoring of medicinal products. World Health Organization, 2002, (17), (http://apps.who.int/medicinedocs/pdf/s4893e/s4893e.pdf)
Framework:	Structure/Foundation/Input
Rating Scale:	➜ NOT IMPLEMENTED: There are no legal provisions or regulations to satisfy the requirement of the sub- indicator. ➜ ONGOING IMPLEMENTATION (OI): The NRA is taking steps towards establishment of legal provisions and regulations to satisfy the requirement of the sub-indicator; however no results exist yet. ➜ PARTIALLY IMPLEMENTED (PI): Legal provisions and regulations to satisfy the requirement of the sub-indicator were recently established and are in early implementation phase so no consolidated results exist yet. ➜ IMPLEMENTED (I): There are legal provisions and regulations which satisfy the requirement of the sub-indicator and which are actually implemented and enforced.
Limitations and remarks:	Scoring this sub-indicator as "not applicable NA" is excluded (i.e. this sub-indicator will always apply for all benchmarked NRAs).

Sub Indicator:	**VL01.03: Guidelines ensure that distributors, importers, exporters, healthcare institutions, consumers and other stakeholders are encouraged to report adverse drug reactions (ADRs) and AEs to the MAH and/or NRA.**
Maturity Level:	1
Scope:	1. Medicines 2. Vaccines
Description:	The assessor should verify the existence of guidelines (including any sort of formal documentation) for encouragement of different stakeholders (e.g., importers, exporters, distributors, health care professionals and institutions, consumers and patients) to report ADRs and AEs to the MAH and/or the NRA. The regulation should ideally be widely distributed and communicated to the public community in order to be meaningful and to be implemented.
Objective:	The objective of this sub-indicator is to ensure reporting of vigilance events by different stakeholders as an essential block of the vigilance function which significantly contributes to its effectiveness and impact.
Requirement:	Guidelines encouraging different stakeholders (including importers, exporters, distributors, health care professionals and institutions, public health programmes, consumers and patients) to report vigilance events to the MAH and/or the NRA.
Evidence to review:	The assessor should ask for and review: 1. Guidelines or other documentation encouraging reporting of vigilance events to the MAH and/or the NRA.
References:	1. Safety Monitoring of Medicinal Products: Guidelines for Setting Up and Running a Pharmacovigilance Centre. UMC, WHO, 2000, (26), (http://apps.who.int/medicinedocs/en/d/Jh2934e/) 2. WHO guidelines on safety monitoring of herbal medicines in pharmacovigilance systems. World Health Organization; 2004, (18), (http://apps.who.int/medicinedocs/documents/s7148e/s7148e.pdf)
Framework:	Structure/Foundation/Input
Rating Scale:	➜ NOT IMPLEMENTED: There are no guidelines to satisfy the requirement of the sub-indicator. ➜ ONGOING IMPLEMENTATION (OI): The NRA is taking steps towards establishment of guidelines to satisfy the requirement of the sub-indicator; however no results exist yet. ➜ PARTIALLY IMPLEMENTED (PI): guidelines to satisfy the requirement of the sub-indicator were recently established and are in early implementation phase so no consolidated results exist yet. ➜ IMPLEMENTED (I): There are guidelines which satisfy the requirement of the sub-indicator and which are actually implemented and enforced.
Limitations and remarks:	▪ Event: a specific identifiable happening or occurrence, e.g., the taking of a medicine or the experience of an adverse effect. ▪ Adverse event (AE): Any untoward medical occurrence that may appear during treatment with a pharmaceutical product but which does not necessarily have a causal relationship with the treatment. ▪ Scoring this sub-indicator as "not applicable NA" is excluded (i.e. this sub-indicator will always apply for all benchmarked NRAs).
Sub Indicator:	**VL01.04: Legal provisions and regulations allow NRA to require manufacturers and/or MAHs to conduct specific studies on safety and effectiveness under specific conditions.**
Maturity Level:	2

Scope:	1. Medicines 2. Vaccines
Description:	The assessor should verify that legal provisions and regulations provide the suitable and proportionate mandate for the NRA to require the manufacturers and/or MAHs to perform specific post-authorization safety activities to further characterize the safety profile of the product. For example, these may include the conduct of additional studies on safety and effectiveness under specific conditions, establishment of registries, and specific data analyses at time points post authorization. The assessor should verify that such legislation exists and is endorsed.
Objective:	The objective of this sub-indicator is to ensure that legal provisions and regulations are providing the necessary mandate for the NRA to request the manufacturers and/or MAHs to conduct specific safety and effectiveness studies under specific conditions.
Requirement:	Legal provisions and regulations allowing the NRA to require MAHs to perform specific post-authorization safety activities to further characterize the safety profile of the product. These may include, for example, the conduct of additional studies on safety and effectiveness under specific conditions, establishment of registries, or specific data analyses at time points post authorization, etc.).
Evidence to review:	The assessor should ask for and review: 1. Legal provisions and regulations authorizing the NRA to request specific post-marketing phase safety and/or effectiveness studies.
References:	26- Safety Monitoring of Medicinal Products: Guidelines for Setting Up and Running a Pharmacovigilance Centre. UMC, WHO, 2000, (26), (http://apps.who.int/medicinedocs/en/d/Jh2934e/)
Framework:	Structure/Foundation/Input
Rating Scale:	➜ NOT IMPLEMENTED: There are no legal provisions or regulations to satisfy the requirement of the sub- indicator. ➜ ONGOING IMPLEMENTATION (OI): The NRA is taking steps towards establishment of legal provisions and regulations to satisfy the requirement of the sub-indicator ; however no results exist yet. ➜ PARTIALLY IMPLEMENTED (PI): Legal provisions and regulations to satisfy the requirement of the sub-indicator were recently established and are in early implementation phase so no consolidated results exist yet. ➜ IMPLEMENTED (I): There are legal provisions and regulations which satisfy the requirement of the sub-indicator and which are actually implemented and enforced.
Limitations and remarks:	▪ Effectiveness: a measure of the chances or odds (i.e., probability) of a medicine working positively as expected for patients. ▪ Scoring this sub-indicator as "not applicable NA" is excluded (i.e. this sub-indicator will always apply for all benchmarked NRAs).
Sub Indicator:	**VL01.05: Legal provisions, regulations and guidelines require manufacturers and/or MAHs to designate an individual person to be in charge of vigilance system.**
Maturity Level:	3
Scope:	1. Medicines 2. Vaccines
Description:	The assessor should verify that legal provisions require the manufacturers and/or MAHs to designate an individual to be in charge of all vigilance activities relevant to their medical products placed on the market. This person should have oversight of the vigilance system in terms of structure and performance. In addition, the assessor should check the requirements for designation of that person and the responsibilities assigned to that

	person. Assessors should note that the qualifications for being designated as an individual person in charge of medical products vigilance may vary from one country or region to another; however in all cases the requirements should ensure the competence of the person responsible for these assigned roles and responsibilities.
Objective:	The objective of this sub-indicator is to ensure that legal provisions and regulations provide the necessary mandate for the NRA to obligate the manufacturers and/or MAHs to designate an individual person to be in charge of medical products vigilance.
Requirement:	Legal provisions and regulations mandating the manufacturers and/or MAHs to designate an individual person in charge of medical products vigilance.
Evidence to review:	The assessor should ask for and review: 1. Legal provisions and regulations obligating the manufacturers and/or MAHs to designate an individual person to be in charge of medical products vigilance. 2. Documents that define the qualifications for being designated as an individual person in charge of medical products vigilance. 3. Documents that define the responsibilities of the individual person in charge of medical products vigilance.
References:	1. WHO Pharmacovigilance indicators: A practical manual for the assessment of pharmacovigilance systems. World Health Organization. 2015, (85), (http://apps.who.int/medicinedocs/documents/s21970en/s21970en.pdf)
Framework:	Structure/Foundation/Input
Rating Scale:	➜ NOT IMPLEMENTED: There are no legal provisions, regulations or guidelines to satisfy the requirement of the sub-indicator. ➜ ONGOING IMPLEMENTATION (OI): The NRA is taking steps towards establishment of legal provisions, regulations and guidelines to satisfy the requirement of the sub-indicator; however no results exist yet. ➜ PARTIALLY IMPLEMENTED (PI): Legal provisions, regulations and guidelines to satisfy the requirement of the sub-indicator were recently established and are in early implementation phase so no consolidated results exist yet. ➜ IMPLEMENTED (I): There are legal provisions, regulations and guidelines which satisfy the requirement of the sub-indicator and which are actually implemented and enforced.
Limitations and remarks:	▪ The title of the individual person in charge of medical products vigilance may vary from one country or region to another. For example, this person may be called a Qualified Person for Pharmacovigilance in one country or region, while a different title may be used in another. ▪ Scoring this sub-indicator as "not applicable NA" is excluded (i.e. this sub-indicator will always apply for all benchmarked NRAs).
Sub Indicator:	**VL01.06: There are guidelines for planning, conducting, monitoring, and reporting of vigilance activities.**
Maturity Level:	3
Scope:	1. Medicines 2. Vaccines
Description:	The assessor should verify that guidelines exist and are endorsed for different vigilance activities, including planning, conducting, monitoring and reporting. The assessor should verify that the guidance is in agreement with other internationally accepted guidance such as that from the World Health Organization (WHO) or International Conference on Harmonization. As a general principle, harmonization of the safety regulatory framework is expected in order to facilitate the exchange of information and experience across NRAs. When applicable, differences should be identified.

	The assessor should identify and review these guidelines and make sure they include: 1. Objectives of the vigilance system; 2. List of events (ADRs and adverse events following immunization (AEFIs)) to be reported; 3. For vaccines, case definitions of events to be reported; 4. Clear definitions of terminology relevant for analysis and response (e.g., AE, adverse reaction, medication error, coincidental error, program error, serious event, and cluster event); 5. Information on how to report (i.e., who, how, where, when and to whom); 6. All medical products to be included in the reporting system (i.e., reporting is not restricted to certain products or sectors); 7. Procedures for analyzing data; 8. Procedures for providing feedback of findings to key players (e.g. reporters of complaints, informers, parents, caregivers, associations and communities) and for relevant follow-up actions; 9. Guidance for investigations and actions to be taken in case of serious events or a cluster of events 10. Guidance on assessment of the balance between risks and benefits for medical products; 11. Guidance on crisis prevention and management; 12. Guidance on communication of vigilance information; 13. Definition of the individuals in charge; 14. Guidance on potential vigilance-related differences and particularities among different medical products (e.g. medicines versus vaccines).
Objective:	The objective of this sub-indicator is to ensure that the guidelines reflect the current thinking of the NRA on different vigilance activities and are facilitating and promoting Good Vigilance Practices. This significantly contributes to vigilance effectiveness and consistency.
Requirement:	Guidelines relevant to vigilance including planning, conducting and reporting activities.
Evidence to review:	The assessor should ask for and review: 1. Guidelines for MAH and competent authorities on vigilance activities. 2. Guidelines for planning, conducting and reporting of vigilance activities. Ideally, these should include the items listed in the description section of this fact sheet.
References:	1. The importance of Pharmacovigilance: safety monitoring of medicinal products. World Health Organization, 2002, (17), (http://apps.who.int/medicinedocs/pdf/s4893e/s4893e.pdf) 2. WHO Pharmacovigilance indicators: A practical manual for the assessment of pharmacovigilance systems. World Health Organization. 2015, (85), (http://apps.who.int/medicinedocs/documents/s21970en/s21970en.pdf)
Framework:	Structure/Foundation/Input
Rating Scale:	➜ NOT IMPLEMENTED: There are no guidelines to satisfy the requirement of the sub-indicator. ➜ ONGOING IMPLEMENTATION (OI): The NRA is taking steps towards establishment of guidelines to satisfy the requirement of the sub-indicator; however no results exist yet. ➜ PARTIALLY IMPLEMENTED (PI): Guidelines to satisfy the requirement of the sub-indicator were recently established and are in early implementation phase so no consolidated results exist yet. ➜ IMPLEMENTED (I): There are guidelines which satisfy the requirement of the sub-indicator and which are actually implemented and enforced.
Limitations and remarks:	Scoring this sub-indicator as “not applicable NA” is excluded (i.e. this sub-indicator will always apply for all benchmarked NRAs)

Sub Indicator:	**VL01.07: Legal provisions and regulations allow recognition and/or reliance on vigilance-related decisions, reports or information from other countries or regional or international bodies.**
Maturity Level:	1
Scope:	1. Medicines 2. Vaccines
Description:	The assessor should verify that legal provisions and regulations permit the application of a recognition and/or reliance regulatory model to the vigilance-related national decisions. Although there is an ultimate need to establish a national vigilance system for medical products, recognition and/or reliance on vigilance-related information and decisions from other countries or regional or international entities would significantly contribute to the safety of medical products in the country. This would, in turn contribute to the public health. While recognition considers regulatory decisions from other sources in an automatic way with minimal sharing of information and justification, reliance depends heavily on information-sharing, communication, and scientific rationale and reasoning. Both approaches (i.e., recognition and reliance) might be applied in passive or active modes. However, the active mode is encouraged and preferred over the passive one.
Objective:	The objective of this sub-indicator is to ensure that legal provisions and regulations are providing the necessary mandate for the NRA to apply recognition and/or reliance regulatory model.
Requirement:	Legal provisions and regulations authorize the NRA to recognize and/or rely on vigilance-related decisions, reports or information from other countries or regional or international entities when making national vigilance decisions.
Evidence to review:	The assessor should ask for and review: 1. Legal provisions and regulations relevant to reliance and/or recognition as applied to vigilance. 2. Legal provisions and regulations relevant to information sharing, reliance and/or recognition as applied to vigilance.
References:	
Framework:	Structure/Foundation/Input
Rating Scale:	➜ NOT IMPLEMENTED: There are no legal provisions or regulations to satisfy the requirement of the sub- indicator. ➜ ONGOING IMPLEMENTATION (OI): The NRA is taking steps towards establishment of legal provisions and regulations to satisfy the requirement of the sub-indicator; however no results exist yet. ➜ PARTIALLY IMPLEMENTED (PI): Legal provisions and regulations to satisfy the requirement of the sub-indicator were recently established and are in early implementation phase so no consolidated results exist yet. ➜ IMPLEMENTED (I): There are legal provisions and regulations which satisfy the requirement of the sub-indicator and which are actually implemented and enforced.
Limitations and remarks:	In some countries, legal provisions and regulations might not support such recognition or reliance. In this case, the scoring of the sub-indicator should be NOT APPLICABLE provided that national vigilance system is able to respond to vigilance events elsewhere.
Indicator:	**VL02 Arrangement for effective organization and good governance.**
Objective:	The objective of this indicator is to ensure effective organization and good governance practices at the entities in charge of vigilance activities. Effective organization and practices in turn contribute to the effective and efficient functioning of the vigilance activities.

Category:	02. Organization and governance
Sub Indicator:	**VL02.01: There is a defined organizational structure with clear responsibilities to conduct vigilance activities.**
Maturity Level:	2
Scope:	1. Medicines 2. Vaccines
Description:	The assessor should identify the organization set in place to establish, implement or maintain the vigilance regulatory function including the defined organizational structures that undertake different relevant activities. Responsibilities, duties and roles of these structures should be clearly defined and documented. In case of involvement of more than one entity, the assessor should check the ways and approaches by which coordination among these structures is managed.
Objective:	The objective of this sub-indicator is to ensure effective organization and good governance of vigilance activities and that these are taken over by defined structures with clear roles and responsibilities.
Requirement:	Roles and responsibilities of the organizational structures in charge of vigilance activities.
Evidence to review:	The assessor should ask for and review: 1. Organization chart of the organizations responsible for the implementation of vigilance activities along with identification of the particular structures implementing the function. 2. Documentation clarifying roles and responsibilities of the structures implementing vigilance activities. This may include, for example, administrative decrees, terms of reference, and position descriptions. 3. Documentation identifying established mechanisms of coordination (e.g., committees, internal work-sharing, and workflow) among structures, if any, which take part in vigilance activities.
References:	1. National drug regulatory legislation: guiding principles for small drug regulatory authorities. In: WHO Expert Committee on Specifications for Pharmaceutical Preparations: thirty-fifth report. Geneva: World Health Organization; 1999: Annex 8 (WHO Technical Report Series, No. 885), (1), (http://apps.who.int/medicinedocs/documents/s21964en/s21964en.pdf)
Framework:	Structure/Foundation/Input
Rating Scale:	➜ NOT IMPLEMENTED: There is no defined structure in charge of vigilance activities. ➜ ONGOING IMPLEMENTATION (OI): A mandate to establish a structure in charge of vigilance activities is available; however the structure itself is not yet established. ➜ PARTIALLY IMPLEMENTED (PI): Structure in charge of vigilance activities is newly established and mandated; however the regular work and practice of this structure is not yet consolidated. ➜ IMPLEMENTED (I): There is defined structure in charge of vigilance activities with clear, well-documented roles and responsibilities.
Limitations and remarks:	Scoring this sub-indicator as "not applicable NA" is excluded (i.e. this sub-indicator will always apply for all benchmarked NRAs).
Sub Indicator:	**VL02.02: Documented procedures and mechanisms are implemented to ensure the involvement, coordination and communication among all stakeholders relevant to vigilance activities**
Maturity Level:	3
Scope:	1. Medicines 2. Vaccines

Description:	The assessor should verify that different stakeholders relevant to vigilance regulatory function are identified. These stakeholders would include not only the different structures (e.g., organizations, institutions, and departments) implementing the regulatory function, but also other entities (e.g., manufacturers and MAHs), governmental agencies (e.g., supply divisions, procurement divisions, and public health programmes including EPI), international organizations (e.g., WHO or the Uppsala Monitoring Centre), non-governmental organizations, professional associations, and customer representative associations. In addition, the assessor should verify the availability and implementation of agreements, memoranda of understanding (MOUs) or documented procedures ensuring the active involvement, communication and collaboration among the identified stakeholders relevant to vigilance of medical products.
Objective:	The objective of this sub-indicator is to ensure that documented procedures and other mechanisms are implemented to ensure the involvement, coordination and communication among different organizations, institutions, and departments for appropriate organization and good governance of the function.
Requirement:	Agreements, MOUs and procedures for ensuring involvement of and communication among stakeholders relevant to vigilance regulatory function.
Evidence to review:	The assessor should ask for and review: 1. List of stakeholders relevant to vigilance of different medical product streams. 2. Agreements, MOUs and standard operating procedures (SOPs) defining the means of communication and collaboration among the identified stakeholders. 3. Example records of communication and collaboration demonstrating implementation of the above-mentioned procedures. 4. Guidelines or SOPs defining procedures for external and internal communications. 5. Documentation that regular meetings and other formal or official communication among above-mentioned stakeholders take place. This documentation should provide evidence for a systematic and well-established communication process. 6. Documentation of paths of communication and reporting. 7. Platforms for information sharing and exchange.
References:	1. The importance of Pharmacovigilance: safety monitoring of medicinal products. World Health Organization, 2002, (17), (http://apps.who.int/medicinedocs/pdf/s4893e/s4893e.pdf) 2. WHO Pharmacovigilance indicators: A practical manual for the assessment of pharmacovigilance systems. World Health Organization. 2015, (85), (http://apps.who.int/medicinedocs/documents/s21970en/s21970en.pdf)
Framework:	Structure/Foundation/Input
Rating Scale:	➜ NOT IMPLEMENTED: There are no coordination and information exchange procedures or mechanisms among different stakeholders of the vigilance function or among the central authority and the decentralized entities. ➜ ONGOING IMPLEMENTATION (OI): The NRA is developing a coordination and information exchange mechanism, but it is not yet ready or exchanges are being conducted without an established methodology. ➜ PARTIALLY IMPLEMENTED (PI): The NRA recently established a coordination and information exchange procedure and mechanism that is at the implementation stage; however, this practice is not yet consolidated. ➜ IMPLEMENTED (I): There are established, implemented and well-maintained coordination and information exchange procedures and mechanisms among different stakeholders of the vigilance function and among the central authority and the decentralized entities.
Limitations and remarks:	Scoring this sub-indicator as "not applicable NA" is excluded (i.e. this sub-indicator will always apply for all benchmarked NRAs).

Indicator:	**VL03 Human resources to perform vigilance activities.**
Objective:	The objective of this indicator is to ensure that all entities within a National Regulatory Authority (NRA) that are concerned with vigilance activities are adequately resourced with a trained, experienced and skilled workforce, and that this workforce has the authority to fully perform the assigned responsibilities. This will ensure that vigilance processes and activities are performed in accordance with international best practices. This indicator is assessed through the evaluation of the human resource capacity of the entities with respect to the number of personnel, the composition, skills and experience of the personnel, and the expertise in those specific areas required to perform the vigilance function.
Category:	06. Resources (HR, FR, infrastructure and equipment)
Sub Indicator:	**VL03.01: Sufficient competent staff (i.e., education, training, skills and experience) are assigned to perform vigilance activities**
Maturity Level:	3
Scope:	1. Medicines 2. Vaccines
Description:	The assessor should verify that the human resources assigned to perform vigilance activities should be sufficient with respect to numbers and competent with respect to the requisite skills, education, experience and training. There should be technical documents and SOPs that provide guidance on the required background for vigilance activities and that consider the requirements for educational background, competencies, skills, experience, and training. The assessor should verify that the NRA estimated the number of staff required to effectively and efficiently perform vigilance function and that the NRA actually recruited that number. In addition, the assessor should verify that these competency requirements are well-established and maintained by the NRA. Metrics and statistics on the different activities performed as well as performance indicators can be used for estimating the adequacy of the number of the assigned staff. The assessor should also verify that the competency of the assigned staff is built, maintained and improved through recruitment as well as continuous on-the-job training.
Objective:	The objective of this sub-indicator is to ensure the existing human resources for vigilance is sufficient, in terms of numbers, experience, and specific competencies, to perform all the activities along the entire vigilance chain.
Requirement:	Sufficient number of competent human resources in charge of vigilance activities.
Evidence to review:	The assessor should ask for and review: 1. Evidence that the number of staff members involved in each of the documented activities along the entire vigilance process flow is adequate. 2. Evidence that the systems and structures are in place to ensure appropriate placement of staff with respect to competence and skills. 3. Evidence that the system and structures have been implemented. The documentation should include the records to verify that the staff competence is appropriate for the job requirements. 4. Evidence that the professional profiles of the human resources engaged in vigilance activities are appropriate with respect to education, skills, and expertise, to perform a particular function along the vigilance chain. Documentation should include a list of the requisite skills and training for each position. 5. Recruitment plan.
References:	1. Quality management systems — Requirements. International Standard ISO 9001:2015. International Organization for Standardization, 2015, (4), (https://www.iso.org/iso-9001-quality-management.html)
Framework:	Structure/Foundation/Input

Rating Scale:	➜ NOT IMPLEMENTED: The NRA does not have enough competent staff (i.e., education, training, skills and experience) to perform vigilance activities ➜ ONGOING IMPLEMENTATION (OI): The NRA has recently developed a plan to recruit adequate competent staff; however, the plan has not been implemented. ➜ PARTIALLY IMPLEMENTED (PI): The NRA has initiated the implementation of the human resources development plan; however, there is need to complete the competency profile. ➜ IMPLEMENTED (I): The NRA has a sustained number of competent staff (i.e., education, training, skills and experience) assigned to perform vigilance activities.
Limitations and remarks:	▪ Assessment of the adequacy and appropriateness of the number of staff members is quite subjective and should be linked to some process or output indicators. When estimating staff adequacy, the assessor should consider the workload, backlog, and delays in delivery based on established timeframes. ▪ Scoring this sub-indicator as "not applicable NA" is excluded (i.e. this sub-indicator will always apply for all benchmarked NRAs).
Sub Indicator:	**VL03.02: Duties, functions, and responsibilities of the staff in charge of vigilance activities are established and updated in the respective job descriptions.**
Maturity Level:	3
Scope:	1. Medicines 2. Vaccines
Description:	The assessor should verify that procedures are in place to maintain a current and updated structure for managing job descriptions for personnel participating in vigilance activities. In addition, job descriptions should address current staff duties, responsibilities and the requisite competencies. A job description with this format and content should be established and implemented for all staff. The management of job descriptions should be supported by a guidance document that provides direction on when and how to update the information, and where the information should be kept for easy access. The guidance document should present the appropriate duties and responsibilities that are assigned to each member of the organization involved in vigilance activities. Thus, the professional profiles of staff are reflected in their respective roles and responsibilities within the NRA. There should be procedures to guide responsible persons to document that duties, functions and responsibilities are revised and kept up to date. In addition, procedures should be available to guide the keeping and documenting of up to date work schedules and enforcing the implementation of the documented guidelines and procedures.
Objective:	The objective of this sub-indicator is to ensure that duties and responsibilities of the staff are clear and well defined, that job descriptions are kept up to date with current duties, functions and responsibilities, and that these activities are adequately documented.
Requirement:	Duties, roles and responsibilities of the staff relevant to vigilance activities.
Evidence to review:	The assessor should ask for and review: 1. Procedure and guidelines that guide placement of staff members within the NRA; 2. The professional profiles of staff (i.e., job descriptions) and documentation that they are related to their current roles and duties; 3. The professional profiles of the external experts and documentation that the profiles provide a composition that is complete and consistent with that prescribed in the legal provisions; 4. Procedures to guide the documentation of up to date duties and work schedules, and to enforce the implementation of the documented guidelines and procedures; 5. Job descriptions for designated staff.

References:	1. National drug regulatory legislation: guiding principles for small drug regulatory authorities. In: WHO Expert Committee on Specifications for Pharmaceutical Preparations: thirty-fifth report. Geneva: World Health Organization; 1999: Annex 8 (WHO Technical Report Series, No. 885), (1), (http://apps.who.int/medicinedocs/documents/s21964en/s21964en.pdf) 2. Quality management systems — Requirements. International Standard ISO 9001:2015. International Organization for Standardization, 2015, (4), (https://www.iso.org/iso-9001-quality-management.html) 3. Guiding principles for small national drug regulatory authorities. In: WHO Expert Committee on Specifications for Pharmaceutical Preparations: thirty-first report. Geneva: World Health Organization; 1990: Annex 6 (WHO Technical Report Series, No. 790), (5), (http://apps.who.int/medicinedocs/documents/s21964en/s21964en.pdf) 4. Effective drug regulation: A multicounty study. Geneva: World Health Organization; 2002, (7), (http://apps.who.int/medicinedocs/pdf/s2300e/s2300e.pdf)
Framework:	Structure/Foundation/Input
Rating Scale:	➜ NOT IMPLEMENTED: There is no evidence of defined or established duties, functions, responsibilities, respective job descriptions and necessary required competencies. ➜ ONGOING IMPLEMENTATION (OI): The NRA has recently drafted or developed the role and responsibilities document but it has not yet been implemented. ➜ PARTIALLY IMPLEMENTED (PI): The NRA has initiated implementation of this requirement but it has not been defined or followed for all staff or the roles and responsibilities documents, including staff job descriptions, are not up to date. ➜ IMPLEMENTED (I): The NRA has defined and established all required duties, functions, and responsibilities, and respective job descriptions are up-to-date.
Limitations and remarks:	Scoring this sub-indicator as "not applicable NA" is excluded (i.e. this sub-indicator will always apply for all benchmarked NRAs).
Sub Indicator:	**VL03.03: Training plan developed, implemented and updated at least once a year for staff in charge of vigilance activities.**
Maturity Level:	3
Scope:	1. Medicines 2. Vaccines
Description:	The assessor should verify that training plans are developed, implemented and updated at least once every year to reflect the current situation by considering education and experience of the staff. The training plan should be complemented with guidelines or similar documents that guide the development and implementation of training plans. The assessor should ensure that induction training for new staff as well as continued on- the-job for staff is planned and implemented. There should be procedures to approve the training plan and the budget allocated for implementing and updating the training plan. The plans should present clearly defined training goals, and should include training in certain topics and skills to address identified deficiencies. Learning objectives, training methods and activities, evidence of learning, and evaluation and assessment of training should be documented. This documentation should confirm that the learning objectives were achieved and were designed to address weaknesses within the entities. Procedures should be in place to ensure that a training plan is developed, implemented and updated at least once every year. The assessor should verify that there is a system in place for monitoring the implementation and effectiveness of the training plan and for documenting the skills acquired in training activities for internal and external experts.
Objective:	The objective of this sub-indicator is to ensure that a training plan for staff exists, and that it is implemented and updated annually. Through the training plan, NRA can be sure that competency of staff in charge of vigilance activities is maintained and enhanced.

Requirement:	Implementation of training plan
Evidence to review:	The assessor should ask for and review: 1. Guidelines for development, implementation and annual update (i.e., at least once per year) of the training plan. Guidelines should also provide for a mechanism to measure effectiveness of training. 2. Documentation for the system or structures used to approve the training plan and to evaluate the adequacy of the budget allocated to the training activities. 3. The current or existing staff training plan (or matrix) for staff. The assessor should assess this in in relation to the respective individual job descriptions. 4. SOP for developing and maintaining the training plan. 5. Evidence that the NRA has investigated and identified training needs. 6. List of trainings performed. 7. Example records for training activities.
References:	1. National drug regulatory legislation: guiding principles for small drug regulatory authorities. In: WHO Expert Committee on Specifications for Pharmaceutical Preparations: thirty-fifth report. Geneva: World Health Organization; 1999: Annex 8 (WHO Technical Report Series, No. 885), (1), (http://apps.who.int/medicinedocs/documents/s21964en/s21964en.pdf) 2. Quality management systems — Requirements. International Standard ISO 9001:2015. International Organization for Standardization, 2015, (4), (https://www.iso.org/iso-9001-quality-management.html) 3. Guiding principles for small national drug regulatory authorities. In: WHO Expert Committee on Specifications for Pharmaceutical Preparations: thirty-first report. Geneva: World Health Organization; 1990: Annex 6 (WHO Technical Report Series, No. 790), (5), (http://apps.who.int/medicinedocs/documents/s21964en/s21964en.pdf) 4. Effective drug regulation: A multicounty study. Geneva: World Health Organization; 2002, (7), (http://apps.who.int/medicinedocs/pdf/s2300e/s2300e.pdf) 5. Quality systems requirements for national good manufacturing practice inspectorates. In: WHO Expert Committee on Specifications for Pharmaceutical Preparations: thirty-sixth report. Geneva: World Health Organization; 2002: Annex 8 (WHO Technical Report Series, No. 902), (8), (http://apps.who.int/medicinedocs/documents/s22112en/s22112en.pdf)
Framework:	Process
Rating Scale:	➜ NOT IMPLEMENTED: There is no systematic training program including training plan (or matrix). ➜ ONGOING IMPLEMENTATION (OI): The NRA has recently drafted or developed the training plan but there is no evidence of implementation. ➜ PARTIALLY IMPLEMENTED (PI): The NRA has developed and initiated the training plan implementation. However, the NRA has not fulfilled all required planned training or has been applying the plan for less than two years. ➜ IMPLEMENTED (I): The NRA has an updated training plan developed that is supported by adequate records to demonstrate effective plan implementation, including induction training for new staff and routine on-the-job training for recruited staff.
Limitations and remarks:	▪ Training plans must be updated regularly; ideally on an annual basis, but not less frequently that once every two years. ▪ Some regulatory functions may include many training activities that are not incorporated in the institutional training programme. Such training normally is offered by invitation. In this case, the assessor should recognize reports from non-routine vigilance -relevant training not included in the NRA training plan. ▪ Scoring this sub-indicator as "not applicable NA" is excluded (i.e. this sub-indicator will always apply for all benchmarked NRAs).
Sub Indicator:	**VL03.04: The NRA generates and maintains records of staff training activities and training effectiveness verification.**
Maturity Level:	3

Scope:	1. Medicines 2. Vaccines
Description:	The assessor should verify that records of staff training that is performed or organized by the NRA are generated, maintained, regularly updated. This activity should be supported by guidelines that direct the NRA to generate and maintain records of staff training activities. Procedures should be in place to document and propose staff training needs and to allocate a budget for continuous staff capacity building and development. The assessor should check that there is an evaluation or assessment mechanism to verify the quality of learning, and to confirm that learning objectives are achieved. Documentation should include an inventory (i.e., soft and/or hard) system that records all impactful and non-impactful trainings, and identifies all staff members who participated. A system to measure or estimate impact of trainings should be established.
Objective:	The objective of this sub-indicator is to ensure that training organized by the NRA or responsible regulatory authority is adequately documented and that the training records are adequately maintained and kept. Staff training records are considered an integral part of staff file and are a tool for measuring and tracking staff competency, development and adequacy.
Requirement:	Training records
Evidence to review:	The assessor should ask for and review: 1. Guidelines or similar documents that guide the NRA to generate and maintain records of staff training activities; 2. Evaluations of training effectiveness; 3. The training inventory, and procedures for completing the inventory; 4. Examples of archived records of staff training, and procedures for the archiving system.
References:	1. WHO Pharmacovigilance indicators: A practical manual for the assessment of pharmacovigilance systems. World Health Organization. 2015, (85), (http://apps.who.int/medicinedocs/documents/s21970en/s21970en.pdf) 2. WHO guidelines on safety monitoring of herbal medicines in pharmacovigilance systems. World Health Organization; 2004, (18), (http://apps.who.int/medicinedocs/documents/s7148e/s7148e.pdf) 3. National drug regulatory legislation: guiding principles for small drug regulatory authorities. In: WHO Expert Committee on Specifications for Pharmaceutical Preparations: thirty-fifth report. Geneva: World Health Organization; 1999: Annex 8 (WHO Technical Report Series, No. 885), (1), (http://apps.who.int/medicinedocs/documents/s21964en/s21964en.pdf) 4. Quality management systems — Requirements. International Standard ISO 9001:2015. International Organization for Standardization, 2015, (4), (https://www.iso.org/iso-9001-quality-management.html) 5. Guiding principles for small national drug regulatory authorities. In: WHO Expert Committee on Specifications for Pharmaceutical Preparations: thirty-first report. Geneva: World Health Organization; 1990: Annex 6 (WHO Technical Report Series, No. 790), (5), (http://apps.who.int/medicinedocs/documents/s21964en/s21964en.pdf) 6. Effective drug regulation: A multicounty study. Geneva: World Health Organization; 2002, (7), (http://apps.who.int/medicinedocs/pdf/s2300e/s2300e.pdf)
Framework:	Output
Rating Scale:	➜ NOT IMPLEMENTED: There is no evidence that the NRA generates and maintains records of staff training activities. ➜ ONGOING IMPLEMENTATION (OI): The NRA has recently initiated plans to generate, document and keep records of staff training activities, however they are not yet followed. ➜ PARTIALLY IMPLEMENTED (PI): The NRA has recently initiated plans to generate,

	document and keep records of staff training activities but they are not fully followed for all training activities or they have been established for less than two years. ➔ IMPLEMENTED (I): The NRA generates and maintains records of staff training activities.
Limitations and remarks:	▪ The assessor should note that some NRAs out-source training including staff capacity development activities. In this case the assessor should request the identity of the provider, as well as evaluations of the provider. The assessor may request the professional profiles of tutors or resource persons used to offer training. The assessor may also request records covering the archiving systems in place. ▪ Scoring this sub-indicator as "not applicable NA" is excluded (i.e. this sub-indicator will always apply for all benchmarked NRAs).
Indicator:	**VL04 Procedures established and implemented to perform vigilance activities.**
Objective:	The objective of this indicator is to ensure that required activities of the vigilance system are implemented through standard procedures and work instructions that ensure the consistency, effectiveness, efficiency, impartiality and proportionality of the vigilance system. The NRA should have established a system which allows the regular review of safety and effectiveness aspects of the authorized products on the market, including processes to review and share relevant data between key players and to take appropriate action when necessary. There should be written procedures that define how relevant data are routinely shared among key personnel engaged in vigilance activities and how any actions taken are reviewed for appropriateness. Documented evidence to be assessed include procedures for review of safety and effectiveness aspects of medical products on the market, for review of reports of notifications, investigations, data analyses, and committee meetings, for sharing of relevant data among key players, and for taking appropriate actions.
Category:	07. Regulatory process
Sub Indicator:	**VL04.01: Vigilance procedures and tools are in place and implemented for collection and assessment of ADRs and AEs.**
Maturity Level:	3
Scope:	1. Medicines 2. Vaccines
Description:	The assessor should verify the existence and implementation of standard procedures for different vigilance activities related to collection and assessment of ADRs and AEs including: 1. Existence of a paper-based or an electronic reporting system for ADR- and AEFI-related information that is accessible to MAHs, healthcare professionals and patients 2. Systems for detection and receipt of vigilance events and ADR reports that is complemented with reporting systems (e.g., either active or passive, and either sentinel or country- or state-wide) that have the satisfactory sensitivity to detect serious events or clusters of events. For this point, the assessor should check for the number and rates of reports within defined periods, ADRs following off-label use, and a breakdown of reports that compares district or regional reporting activities for the different products and populations that are involved in vigilance reporting. 3. Timely review, analysis, and causality assessment of ADRs and AEs. For this process, assessor should verify that: a. in 80% of cases an investigation is initiated within 48 hours following reporting (for vaccines); b. preliminary investigation report is available within 1 week (for vaccines); c. Investigation is of adequate quality, procedures are thorough, and findings are clearly-

	described; d. conclusions are scientifically justified and supported by findings. 4. Records of reported ADRs and AEFIs (for vaccines) are stored and maintained. The assessor should verify that the above-mentioned procedures are consistent with the relevant national guidelines which in turn are in coherence with WHO or other international accepted guidance. The assessor should review records that verify the actual implementation of such procedures. In addition, the assessor should verify that all vigilance data received are analyzed on a regular basis. The assessor should check the tools NRA is using to collect and analyze the data (e.g. calculation of incidence rates or the assessment of causality). WHO recommends the following tools: 1. A national database or similar centralized (e.g., regional, sub- regional or global) system, that is compatible with International Conference on Harmonization E2B, to code, collate, and store data and reports and to analyze vigilance data. 2. The adoption of standard case definitions for AEFIs (e.g., Brighton collaboration definitions or national case definitions).
Objective:	The objective of this sub-indicator is to ensure consistency of different activities of the medical products vigilance system through standard procedures which are complemented by the necessary tools.
Requirement:	Procedures and tools necessary for effective implementation of different regulatory activities.
Evidence to review:	The assessor should ask for and review: 1. Procedures and records of reporting systems including reporting forms or platforms used within the country; 2. Codes and case definitions (for vaccines); 3. Procedures and methods used for causality assessment; 4. Numbers and rates of reports within defined period(s), a list of ADRs following off-label use, and a breakdown of reports that compares district or regional reporting activities for the different products and populations involved in vigilance reporting. 5. Number of reports transmitted to WHO database along with the frequency of submission.
References:	1. WHO Pharmacovigilance indicators: A practical manual for the assessment of pharmacovigilance systems. World Health Organization. 2015, (85), (http://apps.who.int/medicinedocs/documents/s21970en/s21970en.pdf) 2. WHO guidelines on safety monitoring of herbal medicines in pharmacovigilance systems. World Health Organization; 2004, (18), (http://apps.who.int/medicinedocs/documents/s7148e/s7148e.pdf) 3. The importance of Pharmacovigilance: safety monitoring of medicinal products. World Health Organization, 2002, (17), (http://apps.who.int/medicinedocs/pdf/s4893e/s4893e.pdf)
Framework:	Process
Rating Scale:	➜ NOT IMPLEMENTED: No procedures exist for collection and assessment of ADRs and AEs. ➜ ONGOING IMPLEMENTATION (OI): The NRA is taking steps towards development and establishment of procedures for collection and assessment of ADRs and AEs; however no results yet exist. ➜ PARTIALLY IMPLEMENTED (PI): Procedures for collection and assessment of ADRs and AEs were recently established by the NRA and are in early implementation phase so no consolidated results exist yet. ➜ IMPLEMENTED (I): Standard procedures exist and are implemented for collection and assessment of ADRs and AEs.
Limitations and remarks:	Scoring this sub-indicator as "not applicable NA" is excluded (i.e. this sub-indicator will always apply for all benchmarked NRAs).

Sub Indicator:	**VL04.02: Vigilance procedures and tools are in place for investigation, interpretation of and response to ADRs and AEs.**
Maturity Level:	3
Scope:	1. Medicines 2. Vaccines
Description:	The assessor should verify the existence and implementation of standard procedures for different vigilance activities related to investigation and interpretation of and response to ADRs and AEs including: 1. Investigation and assessment of ADRs and AEs 2. Assessment of risk, analysis and evaluation of vigilance data, and identification of trends 3. Processes for signal detection; 4. Use of statistical tools to calculate reporting disproportionalities such as Proportional Reporting Ratio 5. Initiation of appropriate actions at the national or sub-national level when needed. For this particular process, the assessor should verify that all vigilance events are screened and triaged by staff that is qualified to assess their impact on public health and to determine the subsequent steps needed. These steps may include one or more of the following: • Addition to national vigilance database • Follow up or further analysis • Referral for comprehensive investigation or systematic causality assessment • Issue of safety alerts and/or batch or product recalls • Other regulatory decisions including product withdrawal and/or revocation of marketing authorization. The assessor should verify that the above mentioned procedures are consistent with the relevant national guidelines, which in turn are in coherence with WHO or other international accepted guidance. The assessor should review records proving the actual implementation of such procedures. In addition, the assessor should verify that all vigilance data received are investigated and interpreted on a regular basis and that any and all necessary actions are taken.
Objective:	The objective of this sub-indicator is to ensure consistency of different activities related to investigation of, interpretation of, and response to ADRs and AEs.
Requirement:	Procedures and tools necessary for investigation, interpretation of and response to ADRs and AEs.
Evidence to review:	The assessor should ask for and review: 1. Procedures for taking action on recommendations arising from causality assessment; 2. Investigation reports; 3. Documentation of actions taken following reporting of vigilance events (ADRs, AE and AEFIs); 4. Reports of notifications, data analyses, committee meetings, and other related records; 5. Documentation regarding the number of signals detected from national, regional or linked international databases, if any; 6. Listing of the AEFIs reported (e.g., from the EPI to the NRA or vigilance center) over the last two years.
References:	1. WHO Pharmacovigilance indicators: A practical manual for the assessment of pharmacovigilance systems. World Health Organization. 2015, (85), (http://apps.who.int/medicinedocs/documents/s21970en/s21970en.pdf) 2. WHO guidelines on safety monitoring of herbal medicines in pharmacovigilance systems. World Health Organization; 2004, (18), (http://apps.who.int/medicinedocs/documents/s7148e/s7148e.pdf) 3. The importance of Pharmacovigilance: safety monitoring of medicinal products. World Health Organization, 2002, (17), (http://apps.who.int/medicinedocs/pdf/s4893e/s4893e.pdf)

Framework:	Process
Rating Scale:	➜ NOT IMPLEMENTED: No procedures exist for investigation of, interpretation of and response to ADRs and AEs. ➜ ONGOING IMPLEMENTATION (OI): The NRA is taking steps towards development and establishment of procedures for investigation of, interpretation of and response to ADRs and AEs; however no results yet exist. ➜ PARTIALLY IMPLEMENTED (PI): Procedures for investigation of, interpretation of and response to ADRs and AEs were recently established by the NRA and are in early implementation phase so no consolidated results exist yet. ➜ IMPLEMENTED (I): Standard procedures exist and are implemented for investigation of, interpretation of and response to ADRs and AEs.
Limitations and remarks:	Scoring this sub-indicator as "not applicable NA" is excluded (i.e. this sub-indicator will always apply for all benchmarked NRAs).
Sub Indicator:	**VL04.03: Standard procedures exist and are implemented for enforcement of the national vigilance system.**
Maturity Level:	4
Scope:	1. Medicines 2. Vaccines
Description:	The assessor should verify the existence and enactment of standard procedures for different vigilance enforcement activities including, for example, product label changes, restrictions of use, product withdrawals or suspensions, or implementation of intensive monitoring. The assessor should confirm that, as part of these procedures, the NRA notifies manufacturers (and vice versa) of significant safety and efficacy issues and that reporting is kept up to date.
Objective:	The objective of this sub-indicator is to ensure consistency of the vigilance function through standard procedures for enforcement activities.
Requirement:	Standard procedures for different vigilance enforcement activities.
Evidence to review:	The assessor should ask for and review: 1. Standard procedures for enforcement activities relevant to vigilance system; 2. Records of vigilance inspections of MAHs and corrective actions and preventive actions issued over the last two years; 3. Records of enactment of these standard procedures (e.g., decisions communicated to manufacturers and MAHs).
References:	1. WHO guidelines on safety monitoring of herbal medicines in pharmacovigilance systems. World Health Organization; 2004, (18), (http://apps.who.int/medicinedocs/documents/s7148e/s7148e.pdf) 2. WHO Pharmacovigilance indicators: A practical manual for the assessment of pharmacovigilance systems. World Health Organization. 2015, (85), (http://apps.who.int/medicinedocs/documents/s21970en/s21970en.pdf) 3. The importance of Pharmacovigilance: safety monitoring of medicinal products. World Health Organization, 2002, (17), (http://apps.who.int/medicinedocs/pdf/s4893e/s4893e.pdf)
Framework:	Process
Rating Scale:	➜ NOT IMPLEMENTED: No standard procedures exist for enforcement of the national vigilance system. ➜ ONGOING IMPLEMENTATION (OI): The NRA is taking steps towards development and establishment of procedures for enforcement of the national vigilance system; however no results yet exist.

	➔ PARTIALLY IMPLEMENTED (PI): Procedures for enforcement of the national vigilance system were recently established by the NRA and are in early implementation phase so no consolidated results exist yet. ➔ IMPLEMENTED (I): Standard procedures exist and are implemented for enforcement of the national vigilance system.
Limitations and remarks:	Scoring this sub-indicator as "not applicable NA" is excluded (i.e. this sub-indicator will always apply for all benchmarked NRAs).
Sub Indicator:	**VL04.04: Risk approach is considered throughout different vigilance activities, including timely response to detected signals for risks or benefits.**
Maturity Level:	3
Scope:	1. Medicines 2. Vaccines
Description:	The assessor should verify that different vigilance activities are implemented with consideration of risk approach. In general, the principle of risk proportionality should be applied in the decision-making process for post-approval activities. This entails risk assessment, including identification of different risks along with their analysis and evaluation, risk control, via risk reduction, mitigation or acceptance, and regular risk review, which may include adoption of any necessary changes in the risk management process. Risk communication should also be considered across all steps of the risk management process. Those products, events, or activities of high risk should be given higher attention when establishing risk mitigation and control strategies and procedures.
Objective:	The objective of this sub-indicator is to ensure that a risk approach consideration is contributing to vigilance function efficiency and effectiveness.
Requirement:	Consideration of risk approach in different vigilance activities including timely response to detected signals for risks or benefits.
Evidence to review:	The assessor should ask for and review: 1. Procedures for risk approach consideration in different vigilance activities. 2. Examples of risk management process including risk assessment, risk control and risk review. 3. Examples of risk management strategy for identified high risk products, events or activities.
References:	1. WHO Pharmacovigilance indicators: A practical manual for the assessment of pharmacovigilance systems. World Health Organization. 2015, (85), (http://apps.who.int/medicinedocs/documents/s21970en/s21970en.pdf) 2. WHO guidelines on quality risk management, (55), (http://digicollection.org/whoqapharm/p/about and http://apps.who.int/medicinedocs/en)
Framework:	Process
Rating Scale:	NOT IMPLEMENTED: Risk approach is not considered throughout different vigilance activities. ➔ ONGOING IMPLEMENTATION (OI): The NRA is taking steps towards consideration of risk approach for different vigilance activities; however, no results yet exist. ➔ PARTIALLY IMPLEMENTED (PI): Consideration of risk approach for different vigilance activities was recently established and is in early implementation phase so no consolidated results exist yet. ➔ IMPLEMENTED (I): Risk approach is considered throughout different vigilance activities.

Limitations and remarks:	▪ The risk approach meant herein is that related to NRA. However, employment of risk approach by manufacturers and MAHs is also of great value and should be verified by the NRA as part of its implementation and enforcement of vigilance activities. ▪ Scoring this sub-indicator as "not applicable NA" is excluded (i.e. this sub-indicator will always apply for all benchmarked NRAs).
Sub Indicator:	**VL04.05: Staff access to information resources relevant to vigilance processes (e.g., safety information sources and reference materials) is ensured.**
Maturity Level:	1
Scope:	1. Medicines 2. Vaccines
Description:	The assessor should verify that staff responsible for different vigilance activities, including members of any expert committees, have access to both internal and external sources of information and reference materials, including literature and publications, to allow them to make decisions on vigilance events. Information resources include, among others, all scientific information concerning the use of medicinal products and the outcome of their use, (i.e., quality, nonclinical and clinical data, including pharmacovigilance and pharmaco-epidemiological data). Access to market information might be helpful as well (e.g. medicines utilization statistics).
Objective:	The objective of this sub-indicator is to ensure access of the responsible staff to vigilance relevant information resources, reference materials and literature as an essential contributing factor for effective performance of the function.
Requirement:	Access of vigilance staff to relevant information resources
Evidence to review:	The assessor should ask for and review: 1. Subscriptions to databases of scientific literature with up-to-date studies and information on medical products safety and efficacy; 2. A list of electronic and printed materials consulted during the vigilance event analysis and investigation (e.g., books, international guidelines, or international package inserts), 3. Access to pre-market, preclinical and clinical trial data; 4. Access to risk management plan. 5. Access to Periodic Safety Update Reports and Periodic Benefit Risk Evaluation Reports 6. Access to renewal dossiers
References:	1. WHO Pharmacovigilance indicators: A practical manual for the assessment of pharmacovigilance systems. World Health Organization. 2015, (85), (http://apps.who.int/medicinedocs/documents/s21970en/s21970en.pdf) 2. WHO guidelines on safety monitoring of herbal medicines in pharmacovigilance systems. World Health Organization; 2004, (18), (http://apps.who.int/medicinedocs/documents/s7148e/s7148e.pdf)
Framework:	Process
Rating Scale:	➜ NOT IMPLEMENTED: Staff does not have access to information resources relevant to vigilance processes (e.g., safety information sources and reference materials). ➜ ONGOING IMPLEMENTATION (OI): The NRA is taking steps to guarantee staff access to information resources relevant to vigilance processes (e.g., safety information sources and reference materials); however no results exist yet. ➜ PARTIALLY IMPLEMENTED (PI): Staff access to information resources relevant to vigilance processes (e.g. safety information sources and reference materials) was recently established and is in early implementation phase; however, no consolidated results exist yet. ➜ IMPLEMENTED (I): Staff has reasonable access to information resources relevant to vigilance processes (e.g., safety information sources and reference materials).

Limitations and remarks:	▪ Efficacy is defined as the ability of a drug to produce the purported effect as determined by scientific methods. ▪ Scoring this sub-indicator as "not applicable NA" is excluded (i.e. this sub-indicator will always apply for all benchmarked NRAs).
Sub Indicator:	**VL04.06: The NRA has access to expert committees for review of serious emergent safety concerns, when needed.**
Maturity Level:	3
Scope:	1. Medicines 2. Vaccines
Description:	The assessor should verify access of the NRA to a standing advisory committee or other group of experts for the investigation, assessment and analysis of serious vigilance events (ADRs and AEFIs). The expert members of this committee might be internal or external to the NRA; however in case of external staff, the appropriate measures should be taken to ensure that relevant interests are declared and that that confidentiality is maintained. The assessor should review terms of reference and written standard procedures defining conditions and processes for the election of the members and for assuring their expertise. Confidentiality, independence of the experts and prevention and handling of conflicts of interest should also be regulated. The NRA should have access to any other experts when needed. The assessor should also verify NRA access to external expertise in specific medical fields (e.g., teratology) when needed as part of this sub-indicator.
Objective:	The objective of this sub-indicator is to ensure effective investigations, assessments and analyses of serious vigilance events through the access to an expert committee (unless extensive and sufficient internal expertise is available).
Requirement:	Expert committee for review of serious vigilance events
Evidence to review:	The assessor should ask for and review: 1. Terms of reference and standard procedures for the expert committee for review of serious vigilance events. 2. Records of discussions and decisions of the expert committee for review of serious vigilance events over the last two years or the last 5 to 10 meetings. 3. Procedures for convening the expert committee when needed to provide advice and recommendations. 4. Procedures for follow-up and implementation of the expert committee recommendations, including procedures for re-convening the expert committee as needed to review progress.
References:	1. WHO guidelines on safety monitoring of herbal medicines in pharmacovigilance systems. World Health Organization; 2004, (18), (http://apps.who.int/medicinedocs/documents/s7148e/s7148e.pdf) 2. WHO Pharmacovigilance indicators: A practical manual for the assessment of pharmacovigilance systems. World Health Organization. 2015, (85), (http://apps.who.int/medicinedocs/documents/s21970en/s21970en.pdf) 3. The importance of Pharmacovigilance: safety monitoring of medicinal products. World Health Organization, 2002, (17), (http://apps.who.int/medicinedocs/pdf/s4893e/s4893e.pdf)
Framework:	Process
Rating Scale:	➔ NOT IMPLEMENTED: The NRA does not have access to expert committees for review of serious emergent safety concerns. ➔ ONGOING IMPLEMENTATION (OI): The NRA is taking steps towards guaranteeing access to expert committees for review of serious emergent safety concerns; however no results exist yet.

	➔ PARTIALLY IMPLEMENTED (PI): NRA access to expert committees for review of serious emergent safety concerns was recently established and is in early implementation phase, so no consolidated results exist yet. ➔ IMPLEMENTED (I): The NRA has access to expert committees for review of serious emergent safety concerns, when needed.
Limitations and remarks:	There might be a limitation if the expert committee is not formalized or does not meet frequently.
Sub Indicator:	**VL04.07: With respect to vigilance data, assessment of the risk-benefit balance of medical products is regularly conducted.**
Maturity Level:	4
Scope:	1. Medicines 2. Vaccines
Description:	The assessor should verify that safety and/or effectiveness of medical products placed on the market are regularly evaluated through periodic assessment of the risk-benefit balance of medical products. Towards this end, the assessor should verify the availability of risk-benefit analysis tools and processes, including descriptions of their application to regulatory decision making. The assessor should also confirm that vigilance data are informing such risk-benefits assessments, and that informed, science-based decisions are taken when necessary. Risk-benefit assessment is an important regulatory tool that highlights the risk-regulations such as withdrawal from the market or suspension of license and sale. benefit of therapeutic products. Industry (i.e., the MAH) is primarily responsible for developing risk-benefit assessments. Product vigilance evaluation involves the ongoing assessment of the risk-benefit of a product (including, for example, data from adverse reaction reports, clinical trials, meta-analysis, and observational studies). These assessments provide the assurance that benefits outweigh the risks for a given population during clinical trials and following market authorization. The frequency of this evaluation varies significantly depending on the maturity of the national vigilance system. In addition, the assessor should verify that after the risk-benefit assessment of the medical products, the NRA is making well-justified decisions based on scientifically sound evidence and is taking necessary regulatory in response to the risks detected. The goals of the actions are to minimize risk and maintain a favorable risk-benefit profile. With the current regulatory landscape, these interventions generally fall within the following options: • Issuance of a risk communication; • Revision of market authorization (e.g., terms and conditions, naming, labelling, or packaging); • Further investigation by the regulator; • Enforcement of
Objective:	The objective of this sub-indicator is to ensure the sustained and effective evaluation of medical products safety and effectiveness, and the ongoing evaluation of their risk- benefit balance with full consideration of national and international vigilance data.
Requirement:	Risk-benefit assessment of medical products with consideration of vigilance data
Evidence to review:	The assessor should ask for and review: 1. Standard procedures relevant to the risk- benefit assessment of medical products; 2. Documented evidence of the consideration of the vigilance data in these processes; 3. Regulatory decisions and actions for maintaining the favorable risk-benefit balance of the medical products placed on the market.
References:	
Framework:	Process

Rating Scale:	➜ NOT IMPLEMENTED: Assessment of risk-benefit balance of medical products is not regularly conducted at all. ➜ ONGOING IMPLEMENTATION (OI): The NRA is taking steps towards assessment of risk-benefit balance of medical products on regular basis; however no results exist yet. ➜ PARTIALLY IMPLEMENTED (PI): Assessment of risk-benefit balance of medical products is regularly conducted; however consideration of vigilance data is not fully utilized or consideration of vigilance data for risk-benefit assessment was recently established and remains in early implementation phase. For these reasons, no consolidated results yet exist. ➜ IMPLEMENTED (I): Risk-benefit balance of medical products is regularly conducted with full consideration of vigilance data.
Limitations and remarks:	Scoring this sub-indicator as "not applicable NA" is excluded (i.e. this sub-indicator will always apply for all benchmarked NRAs).
Sub Indicator:	**VL04.08: Active vigilance activities, as well as proactive monitoring programmes (when needed) have been developed and implemented.**
Maturity Level:	4
Scope:	1. Medicines 2. Vaccines
Description:	The assessor should verify the existence and implementation of active surveillance systems as well as proactive vigilance systems for early detection of events. The goal is to initiate corrective actions and preventive actions to manage use of medical products of significant public health impact and medical products of potential high risk. Passive surveillance means that no active measures are taken to look for AEs other than the encouragement of health professionals and others to report safety concerns. Reporting is entirely dependent on the initiative and motivation of the potential reporters. This is the most common form of vigilance. It is commonly referred to as "spontaneous" or "voluntary" reporting. In some countries, this form of reporting is mandatory. Active safety surveillance, on the other hand, means that active measures are taken to detect AEs. This is managed by active follow-up after treatment and the events may be detected by asking patients directly or by screening patient records. Such follow-up is best done prospectively. Active vigilance is sometimes very descriptively referred to as, "hot pursuit". The most comprehensive method is cohort event monitoring. Examples of this are the Intensive Medicines Monitoring Programme in New Zealand and Prescription Event Monitoring in England. Other methods used include the use of registers, record linkage and screening of laboratory results in medical laboratories. Active surveillance may entail several activities including signal detection and field research. One of the most important activities in the vigilance system is the ability to detect safety issues as quickly as possible. Safety management programs should be then established. Active surveillance might be applied to all medical products or to selected high risk medical products. Proactive approach is mainly related to and based on the assessment of pre-market data which could contribute to risk management, risk mitigation or risk minimization when necessary.
Objective:	The objective of this sub-indicator is to ensure that vigilance systems are implemented in active and/or proactive manners, rather than reactively, when needed for protecting public health.
Requirement:	Active vigilance monitoring and surveillance programme.
Evidence to review:	The assessor should ask for and review: 1. Standard procedures and mechanisms relevant to proactive vigilance systems; 2. Standard procedures and mechanisms relevant to active vigilance activities; 3. Risk management plans from the manufacturers.

References:	1. WHO guidelines on safety monitoring of herbal medicines in pharmacovigilance systems. World Health Organization; 2004, (18), (http://apps.who.int/medicinedocs/documents/s7148e/s7148e.pdf) 2. WHO Pharmacovigilance indicators: A practical manual for the assessment of pharmacovigilance systems. World Health Organization. 2015, (85), (http://apps.who.int/medicinedocs/documents/s21970en/s21970en.pdf) 3. The importance of Pharmacovigilance: safety monitoring of medicinal products. World Health Organization, 2002, (17), (http://apps.who.int/medicinedocs/pdf/s4893e/s4893e.pdf)
Framework:	Process
Rating Scale:	➜ NOT IMPLEMENTED: No active surveillance or proactive vigilance systems are implemented at all. ➜ ONGOING IMPLEMENTATION (OI): The NRA is taking steps towards development of procedures for active surveillance and/or proactive vigilance systems; however no results exist yet. ➜ PARTIALLY IMPLEMENTED (PI): Procedures and mechanisms for active surveillance and/or proactive vigilance system were recently established by the NRA and are in early implementation phase so no consolidated results exist yet. ➜ IMPLEMENTED (I): Active surveillance and/or proactive vigilance system are implemented based on well-established criteria.
Limitations and remarks:	Scoring this sub-indicator as "not applicable NA" is excluded (i.e. this sub-indicator will always apply for all benchmarked NRAs).
Indicator:	**VL05 Mechanism in place to monitor regulatory performance and output.**
Objective:	The objective of this indicator is to ensure the effectiveness of the different medical-product related vigilance activities, to measure relevant advancements, and to ensure that performance indicators are established, implemented and verified on a regular basis.
Category:	09. Monitoring progress and assessing outcomes & impact
Sub Indicator:	**VL05.01: Vigilance information is used in timely manner to amend existing regulatory decisions or to issue new regulatory decisions or actions.**
Maturity Level:	3
Scope:	1. Medicines 2. Vaccines
Description:	The assessor should verify that corrective regulatory decisions and actions (e.g., suspensions, recalls, updates of product leaflet, product withdrawals or revocations of marketing authorization) are based on vigilance findings and are in accordance with national regulations and WHO recommendations. Furthermore, the assessor should verify that the regulatory actions related to the vigilance function are implemented and monitored.
Objective:	The objective of this sub-indicator is to ensure that the vigilance function provides the scientific basis for regulatory decisions and actions and serves to maintain a favorable risk-benefit balance for medical products placed on the market.
Requirement:	Regulatory decisions and actions in response to vigilance information.
Evidence to review:	The assessor should ask for and review: 1. List of regulatory decisions based on vigilance events in the last two years. 2. Examples of decisions and actions taken in response to vigilance events in the last two years.

	3. Communications and publications of regulation decisions and actions that were provided to different entities within or outside the NRA. 4. List of investigated, detected or analyzed signals in the last two years.
References:	1. WHO Pharmacovigilance indicators: A practical manual for the assessment of pharmacovigilance systems. World Health Organization. 2015, (85), (http://apps.who.int/medicinedocs/documents/s21970en/s21970en.pdf) 2. The importance of Pharmacovigilance: safety monitoring of medicinal products. World Health Organization, 2002, (17), (http://apps.who.int/medicinedocs/pdf/s4893e/s4893e.pdf)
Framework:	Output
Rating Scale:	➜ NOT IMPLEMENTED: no evidence exists for the confirmation that vigilance information is used to amend or issue regulatory decisions and consequent actions in timely manner. ➜ ONGOING IMPLEMENTATION (OI): The NRA is taking steps towards usage of vigilance information to amend or issue regulatory decisions; however no results exist yet. ➜ PARTIALLY IMPLEMENTED (PI): The NRA started recently to use vigilance information to amend or issue regulatory decisions; however, the practice is in the early implementation stage and not yet consolidated. ➜ IMPLEMENTED (I): Evidence exists to confirm that vigilance information is used to amend or issue regulatory decisions and consequent actions in timely manner.
Limitations and remarks:	Scoring this sub-indicator as "not applicable NA" is excluded (i.e. this sub-indicator will always apply for all benchmarked NRAs).
Sub Indicator:	**VL05.02: Performance indicators for vigilance activities are established and implemented.**
Maturity Level:	4
Scope:	1. Medicines 2. Vaccines
Description:	The assessor should verify the existence and implementation of performance indicators for different activities included under the vigilance function. Specifically, the system should define key performance indicators (KPIs) along the entire vigilance activity chain and all indicators should be adequately justified. For the purpose of clarity and consistency, established KPIs should be supported with guidelines for monitoring and maintenance of the KPIs. The guidelines in turn should be supported by SOPs and tools that define the procedures to be used for monitoring and evaluating the necessary, process optimizations should be introduced to avoid recurrence. performance indicators and that define procedures and timelines for reviewing and revising the indicators. Performance indicators for activities included under the medical products vigilance system should include: • detection or receipt of vigilance events from within the reporting system; • timely review, investigation and assessment of vigilance events; • feedback on the vigilance activities to different stakeholders; • storage and management of reported vigilance data; • risk assessment, analysis and evaluation of vigilance data and identification of trends; • initiation of appropriate actions at the national or sub-national level when needed; and • risk management and risk communication plans. Established KPIs might be qualitative, quantitative or combination of both. In general, quantitative indicators are preferred to avoid bias or misinterpretation. However, qualitative indicators are also accepted. Qualitative indicators may or may not include scoring or scaling to render them semi-quantitative and thus more informative. The assessor should ensure that indicators are measured on a regular basis to monitor progress and advancement.

	In addition, the assessor should verify measured indicators are analyzed to identify trends or abnormalities. Justifications for any identified abnormalities should be provided; when necessary, process optimizations should be introduced to avoid recurrence.
Objective:	The objective of this sub-indicator is to ensure that a system, mechanism, or procedure exists to require the NRA to establish performance indicators along the entire vigilance chain. Additionally, the objective is to ensure that KPIs are actually contributing to monitoring of regulatory performance, to measuring effectiveness of vigilance regulatory activities, and to making any necessary adjustments or optimizations.
Requirement:	KPIs for medical products vigilance activities
Evidence to review:	The assessor should ask for and review: 1. Documents supporting the system, mechanism, or procedure compelling the NRA to establish and implement performance indicators along the entire vigilance activity chain. 2. Evidence that the performance indicators have been established and implemented, and that the members of staff involved in the vigilance function are aware of the indicators and the guidelines and SOPs used for monitoring and evaluating their performance. 3. The current performance indicators for vigilance activities 4. Analyses of the measured indicators along with the investigations done to identify trends or abnormalities. 5. Documentation for follow-up of any observed abnormalities, including justifications for any identified abnormalities as well as any process optimizations introduced to avoid recurrence.
References:	1. WHO Pharmacovigilance indicators: A practical manual for the assessment of pharmacovigilance systems. World Health Organization. 2015, (85), (http://apps.who.int/medicinedocs/documents/s21970en/s21970en.pdf) 2. The importance of Pharmacovigilance: safety monitoring of medicinal products. World Health Organization, 2002, (17), (http://apps.who.int/medicinedocs/pdf/s4893e/s4893e.pdf) 3. World Health Organization. European Observatory on Health Systems and Policies. Performance measurement for health system improvement: experiences, challenges and Prospects, (125), (http://www.who.int/management/district/performance/PerformanceMeasurementHealthSystemImprovement2.pdf) 4. World Health Organization. European Observatory on Health Systems and Policies. Health System Performance Comparison: an agenda for policy, information and research, (126), (http://www.euro.who.int/__data/assets/pdf_file/0009/244836/Health-System-Performance-Comparison.pdf)
Framework:	Output
Rating Scale:	➜ NOT IMPLEMENTED: There are no KPIs for vigilance activities. ➜ ONGOING IMPLEMENTATION (OI): The NRA has recently drafted KPIs for vigilance activities but they have not yet been reported. ➜ PARTIALLY IMPLEMENTED (PI): The NRA has developed KPIs for vigilance activities and has been applying them for less than two year or they have not covered all critical steps. ➜ IMPLEMENTED (I): The NRA has established and implemented KPIs for vigilance activities. The indicators are reviewed regularly, and appropriate actions are taken and decisions made.
Limitations and remarks:	▪ When they refer to outcomes, indicators may be ambiguous and difficult to interpret, as outcomes are the result of many factors that are difficult to disentangle. When they refer to processes, indicators are often too specific, as they may focus on a particular intervention or condition or they may quickly become outdated as business models develop. ▪ Different methodologies are used to measure the NRAs performance on vigilance activities. In this case, the assessor should verify that adequate supporting documents are available. The assessor should consider that developed performance

indicators should be Specific, Measurable, Achievable, Realistic, and Time-bound (i.e., "SMART").
- Scoring this sub-indicator as "not applicable NA" is excluded (i.e. this sub-indicator will always apply for all benchmarked NRAs).

Indicator:	**VL06 Mechanism exists to promote transparency, accountability and communication.**
Objective:	The objective of this indicator is to ensure communication within the NRA, transparency and outreach to public, regional and international partners, and accountability of the NRA. Additionally, these contribute to mutual understanding and involvement of all stakeholders that are relevant to the vigilance system and raise the confidence in the regulatory system.
Category:	08. Transparency, accountability and communication
Sub Indicator:	**VL06.01: Vigilance activities and relevant feedback are appropriately communicated to the public.**
Maturity Level:	2
Scope:	1. Medicines 2. Vaccines
Description:	The assessor should verify that a proper mechanism is available, enacted and used to demonstrate that regular feedback and information on the vigilance system, in particular, serious events and clusters of AEs, are communicated appropriately to the public (including patients, parents and caregivers). Furthermore, guidance to the public community on ways and approaches to manage any potential risks, may contribute significantly to risk reduction or elimination. Investigation reports of public concerns and summaries of these reports should be made available to the public. Regular publications (e.g., bulletins) or awareness sessions would serve the above-mentioned communication mechanism. In addition, considering the fact that medical professionals and the public community play a crucial role in the vigilance system, activities for raising their awareness is necessary. The assessor should verify that regular meetings, trainings, educational sessions, educational materials, and media aids are provided for a wide audience, including undergraduate, postgraduate medical, pharmacy and nursing students, staff and healthcare providers in public and private sectors, staff from immunization programs, and the general public community.
Objective:	The objective of this sub-indicator is to ensure the implementation and effectiveness of the overall vigilance system, in particular, to ensure that the risk management and risk communication plans are regularly and systematically implemented (i.e., not on ad hoc basis).
Requirement:	Communication mechanism for the public community on vigilance events, especially serious ones.
Evidence to review:	The assessor should ask for and review: 1. Records of communications to the public community (e.g., social media, newsletters, and websites); 2. Information bulletins and documentation of public awareness sessions and campaigns; 3. Published alerts, assessments and investigation reports.
References:	1. WHO guidelines on safety monitoring of herbal medicines in pharmacovigilance systems. World Health Organization; 2004, (18), (http://apps.who.int/medicinedocs/documents/s7148e/s7148e.pdf) 2. WHO Pharmacovigilance indicators: A practical manual for the assessment of pharmacovigilance systems. World Health Organization. 2015, (85), (http://apps.who.int/medicinedocs/documents/s21970en/s21970en.pdf)

	3. The importance of Pharmacovigilance: safety monitoring of medicinal products. World Health Organization, 2002, (17), (http://apps.who.int/medicinedocs/pdf/s4893e/s4893e.pdf)
Framework:	Output
Rating Scale:	➜ NOT IMPLEMENTED: Vigilance activities and feedback are not communicated to the public community. ➜ ONGOING IMPLEMENTATION (OI): The NRA is taking steps towards sharing of vigilance activities and providing feedback to the public community, but no results yet exist. ➜ PARTIALLY IMPLEMENTED (PI): The NRA started recently to share vigilance activities and provide feedback to the public community; however, it has only limited experience or a limited number of documented events. ➜ IMPLEMENTED (I): Vigilance activities and feedback, especially for serious events and clusters of AEs, are appropriately communicated to the public community.
Limitations and remarks:	Scoring this sub-indicator as "not applicable NA" is excluded (i.e. this sub-indicator will always apply for all benchmarked NRAs).
Sub Indicator:	**VL06.02: Mechanism for regular feedback to all stakeholders on vigilance events exists and is complemented with a risk communication plan.**
Maturity Level:	3
Scope:	1. Medicines 2. Vaccines
Description:	The assessor should verify that a proper mechanism is available, enacted and used to demonstrate that information on vigilance system, especially serious events and clusters of AEs, are shared among all stakeholders engaged in medical products vigilance. Key players include the NRA or the vigilance center, manufacturers, MAHs, purchasers and supply divisions (including the EPI in case of vaccines), distributors, and other health care professionals. The assessor should verify that the process for feedback is established, endorsed and followed down to health facility level. The assessor should note that the regularity of outreach to the stakeholders depends on the availability of data, decisions, or actions. In addition, the assessor should verify that regular formal or official communications and meetings take place among above-mentioned key players when dealing with vigilance events. The assessor should check that periodic feedback is offered from the NRA or the responsible authority to all levels country-wide, especially to medical and health professionals. Particularly for vaccines, the NRA should be informed about in-country vaccine safety and performance information including vaccine preventable diseases surveillance data, EPI coverage data, information on number of doses shipped and administered, seroprevalence study reports, outbreak investigation reports, EPI reports on vaccine supply and storage (i.e., cold chain), special instructions, and recall notifications.
Objective:	The objective of this sub-indicator is to ensure the implementation and effectiveness of the overall vigilance system, particularly the risk management and risk communication plans.
Requirement:	Risk communication plan as a part of an overall mechanism for regular feedback to all stakeholders on vigilance system
Evidence to review:	The assessor should ask for and review: 1. Risk communication plan and procedures for communication with different stakeholders involved in the vigilance system. 2. Examples of shared information among those stakeholders. 3. Records of communication (e.g., social media, newsletters, websites, or publications) among the NRA and those stakeholders. 4. Records of regular meetings among the vigilance relevant stakeholders.

References:	1. WHO guidelines on safety monitoring of herbal medicines in pharmacovigilance systems. World Health Organization; 2004, (18), (http://apps.who.int/medicinedocs/documents/s7148e/s7148e.pdf) 2. WHO Pharmacovigilance indicators: A practical manual for the assessment of pharmacovigilance systems. World Health Organization. 2015, (85), (http://apps.who.int/medicinedocs/documents/s21970en/s21970en.pdf) 3. The importance of Pharmacovigilance: safety monitoring of medicinal products. World Health Organization, 2002, (17), (http://apps.who.int/medicinedocs/pdf/s4893e/s4893e.pdf)
Framework:	Output
Rating Scale:	➔ NOT IMPLEMENTED: Feedback on vigilance events and activities are not communicated to all relevant stakeholders. ➔ ONGOING IMPLEMENTATION (OI): The NRA is taking steps towards providing feedback on vigilance events and activities to all relevant stakeholders, but no risk communication plan or results yet exist. ➔ PARTIALLY IMPLEMENTED (PI): The NRA started recently to provide feedback on vigilance events and activities to all relevant stakeholders; however, the NRA has only limited experience or it has a limited number of documented events. ➔ IMPLEMENTED (I): Feedback on vigilance events and activities are communicated to all relevant stakeholders. These activities are based on a well-developed risk communication plan.
Limitations and remarks:	Scoring this sub-indicator as "not applicable NA" is excluded (i.e. this sub-indicator will always apply for all benchmarked NRAs).
Sub Indicator:	**VL06.03: Vigilance data and findings are shared with relevant regional and international partners.**
Maturity Level:	3
Scope:	1. Medicines 2. Vaccines
Description:	The assessor should verify that national vigilance data and findings and conclusions are shared with relevant regional and international partners (e.g. WHO Collaborating Centers). The assessor should confirm that the national vigilance staff have access to the regional and international tools (e.g., databases) and should verify that these tools facilitate information sharing and analysis. In addition, the assessor should confirm that there is two-way collaboration and interaction among the national vigilance system and relevant regional and international partners.
Objective:	The objective of this sub-indicator is to ensure medical products safety and efficacy through sharing of global concerns and relevant vigilance data and findings among the national and international communities; such sharing will benefit all stakeholders. This sharing also fosters regulatory convergence and harmonization.
Requirement:	Regional and international sharing of vigilance data and findings.
Evidence to review:	The assessor should ask for and review: 1. Proof of membership of the national vigilance system in relevant regional and international organizations or partnerships. 2. Proof of regular communications and interactions with those regional and international partners. 3. Proof of engagement of national vigilance system in regional or international meetings, conferences, or symposia. 4. Publication of vigilance data in scientific publications as a means of communication with international and regional partners. 5. List of serious ADRs and AEFIs submitted to WHO Collaborating Centers in the last two years.

References:	1. WHO guidelines on safety monitoring of herbal medicines in pharmacovigilance systems. World Health Organization; 2004, (18), (http://apps.who.int/medicinedocs/documents/s7148e/s7148e.pdf) 2. WHO Pharmacovigilance indicators: A practical manual for the assessment of pharmacovigilance systems. World Health Organization. 2015, (85), (http://apps.who.int/medicinedocs/documents/s21970en/s21970en.pdf) 3. The importance of Pharmacovigilance: safety monitoring of medicinal products. World Health Organization, 2002, (17), (http://apps.who.int/medicinedocs/pdf/s4893e/s4893e.pdf)
Framework:	Output
Rating Scale:	➜ NOT IMPLEMENTED: Vigilance data and findings are not shared with relevant regional and international partners. ➜ ONGOING IMPLEMENTATION (OI): The NRA is taking steps towards sharing of vigilance data and findings with other regional and international partners, but results do not yet exist. ➜ PARTIALLY IMPLEMENTED (PI): The NRA started recently to share vigilance data and findings with other regional and international partners; however, it has only limited experience or a limited number of documented events. ➜ IMPLEMENTED (I): Vigilance data and findings are shared with relevant regional and international partners.
Limitations and remarks:	Scoring this sub-indicator as “not applicable NA” is excluded (i.e. this sub-indicator will always apply for all benchmarked NRAs).

04

Market Surveillance and Control (MC): Indicators and Fact Sheets

WHO Global Benchmarking Tool (GBT) for Evaluation of National Regulatory System of Medical Products

04. Market Surveillance and Control (MC): Indicators and Fact Sheets

Function:	04 — MARKET SURVEILLANCE AND CONTROL (MC)
Description:	Market surveillance and control function plays a crucial role in assuring medical products consumer safety since its objective is to ensure compliance of the products placed on the market with pre-set criteria for quality, safety and efficacy (i.e., verify compliance with marketing authorization and good practices guidelines). Market surveillance and control function activities are primarily concerned with four themes: (1) control of import activities, (2) prevention and detection of and response to substandard and falsified medical products, (3) market surveillance program for monitoring the quality of medical products throughout the supply chain, and (4) control of promotional, marketing and advertising activities. The aforementioned activities may or may not be undertaken by a single entity (e.g., organization, division, or department). A general limitation to one of the market surveillance and control function activities exists in countries where advertisement is not allowed or is restricted to specific medical products (e.g. over-the-counter medical products). However, in all cases, control of marketing and promotional materials (i.e., in its wider meaning that includes promotion to healthcare professionals) will always apply.
Indicator:	**MC01 Legal provisions, regulations and guidelines required to define regulatory framework of market surveillance and control activities.**
Objective:	The objective of this indicator is to ensure that market surveillance and control activities are backed up by a comprehensive set of legal provisions, regulations and guidelines that provide the necessary mandate to implement all activities related to this regulatory function.
Category:	01. Legal provisions, regulations and guidelines
Sub Indicator:	**MC01.01: Legal provisions and regulations are in place with respect to import activities including permanent regulatory intervention at designated entry and exit ports where medical products are being moved.**
Maturity Level:	1
Scope:	1. Medicines 2. Vaccines
Description:	The assessor should verify that the medical products importation activities should be conducted in conformity with the mandate promulgated under the relevant legal provisions, regulations and guidelines as implemented and enforced by the National Regulatory Authority (NRA). These activities may be conducted in collaboration with other relevant authorities, e.g. customs. These mandates should require that transactions relating to importation of consignments of medical products be conducted by licensed entities and that good storage and distribution practices be followed. In exceptional cases (e.g., emergency situations for the public health interest), the NRA may retain the discretionary power to waive some licensing or authorization requirements for some medical product consignments. Such waivers should be properly justified and should not compromise patient safety or the risk-benefit balance of the medical products. Importation of medical products should be channeled exclusively through designated air, sea, or land ports. These designated entry and exit ports (i.e., air, sea, or land) should have permanent capacity for the regulatory intervention that is essential to ensure

	compliance with and enforcement of the relevant mandates. When justified by the workload, either full-time or part-time inspectors may be stationed at one or more of these designated ports.
Objective:	The objective of this sub-indicator is to ensure that the NRA has the necessary mandate, supported by the appropriate legal provisions and regulations, to control import activities of medical products. This control will, in turn, contribute to a positive public health impact. In the interest of public health, import activities related to medical products, unlike that of ordinary commodities, need to be controlled and under the proper oversight of the NRA. Hence, the NRA needs to be supported with the mandate needed to assume this responsibility. Import activities should then comply with this mandate, including the relevant legal provisions, regulations and guidelines. The activities should be supported by a regulatory presence at the entry and exit ports to enforce these mandates.
Requirement:	Legal provisions and regulations relevant to import activities of all medical products to or from the country.
Evidence to review:	The assessor should ask for and review: 1. Legal provisions relevant to medical products import activities. 2. Regulations relevant to medical products import and. 3. Guidelines relevant to medical products import activities including good storage and good distribution practices. 4. Evidence of permanent regulatory intervention at the entry and exit ports.
References:	1. Guidelines on import procedures for pharmaceutical products, World Health Organization (WHO), (22), (http://digicollection.org/whoqapharm/p/about and http://apps.who.int/medicinedocs/en)
Framework:	Structure/Foundation/Input.
Rating Scale:	➜ NOT IMPLEMENTED (NI): There are no legal provisions or regulations to satisfy the requirement of the sub- indicator. ➜ ONGOING IMPLEMENTATION (OI): The NRA is taking steps towards establishment of legal provisions and regulations to satisfy the requirement of this sub-indicator; however no results exist so far. ➜ PARTIALLY IMPLEMENTED (PI): Legal provisions and regulations to satisfy the requirement of this sub-indicator were recently established, and are in an early implementation phase, so no documented results exist so far. ➜ IMPLEMENTED (I): There are legal provisions and regulations which satisfy the requirement of the sub-indicator and which are actually implemented and enforced.
Limitations and remarks:	▪ Permanent regulatory intervention at the entry and exit ports may or may not entail physical presence of regulators at these ports. Other acceptable alternatives include, but are not limited to, close cooperation between regulators and custom authorities with proper documentation and authorization controls or electronic systems. ▪ Scoring this sub-indicator as "not applicable NA" is excluded (i.e. this sub-indicator will always apply for all benchmarked NRAs).
Sub Indicator:	**MC01.02: Legal provisions and regulations authorize market surveillance and control activities which include product sampling from different points of the supply chain.**
Maturity Level:	1
Scope:	1. Medicines 2. Vaccines
Description:	The assessor should verify the existence and implementation of legal provisions and regulations which establish a market surveillance program. Such market surveillance should normally include sampling of different medical products from different points

	across the supply chain, from the manufacturer, through the distributors and wholesalers, and up to the last point of sale or dispensing. In addition, the assessor should ensure that market control activities extend to the internet sales of medical products. It should be noted that testing is not limited to laboratory testing, but is extended to all types of testing including innovative technologies.
Objective:	The objective of this sub-indicator is to ensure the quality, safety and efficacy of medical products placed on the market. The ultimate goal of the overall medical products regulatory system is to ensure public accessibility and affordability of safe, effective and high quality products. Hence, a market surveillance program, combined with market control activities, is necessary to regularly check the quality of medical products available on the market and to take any necessary regulatory actions. Market surveillance and control activities should be based on and supported by an appropriate legal mandate.
Requirement:	Legal provisions, regulations and guidelines relevant to market surveillance and control activities of all medical products.
Evidence to review:	The assessor should ask for and review: 1. Legal provisions relevant to surveillance program which includes sampling and testing of samples of medical products. 2. Regulations relevant to surveillance program which includes sampling and testing of samples of medical products. 3. Guidelines relevant to surveillance program which includes sampling and testing of samples of medical products. 4. Legal provisions, regulations or guidelines relevant to market control of internet sales of medical products.
References:	1. Guidelines on the conduct of surveys of the quality of medicines, World Health Organization (WHO), (86), (http://apps.who.int/medicinedocs/en/q/ and http://digicollection.org/whoqapharm/) 2. WHO guidelines for sampling of pharmaceutical products and related materials, World Health Organization (WHO), (31), (http://digicollection.org/whoqapharm/p/about and http://apps.who.int/medicinedocs/en)
Framework:	Structure/Foundation/Input.
Rating Scale:	➜ NOT IMPLEMENTED (NI): There are no legal provisions or regulations to satisfy the requirement of the sub- indicator. ➜ ONGOING IMPLEMENTATION (OI): The NRA is taking steps towards establishment of legal provisions and regulations to satisfy the requirement of this sub-indicator; however no results exist so far. ➜ PARTIALLY IMPLEMENTED (PI): Legal provisions and regulations to satisfy the requirement of this sub-indicator were recently established, and are in an early implementation phase, so no documented results yet exist. ➜ IMPLEMENTED (I): There are legal provisions and regulations which satisfy the requirement of the sub-indicator and which are actually implemented and enforced.
Limitations and remarks:	▪ nternet sales might be prohibited in some countries. In this case, the sub-indicator would not apply to internet sales provided that some legal provisions or regulations are in place to prohibit internet sales. ▪ Sampling activities at manufacturers, distributers and points of sale or dispensing might be undertaken during a regulatory inspection programme. ▪ Scoring this sub-indicator as "not applicable NA" is excluded (i.e. this sub-indicator will always apply for all benchmarked NRAs).
Sub Indicator:	**MC01.03: Legal provisions and regulations address the role of NRA in dealing with substandard or falsified (SF) medical products.**
Maturity Level:	1

Scope:	1. Medicines 2. Vaccines
Description:	The assessor should verify that legal provisions, regulations and guidelines that address the role of the NRA in dealing with SF medical products are available and enacted. Examples of possible actions to be taken include: suspension of a drug's marketing authorization, recall of certain batches, a warning in national drug bulletins, or a separate warning sent out to a list of institutions and key persons that deal with or prescribe pharmaceutical products. The legislation should provide for adequate and proportional sanctions, penalties and prosecutions for violations of the applicable legislation. The assessor should review the guidance published for all categories of stakeholders and find out if the guidance covers the scope of the applicable legislation and regulations. Consistency with World Health Organization (WHO) guidance should be checked as well and any differences should be identified.
Objective:	The objective of this sub-indicator is to ensure that the NRA is empowered with the proper legal provisions and regulations to work on prevention, detection and response to SF medical products.
Requirement:	Legal provisions, regulations and guidelines addressing products and personnel involved in SF medical products.
Evidence to review:	The assessor should ask for and review: 1. Legal provisions relevant to the role of the NRA in dealing with SF medical products; 2. Regulations relevant to the role of the NRA in dealing with SF medical products; 3. Guidelines relevant to the role of the NRA in dealing with SF medical products.
References:	1. Addressing the barriers to effective monitoring, reporting and containment of spurious/ substandard/falsely-labelled/ falsified/counterfeit medical products. A report prepared for the Medicines Transparency Alliance, Philippines: 2016, (88), (http://apps.who.int/medicinedocs/documents/s22331en/s22331en.pdf) 2. SF- Frequently asked questions. Scope, scale and harm. How big is the problem of SF medical products?, (87), (https://www.who.int/medicines/regulation/ssffc/faq-ssffc_1-10/en/) 3. Substandard and falsified medical products. Fact sheet, (134), (https://www.who.int/en/news-room/fact-sheets/detail/substandard-and-falsified-medical-products) 4. WHO Member State Mechanism on substandard/spurious/falsely-labelled/falsified/counterfeit medical products, A70/23, appendix 3, Working Definitions, (128), (https://www.who.int/medicines/regulation/ssffc/A70_23-en1.pdf) 5. Recommendations for health authorities to detect and deal with actions, activities and behaviors that result in substandard/spurious/falsely-labelled/falsified/counterfeit medical products, A68/33, annex 1, (129), (http://apps.who.int/gb/ebwha/pdf_files/WHA68/A68_33-en.pdf) 6. Guidance on developing a national plan for preventing, detecting and responding to actions, activities and behaviors that result in SF medical products. WHO (document A70/23), (130), (https://www.who.int/medicines/regulation/ssffc/mechanism/A70_23-en6-14.pdf) 7. WHO Global Surveillance and Monitoring System for substandard and falsified medical products, (133), (https://www.who.int/medicines/regulation/ssffc/publications/gsms-report-sf/en/)
Framework:	Structure/Foundation/Input.
Rating Scale:	➜ NOT IMPLEMENTED (NI): There are no legal provisions or regulations to satisfy the requirement of the sub- indicator. ➜ ONGOING IMPLEMENTATION (OI): The NRA is taking steps towards establishment of legal provisions and regulations to satisfy the requirement of this sub-indicator; however no results exist so far. ➜ PARTIALLY IMPLEMENTED (PI): Legal provisions and regulations to satisfy the requirement of the sub-indicator were recently established and are in early implementation phase so no documented results yet exist. ➜ IMPLEMENTED (I): There are legal provisions and regulations which satisfy the requirement of the sub-indicator and which are actually implemented and enforced.

Limitations and remarks:	▪ Formal guidelines might not exist, however relevant guidance may be provided in other types of documentation (e.g., regulations). ▪ Scoring this sub-indicator as "not applicable NA" is excluded (i.e. this sub-indicator will always apply for all benchmarked NRAs).
Sub Indicator:	**MC01.04: Legal provisions and regulations exist for the control of promotion, marketing and advertising of medical products to avoid communication of false or misleading information.**
Maturity Level:	2
Scope:	1. Medicines 2. Vaccines
Description:	The assessor should verify the availability of legal provisions, regulations and guidelines which set the rules for control of promotional, marketing and advertising activities of medical products. These rules should ensure that communication of false or misleading information to health professionals, the public, or any other stakeholders is avoided.
Objective:	The objective of this sub-indicator is to ensure that medical professionals and the public have access to accurate data about the medical products through different promotional, marketing and advertising activities. Inappropriate promotion and advertisement of medicines may contribute to the irrational or incorrect use of medicinal products. The impact of accurate and science-based promotional activities is related to the existence of trustworthy and accessible information sources and the level of medical knowledge of the population. Hence, the control of promotion and advertisement of medical products is necessary and should be sustained by a legal and regulatory framework.
Requirement:	Legal provisions, regulations and guidelines for the control of promotion, marketing and advertising of medical products.
Evidence to review:	The assessor should ask for and review: 1. Legal provisions relevant to control of promotion, marketing and advertising of medical products. 2. Regulations relevant to control of promotion, marketing and advertising of medical products. 3. Guidelines relevant to control of promotion, marketing and advertising of medical products.
References:	1. Drug Promotion: Push, Promote or Educate? Essential Drugs Monitor, No. 020, 1995, World Health Organization (WHO), (91), (http://apps.who.int/medicinedocs/documents/s21265en/s21265en.pdf) 2. Ethical Criteria for the Promotion, Advertisement, and Publicity of Medicines - PANDRH Series Technical Document No 12 (Pan American Network for Drug Regulatory Harmonization), (94), (http://apps.who.int/medicinedocs/documents/s22161en/s22161en.pdf) 3. CIOMS/WHO Meeting on Ethical Criteria for Medicinal Drug Promotion. Essential Drugs Monitor No. 017, 1994, (90), (http://apps.who.int/medicinedocs/documents/s21142en/s21142en.pdf) 4. Ethical Criteria for Medicinal Drug Promotion, World Health Organization, 1988, (13), (http://apps.who.int/medicinedocs/documents/whozip08e/whozip08e.pdf) 5. Drug Promotion - What We Know, What We Have Yet to Learn - Reviews of Materials in the WHO/HAI Database on Drug Promotion, World Health Organization (WHO), (89), (http://apps.who.int/medicinedocs/pdf/s8109e/s8109e.pdf) 6. Cross-border Advertising, Promotion and Sale of Medical Products Using the Internet. WHA Resolution; Fifty-First World Health Assembly, WHA51.9, (93), (http://apps.who.int/medicinedocs/documents/s21471en/s21471en.pdf) 7. Alternative Regulatory Models for Pharmaceutical Promotions Involving Civil Society and Other Non-Government Stakeholders, Medicines Transparency Alliance, (96), (http://apps.who.int/medicinedocs/documents/s22327en/s22327en.pdf)

	8. Educational initiatives for medical and pharmacy students about drug promotion: an international cross-sectional survey. Geneva. World Health Organization, (92), (http://apps.who.int/medicinedocs/pdf/s8110e/s8110e.pdf)
Framework:	Structure/Foundation/Input.
Rating Scale:	➜ NOT IMPLEMENTED (NI): There are no legal provisions or regulations to satisfy the requirement of the sub- indicator. ➜ ONGOING IMPLEMENTATION (OI): The NRA is taking steps towards establishment of legal provisions and regulations to satisfy the requirement of this sub-indicator; however no results exist so far. ➜ PARTIALLY IMPLEMENTED (PI): Legal provisions and regulations to satisfy the requirement of this sub-indicator were recently established, and are in early implementation phase so no documented results yet exist. ➜ IMPLEMENTED (I): There are legal provisions and regulations which satisfy the requirement of the sub-indicator and which are actually implemented and enforced.
Limitations and remarks:	▪ Formal guidelines might not exist, however relevant guidance may be provided in other types of documentation (e.g., regulations). ▪ Scoring this sub-indicator as "not applicable NA" is excluded (i.e. this sub-indicator will always apply for all benchmarked NRAs).
Sub Indicator:	**MC01.05: Legal provisions and regulations exist for placement of a product's unique identification number on its outer packaging.**
Maturity Level:	4
Scope:	1. Medicines 2. Vaccines
Description:	The assessor should verify the availability of legal provisions and regulations setting the rules for placement of a unique identification number on the outer package of each medical product. Legal provisions and regulations should indicate that an identification number is assigned to each product that receives marketing authorization.
Objective:	The objective of this sub-indicator is to ensure the placement of a unique identification number on each outer packaging in order to facilitate tracking and tracing activities of medical products throughout the supply chain. These activities, in turn, support the detection and response activities related to SF medical products.
Requirement:	Legal provisions, regulation and guidelines for the placement of product's unique identification number on outer packaging.
Evidence to review:	The assessor should ask for and review: 1. Legal provisions relevant to placement of unique identification number on outer packaging of medical products. 2. Regulations relevant to placement of unique identification number on outer packaging of medical products. 3. Guidelines relevant to placement of unique identification number on outer packaging of medical products.
References:	1. WHO good manufacturing practices for pharmaceutical products: main principles, (51), (http://digicollection.org/whoqapharm/p/about and http://apps.who.int/medicinedocs/en) 2. WHO good distribution practices for pharmaceutical products, World Health Organization (WHO), (27), (http://digicollection.org/whoqapharm/p/about and http://apps.who.int/medicinedocs/en) 3. Existing technologies and "track and trace" models in use and to be developed by Member States. Appendix 2. World Health Organization. Executive Board B 138/40, (101), (http://apps.who.int/gb/ebwha/pdf_files/EB138/B138_40-en.pdf)

	4. WHO Member State Mechanism on substandard/spurious/falsely-labelled/falsified/ counterfeit medical products, A70/23, appendix 2, Available authentication technologies for the prevention and detection of SSFFC medical products, (139), (http://apps.who.int/gb/ebwha/pdf_files/WHA70/A70_23-en.pdf)
Framework:	Structure/Foundation/Input.
Rating Scale:	➜ NOT IMPLEMENTED (NI): There are no legal provisions or regulations to satisfy the requirement of the sub- indicator. ➜ ONGOING IMPLEMENTATION (OI): The NRA is taking steps towards establishment of legal provisions and regulations to satisfy the requirement of this sub-indicator; however no results exist so far. ➜ PARTIALLY IMPLEMENTED (PI): Legal provisions and regulations to satisfy the requirement of the sub-indicator were recently established and are in early implementation phase so no documented results yet exist. ➜ IMPLEMENTED (I): There are legal provisions and regulations which satisfy the requirement of the sub-indicator and which are actually implemented and enforced.
Limitations and remarks:	Scoring this sub-indicator as "not applicable NA" is excluded (i.e. this sub-indicator will always apply for all benchmarked NRAs).
Sub Indicator:	**MC01.06: Guidelines exist for importers that specify the format and content of the relevant applications and procedures to receive the necessary authorizations or permissions.**
Maturity Level:	2
Scope:	1. Medicines 2. Vaccines
Description:	The assessor should verify the existence and implementation of guidelines for importers that specify the format and content of the relevant applications and procedures to receive the necessary authorizations or permissions.
Objective:	The objective of this sub-indicator is to ensure the existence of guidelines for import activities as a tool for ensuring the quality and effectiveness of NRA's actions of surveillance and market control. The guidelines are necessary to establish clearly the rules that importers have to follow to obtain the necessary authorizations or permissions from the NRA.
Requirement:	Guidelines for the format and content of import authorizations or permissions.
Evidence to review:	The assessor should ask for and review: 1. Guidelines for applicants on the format and content of import authorizations or permissions
References:	1. Guidelines on import procedures for pharmaceutical products, World Health Organization (WHO), (22), (http://digicollection.org/whoqapharm/p/about and http://apps.who.int/medicinedocs/en)
Framework:	Structure/Foundation/Input.
Rating Scale:	➜ NOT IMPLEMENTED (NI): There are no guidelines to satisfy the requirement of the sub-indicator. ➜ ONGOING IMPLEMENTATION (OI): The NRA is taking steps towards establishment of guidelines to satisfy the requirement of this sub-indicator; however no results exist so far. ➜ PARTIALLY IMPLEMENTED (PI): Guidelines to satisfy the requirement of the sub-indicator were recently established and are in early implementation phase so no documented results yet exist. ➜ IMPLEMENTED (I): There are guidelines which satisfy the requirement of the sub-indicator and which are actually implemented and enforced.

Limitations and remarks:	▪ Formal guidelines might not exist, however relevant guidance may be provided in other types of documentation (e.g., regulations). ▪ Scoring this sub-indicator as "not applicable NA" is excluded (i.e. this sub-indicator will always apply for all benchmarked NRAs).
Sub Indicator:	**MC01.07: Guidelines exist on the recall, storage and disposal of SF medical products.**
Maturity Level:	2
Scope:	1. Medicines 2. Vaccines
Description:	The assessor should verify the existence of national guidelines for relevant entities on the best practices for effective recall of SF medical products. The guidelines should cover recalls throughout the supply chain up to the desired point (e.g. distributor, wholesaler, or point of sale or use) so that the detected SF medical products are removed from the supply chain. In addition, the assessor should check if a guideline on the best practices for handling recalled SF medical products includes provisions for safe storage and disposal that provide a high degree of assurance that the detected SF medical products will not be re-introduced to the supply chain. Furthermore, the guidelines should ideally provide guidance on the ways by which recall effectiveness is measured in terms of time, recalled units and other relevant aspects.
Objective:	The objective of this sub-indicator is to ensure the existence of guidelines for recall, storage and disposal of SF medical products. These guidelines should ideally reflect the NRA thinking and provide guidance to the responsible entity about effective actions that prevent re-introduction of detected SF medical products into the market.
Requirement:	Guidelines for recall, storage and disposal of SF medical products.
Evidence to review:	The assessor should ask for and review: 1. Guidelines relevant to recall and safe disposal of SF medical products.
References:	1. WHO good manufacturing practices for pharmaceutical products: main principles, (51), (http://digicollection.org/whoqapharm/p/about and http://apps.who.int/medicinedocs/en) 2. WHO good distribution practices for pharmaceutical products, World Health Organization (WHO), (27), (http://digicollection.org/whoqapharm/p/about and http://apps.who.int/medicinedocs/en) 3. Guidelines for Safe Disposal of Unwanted Pharmaceuticals in and after Emergencies, (97), (http://apps.who.int/medicinedocs/pdf/whozip51e/whozip51e.pdf)
Framework:	Structure/Foundation/Input.
Rating Scale:	➔ NOT IMPLEMENTED (NI): There are no guidelines to satisfy the requirement of the sub-indicator. ➔ ONGOING IMPLEMENTATION (OI): The NRA is taking steps towards establishment of guidelines to satisfy the requirement of the sub-indicator however no results are yet exist. ➔ PARTIALLY IMPLEMENTED (PI): Guidelines to satisfy the requirement of the sub-indicator were recently established and are in early implementation phase so no documented results yet exist. ➔ IMPLEMENTED (I): There are guidelines which satisfy the requirement of the sub-indicator and which are actually implemented and enforced.
Limitations and remarks:	▪ Formal guidelines might not exist, however relevant guidance may be provided in other types of documentation (e.g., regulations). ▪ Scoring this sub-indicator as "not applicable NA" is excluded (i.e. this sub-indicator will always apply for all benchmarked NRAs).

Indicator:	**MC02 Arrangement for effective organization and good governance.**
Objective:	The objective of this indicator is to ensure the implementation of effective organization and good governance practices at the organizational structures in charge of establishment licensing activities, which in turn contributes to effective and efficient functioning of the market surveillance and control activities.
Category:	02. Organization and governance
Sub Indicator:	**MC02.01: There is a defined structure, with clear responsibilities, to conduct market surveillance and control activities.**
Maturity Level:	2
Scope:	1. Medicines 2. Vaccines
Description:	The assessor should identify the organization with responsibility to establish, implement and maintain the market surveillance and control regulatory function, including the specific organizational structures assigned the different relevant activities. Responsibilities, duties and roles of these structures should be clearly defined and documented. If more than one organizational structure is involved, the assessor should check the ways and approaches by which coordination among these structures takes place.
Objective:	The objective of this sub-indicator is to ensure effective organization and good governance of market surveillance and control activities and that these activities are taken over by defined organizational structures with clear roles and responsibilities.
Requirement:	Roles and responsibilities of the structures in charge of market surveillance and control activities.
Evidence to review:	The assessor should ask for and review: 1. Organization chart of the institution responsible for the implementation of market surveillance and control activities. The chart and related information should identify the particular structures responsible for implementing the function. 2. Documentation clarifying roles and responsibilities of the structures implementing market surveillance and control activities. These may include administrative decrees, terms of reference, or other relevant documentation. 3. Documentation identifying and establishing mechanisms of coordination (e.g., committees, internal work-sharing and workflow) among the structures, if any, that take part in market surveillance and control activities.
References:	1. National drug regulatory legislation: guiding principles for small drug regulatory authorities. In: WHO Expert Committee on Specifications for Pharmaceutical Preparations: thirty-fifth report. Geneva: World Health Organization; 1999: Annex 8 (WHO Technical Report Series, No. 885), (1), (http://apps.who.int/medicinedocs/documents/s21964en/s21964en.pdf)
Framework:	Structure/Foundation/Input.
Rating Scale:	➜ NOT IMPLEMENTED (NI): There is no defined structure in charge of market surveillance and control activities. ➜ ONGOING IMPLEMENTATION (OI): A mandate to establish a structure in charge of market surveillance and control activities is available; however the structure itself is not established yet. ➜ PARTIALLY IMPLEMENTED (PI): A structure in charge of market surveillance and control activities is newly established and mandated; however the regular work and practice of this structure is not consolidated yet. ➜ IMPLEMENTED (I): There is a defined structure in charge of market surveillance and control activities with clear and well documented roles and responsibilities.

Limitations and remarks:	Scoring this sub-indicator as "not applicable NA" is excluded (i.e. this sub-indicator will always apply for all benchmarked NRAs).
Sub Indicator:	**MC02.02: Documented procedures or mechanisms are implemented to ensure the involvement and communication among all stakeholders relevant to market surveillance and control activities.**
Maturity Level:	3
Scope:	1. Medicines 2. Vaccines
Description:	The assessor should verify that the different stakeholders relevant to market surveillance and control regulatory function are identified. These stakeholders may include not only different organizational structures (e.g., organizations, institutions, or departments) that implement the function, but also other entities such as: other governmental agencies (e.g., laboratories, police departments, and customs and judicial authorities), regional and international organizations (e.g. WHO), non-governmental organizations, professional associations, customer representative associations, and industry representatives (e.g., manufacturers, distributors, and wholesalers). In addition, the assessor should verify the availability and implementation of agreements, memoranda of understanding (MOUs) and other documented procedures that ensure the involvement, communication and collaboration among the identified stakeholders relevant to market surveillance and control activities.
Objective:	The objective of this sub-indicator is to ensure that documented procedures or other mechanisms are implemented to ensure the involvement and communication among different organizations, institutions, and departments, as well as the appropriate organization and good governance of the function.
Requirement:	Agreements, MOUs and procedures for collaboration among stakeholders relevant to market surveillance and control regulatory function.
Evidence to review:	The assessor should ask for and review: 1. List of stakeholders relevant to market surveillance and control. 2. Agreements, MOUs or standard operating procedures (SOPs) that describe the procedures for communication and collaboration among the identified stakeholders. 3. Example records of communications and collaborations that demonstrate implementation of the above mentioned procedures. 4. Guidelines or SOPs that cover external and internal communications. 5. Evidence that demonstrates that there are regular formal meetings or official communications among the above- mentioned key players. These are important to verify that it is a systematic and well established process. 6. Documentation of paths of communication and reporting. 7. Documentation of platforms for information sharing and exchange.
References:	1. National drug regulatory legislation: guiding principles for small drug regulatory authorities. In: WHO Expert Committee on Specifications for Pharmaceutical Preparations: thirty-fifth report. Geneva: World Health Organization; 1999: Annex 8 (WHO Technical Report Series, No. 885), (1), (http://apps.who.int/medicinedocs/documents/s21964en/s21964en.pdf)
Framework:	Structure/Foundation/Input.
Rating Scale:	➔ NOT IMPLEMENTED (NI): There are no information exchange procedures or mechanisms among different stakeholders of the market surveillance and control function or between the central authority and the decentralized entities. ➔ ONGOING IMPLEMENTATION (OI): The NRA is developing an information exchange mechanism, but it is not ready yet or exchanges are being conducted without an established methodology.

	➔ PARTIALLY IMPLEMENTED (PI): The NRA recently established an information exchange procedure or mechanism and it is at the implementation stage, so this practice is not consolidated yet. ➔ IMPLEMENTED (I): There are established, implemented and maintained information exchange procedures or mechanisms among different stakeholders of the market surveillance and control function and between the central authority and the decentralized entities.
Limitations and remarks:	Scoring this sub-indicator as "not applicable NA" is excluded (i.e. this sub-indicator will always apply for all benchmarked NRAs).
Indicator:	**MC03 Human resources to perform market surveillance and control activities.**
Objective:	The objective of this indicator is to ensure to that all entities within a National Regulatory Authority (NRA) are adequately resourced with a trained, experienced and skilled workforce that is empowered to fully perform the market surveillance and control function. This will ensure that market surveillance and control processes and activities are performed in accordance with international best practices. The objective of this indicator is to evaluate the human resource capacity of the entities with respect to the number of personnel, the skills and experience of the personnel, and the overall composition the workforce, with the goal of evaluating whether the workforce possesses the specific expertise required to perform the market surveillance and control function.
Category:	06. Resources (HR, FR, infrastructure and equipment)
Sub Indicator:	**MC03.01: Sufficient competent staff (i.e., education, training, skills and experience) are assigned to perform market surveillance and control activities.**
Maturity Level:	3
Scope:	1. Medicines 2. Vaccines
Description:	The assessor should verify that the human resources assigned to perform market surveillance and control activities should be sufficient with respect to numbers and competent with respect to the requisite skills, education, experience and training. There should be technical documents and SOPs that provide guidance on the required background for market surveillance and control activities and that consider the requirements for educational background, competencies, skills, experience, and training. The assessor should verify that the NRA estimated the number of staff required to effectively and efficiently perform market surveillance and control function and that the NRA actually recruited that number. In addition, the assessor should verify that these competency requirements are well-established and maintained by the NRA. Metrics and statistics on the different activities performed as well as performance indicators can be used for estimating the adequacy of the number of the assigned staff. The assessor should also verify that the competency of the assigned staff is built, maintained and improved through recruitment as well as continuous on-the-job training.
Objective:	The objective of this sub-indicator is to ensure the existing human resources for market surveillance and control are sufficient, in terms of numbers, experience, and specific competencies, to perform all the activities along the entire market surveillance and control chain.
Requirement:	Sufficient number of competent human resources in charge of market surveillance and control activities.
Evidence to review:	The assessor should ask for and review: 1. Evidence that the number of staff members involved in each of the documented activities along the entire market surveillance and control process flow is adequate.

	2. Evidence that the systems and structures are in place to ensure appropriate placement of staff with respect to competence and skills. 3. Evidence that the system and structures have been implemented. The documentation should include the records to verify that the staff competence is appropriate for the job requirements. 4. Evidence that the professional profiles of the human resources engaged in market surveillance and control activities are appropriate with respect to education, skills, and expertise, to perform a particular function along the market surveillance and control chain. Documentation should include a list of the requisite skills and training for each position. 5. Recruitment plan.
References:	1. Quality management systems — Requirements. International Standard ISO 9001:2015. Geneva. International Organization for Standardization, 2015, (4), (https://www.iso.org/iso-9001-quality-management.html)
Framework:	Structure/Foundation/Input.
Rating Scale:	➜ NOT IMPLEMENTED (NI): The NRA does not have enough competent staff (i.e., education, training, skills and experience) to perform market surveillance and control activities ➜ ONGOING IMPLEMENTATION (OI): The NRA has recently developed a plan to recruit adequate competent staff; however, the plan has not been implemented. ➜ PARTIALLY IMPLEMENTED (PI): The NRA has initiated the implementation of the human resources development plan; however, there is need to complete the competency profile. ➜ IMPLEMENTED (I): The NRA has a sustained number of competent staff (i.e., education, training, skills and experience) assigned to perform market surveillance and control activities.
Limitations and remarks:	▪ Assessment of the adequacy and appropriateness of the number of staff members is quite subjective and should be linked to some process or output indicators. When estimating staff adequacy, the assessor should consider the workload, backlog, and delays in delivery based on established timeframes. ▪ In some countries, internal staff might not be sufficient; however external staff (e.g., fellows or interns) may be involved in the performance of the work. ▪ Scoring this sub-indicator as "not applicable NA" is excluded (i.e. this sub-indicator will always apply for all benchmarked NRAs).
Sub Indicator:	**MC03.02: Duties, functions, and responsibilities of the staff in charge of market surveillance and control activities are established and updated in the respective job descriptions**
Maturity Level:	3
Scope:	1. Medicines 2. Vaccines
Description:	The assessor should verify that procedures are in place to maintain a current and updated structure for managing job descriptions for personnel participating in market surveillance and control activities. In addition, job descriptions should address current staff duties, responsibilities and the requisite competencies. A job description with this format and content should be established and implemented for all staff. The management of job descriptions should be supported by a guidance document that provides direction on when and how to update the information, and where the information should be kept for easy access. The guidance document should present the appropriate duties and responsibilities that are assigned to each member of the organization involved in market surveillance and control activities. Thus, the professional profiles of staff are reflected in their respective roles and responsibilities within the NRA. There should be procedures to guide responsible persons to document that duties, functions and responsibilities are revised and kept up to date. In addition, procedures should be available to guide the keeping and documenting of up to date work schedules and enforcing the implementation of the documented guidelines and procedures.

Objective:	The objective of this sub-indicator is to ensure that duties and responsibilities of the staff are clear and well defined, that job descriptions are kept up to date with current duties, functions and responsibilities, and that these activities are adequately documented
Requirement:	Duties, roles and responsibilities of the staff relevant to market surveillance and control activities.
Evidence to review:	The assessor should ask for and review: 1. Procedures and guidelines that guide placement of staff members within the NRA; 2. The professional profiles of staff (i.e., job descriptions) and documentation that they are related to their current roles and duties; 3. The professional profiles of the external experts and documentation that the profiles provide a composition that is complete and consistent with that prescribed in the legal provisions; 4. Procedures to guide the documentation of up to date duties and work schedules, and to enforce the implementation of the documented guidelines and procedures; 5. Job descriptions for designated staff.
References:	1. National drug regulatory legislation: guiding principles for small drug regulatory authorities. In: WHO Expert Committee on Specifications for Pharmaceutical Preparations: thirty-fifth report. Geneva: World Health Organization; 1999: Annex 8 (WHO Technical Report Series, No. 885), (1), (http://apps.who.int/medicinedocs/documents/s21964en/s21964en.pdf) 2. Quality management systems — Requirements. International Standard ISO 9001:2015. Geneva. International Organization for Standardization, 2015, (4), (https://www.iso.org/iso-9001-quality-management.html) 3. Guiding principles for small national drug regulatory authorities. In: WHO Expert Committee on Specifications for Pharmaceutical Preparations: thirty-first report. Geneva: World Health Organization; 1990: Annex 6 (WHO Technical Report Series, No. 790), (5), (http://apps.who.int/medicinedocs/documents/s21964en/s21964en.pdf) 4. Effective drug regulation: A multicounty study. Geneva: World Health Organization; 2002, (7), (http://apps.who.int/medicinedocs/pdf/s2300e/s2300e.pdf)
Framework:	Structure/Foundation/Input.
Rating Scale:	➜ NOT IMPLEMENTED (NI): There is no evidence of defined or established duties, functions, responsibilities, respective job descriptions and necessary required competencies. ➜ ONGOING IMPLEMENTATION (OI): The NRA has recently drafted or developed the role and responsibilities document but it has not yet been implemented. ➜ PARTIALLY IMPLEMENTED (PI): The NRA has initiated implementation of this requirement but it has not been defined or followed for all staff or the roles and responsibilities documents, including staff job descriptions, are not up to date. ➜ IMPLEMENTED (I): The NRA has defined and established all required duties, functions, and responsibilities, and respective job descriptions are up-to-date.
Limitations and remarks:	Scoring this sub-indicator as "not applicable NA" is excluded (i.e. this sub-indicator will always apply for all benchmarked NRAs).
Sub Indicator:	**MC03.03: Training plan developed, implemented and updated at least once a year for staff in charge of market surveillance and control activities.**
Maturity Level:	3
Scope:	1. Medicines 2. Vaccines
Description:	The assessor should verify that training plans are developed, implemented and updated at least once every year to reflect the current situation by considering education and experience of the staff. The training plan should be complemented with guidelines or

	similar documents that guide the development and implementation of training plans. The assessor should ensure that induction training for new staff as well as continued on- the-job for staff is planned and implemented. There should be procedures to approve the training plan and the budget allocated for implementing and updating the training plan. The plans should present clearly defined training goals, and should include training in certain topics and skills to address identified deficiencies. Learning objectives, training methods and activities, evidence of learning, and evaluation and assessment of training should be documented. This documentation should confirm that the learning objectives were achieved and were designed to address weaknesses within the entities. Procedures should be in place to ensure that a training plan is developed, implemented and updated at least once every year. The assessor should verify that there is a system in place for monitoring the implementation and effectiveness of the training plan and for documenting the skills acquired in training activities for internal and external experts.
Objective:	The objective of this sub-indicator is to ensure that a training plan for staff exists, and that it is implemented and updated annually. Through the training plan, NRA can be sure that competency of staff in charge of market surveillance and control activities is maintained and enhanced.
Requirement:	Implementation of training plan
Evidence to review:	The assessor should ask for and review: 1. Guidelines for development, implementation and annual update (i.e., at least once per year) of the training plan. Guidelines should also provide for a mechanism to measure effectiveness of training. 2. Documentation for the system or structures used to approve the training plan and to evaluate the adequacy of the budget allocated to the training activities. 3. The current or existing staff training plan (or matrix) for staff. The assessor should assess this in in relation to the respective individual job descriptions. 4. SOP for developing and maintaining the training plan. 5. Evidence that the NRA has investigated and identified training needs. 6. List of trainings performed. 7. Example records for training activities.
References:	1. National drug regulatory legislation: guiding principles for small drug regulatory authorities. In: WHO Expert Committee on Specifications for Pharmaceutical Preparations: thirty-fifth report. Geneva: World Health Organization; 1999: Annex 8 (WHO Technical Report Series, No. 885), (1), (http://apps.who.int/medicinedocs/documents/s21964en/s21964en.pdf) 2. Quality management systems — Requirements. International Standard ISO 9001:2015. Geneva. International Organization for Standardization, 2015, (4), (https://www.iso.org/iso-9001-quality-management.html) 3. Guiding principles for small national drug regulatory authorities. In: WHO Expert Committee on Specifications for Pharmaceutical Preparations: thirty-first report. Geneva: World Health Organization; 1990: Annex 6 (WHO Technical Report Series, No. 790), (5), (http://apps.who.int/medicinedocs/documents/s21964en/s21964en.pdf) 4. Effective drug regulation: A multicounty study. Geneva: World Health Organization; 2002, (7), (http://apps.who.int/medicinedocs/pdf/s2300e/s2300e.pdf)
Framework:	Process
Rating Scale:	➜ NOT IMPLEMENTED (NI): There is no systematic training program including training plan (or matrix). ➜ ONGOING IMPLEMENTATION (OI): The NRA has recently drafted or developed the training plan but there is no evidence of implementation. ➜ PARTIALLY IMPLEMENTED (PI): The NRA has developed and initiated the training plan implementation. However, the NRA has not fulfilled all required planned training or has been applying the plan for less than two years. ➜ IMPLEMENTED (I): The NRA has an updated training plan developed that is

	supported by adequate records to demonstrate effective plan implementation, including induction training for new staff and routine on-the-job training for recruited staff.
Limitations and remarks:	▪ Training plans must be updated regularly; ideally on an annual basis, but not less frequently that once every two years. ▪ Some regulatory functions may include many training activities that are not incorporated in the institutional training programme. Such training normally is offered by invitation. In this case, the assessor should recognize reports from non-routine market surveillance and control -relevant training not included in the NRA training plan. ▪ Scoring this sub-indicator as "not applicable NA" is excluded (i.e. this sub-indicator will always apply for all benchmarked NRAs).
Sub Indicator:	**MC03.04: The NRA generates and maintains records of staff training activities and training effectiveness verification.**
Maturity Level:	3
Scope:	1. Medicines 2. Vaccines
Description:	The assessor should verify that records of staff training that is performed or organized by the NRA are generated, maintained, regularly updated. This activity should be supported by guidelines that direct the NRA to generate and maintain records of staff training activities. Procedures should be in place to document and propose staff training needs and to allocate a budget for continuous staff capacity building and development. The assessor should check that there is an evaluation or assessment mechanism to verify the quality of learning, and to confirm that learning objectives are achieved. Documentation should include an inventory (i.e., soft and/or hard) system that records all impactful and non-impactful trainings, and identifies all staff members who participated. A system to measure or estimate impact of trainings should be established.
Objective:	The objective of this sub-indicator is to ensure that training organized by the NRA or responsible regulatory authority is adequately documented and that the training records are adequately maintained and kept. Staff training records are considered an integral part of staff file and are a tool for measuring and tracking staff competency, development and adequacy.
Requirement:	Training records
Evidence to review:	The assessor should ask for and review: 1. Guidelines or similar documents that guide the NRA to generate and maintain records of staff training activities; 2. Evaluations of training effectiveness; 3. The training inventory, and procedures for completing the inventory; 4. Examples of archived records of staff training, and procedures for the archiving system
References:	1. National drug regulatory legislation: guiding principles for small drug regulatory authorities. In: WHO Expert Committee on Specifications for Pharmaceutical Preparations: thirty-fifth report. Geneva: World Health Organization; 1999: Annex 8 (WHO Technical Report Series, No. 885), (1), (http://apps.who.int/medicinedocs/documents/s21964en/s21964en.pdf) 2. Quality management systems — Requirements. International Standard ISO 9001:2015. Geneva. International Organization for Standardization, 2015, (4), (https://www.iso.org/iso-9001-quality-management.html) 3. Guiding principles for small national drug regulatory authorities. In: WHO Expert Committee on Specifications for Pharmaceutical Preparations: thirty-first report. Geneva: World Health Organization; 1990: Annex 6 (WHO Technical Report Series, No. 790), (5), (http://apps.who.int/medicinedocs/documents/s21964en/s21964en.pdf) 4. Effective drug regulation: A multicounty study. Geneva: World Health Organization; 2002, (7), (http://apps.who.int/medicinedocs/pdf/s2300e/s2300e.pdf)

Framework:	Output
Rating Scale:	➔ NOT IMPLEMENTED (NI): There is no evidence that the NRA generates and maintains records of staff training activities. ➔ ONGOING IMPLEMENTATION (OI): The NRA has recently initiated plans to generate, document and keep records of staff training activities, however they are not yet followed. ➔ PARTIALLY IMPLEMENTED (PI): The NRA has recently initiated plans to generate, document and keep records of staff training activities but they are not fully followed for all training activities or they have been established for less than two years. ➔ IMPLEMENTED (I): The NRA generates and maintains records of staff training activities.
Limitations and remarks:	▪ The assessor should note that some NRAs out-source training including staff capacity development activities. In this case the assessor should request the identity of the provider, as well as evaluations of the provider. The assessor may request the professional profiles of tutors or resource persons used to offer training. The assessor may also request records covering the archiving systems in place. ▪ Scoring this sub-indicator as "not applicable NA" is excluded (i.e. this sub-indicator will always apply for all benchmarked NRAs).
Indicator:	**MC04 Procedures established and implemented to perform market surveillance and control**
Objective:	The objective of this indicator is to ensure that different activities of the market surveillance and control programme are implemented through standard procedures and work instructions in order to ensure consistency, effectiveness, efficiency, impartiality and proportionality of the programme.
Category:	07. Regulatory process
Sub Indicator:	**MC04.01: Documented and implemented procedures exist to grant the necessary authorizations or permissions for import activities.**
Maturity Level:	3
Scope:	1. Medicines 2. Vaccines
Description:	The assessor should verify the availability of documented standard procedures within the NRA to receive, review and make a decision on import applications of medical products. The assessor should also verify proper implementation of the procedures through review of the relevant records and documentation. The records for an application should include documentation of receipt, screening, review, regulatory decision-making, (i.e., approval or denial), and notification of the applicant. Regulatory decisions should be scientifically justifiable.
Objective:	The objective of this sub-indicator is to ensure that the control of import activities of medical products are an integral part of the overall market surveillance and control regulatory function. Therefore, procedures to handle and decide on (i.e., approve or deny) applications relevant to these activities are essential to ensure the consistency and effectiveness of these regulatory activities.
Requirement:	Procedures along with their relevant records for regulatory decisions on import activities
Evidence to review:	The assessor should ask for and review: 1. SOPs that guide the handling of applications for medical products import activities. 2. List of import applications over a wide range of time (e.g., 6 months or 1 year). 3. Example records and documentation of receiving, processing and decision-making for medical products import applications.

References:	1. Guidelines on import procedures for pharmaceutical products, World Health Organization (WHO), (22), (http://digicollection.org/whoqapharm/p/about and http://apps.who.int/medicinedocs/en) 2. Guidelines on the implementation of the WHO certification scheme on the quality of pharmaceutical products moving in international commerce. In WHO Expert Committee on Specifications for Pharmaceutical Preparations: thirty-fourth report. Geneva. World Health Organization; 1996: Annex 10 (WHO Technical Report Series, No. 863), (29), (http://apps.who.int/medicinedocs/pdf/s5516e/s5516e.pdf)
Framework:	Process
Rating Scale:	➔ NOT IMPLEMENTED (NI): There are no documented procedures in the NRA for the prevention of unauthorized import activities, and no procedures to grant the necessary authorizations or permissions for import activities. ➔ ONGOING IMPLEMENTATION (OI): The NRA has taken some steps to establish procedures to grant the necessary authorizations or permissions for import activities; however no results exist so far. ➔ PARTIALLY IMPLEMENTED (PI): Documented procedures to grant the necessary authorizations or permissions for import activities were recently established; however the procedures are recently implemented and no results associated with this sub-indicator are documented yet. ➔ IMPLEMENTED (I): There are documented procedures to grant the necessary authorizations or permissions for import activities, and these procedures are actually implemented.
Limitations and remarks:	Scoring this sub-indicator as "not applicable NA" is excluded (i.e. this sub-indicator will always apply for all benchmarked NRAs).
Sub Indicator:	**MC04.02: Documented and implemented procedures exist for regulation of promotion and advertisement of medical products**
Maturity Level:	3
Scope:	1. Medicines 2. Vaccines
Description:	The assessor should verify the availability of documented standard procedures within the NRA to receive, review and make a decision on promotion, marketing and advertisement applications. Assessor should also verify proper implementation of the procedures through review of the relevant records and documentation. The records for an application should include documentation of receipt, screening, review and regulatory decision-making, (i.e., approval or denial), and notification of the applicant. Regulatory decisions should be scientifically justifiable.
Objective:	The objective of this sub-indicator is to ensure that the control of promotion and advertisement of medical products is an integral part of the overall market surveillance and control regulatory function. Therefore, procedures to regulate the information that reaches health professionals, as well as the general public, are an important component to promote the rational use of these products.
Requirement:	Procedures along with the relevant records for engagement of regulatory entities in the regulation of promotion and advertisement of medical products.
Evidence to review:	The assessor should ask for and review: 1. SOPs that guide the handling of applications for promotion and advertisement activities. 2. List of promotion, marketing and advertisement applications received and reviewed over a wide range of time (e.g., 6 months or 1 year). 3. Example records and documentation of regulatory decisions on promotion and advertisement applications.

References:	1. Ethical Criteria for the Promotion, Advertisement, and Publicity of Medicines - PANDRH Series Technical Document No 12 (Pan American Network for Drug Regulatory Harmonization), (94), (http://apps.who.int/medicinedocs/documents/s22161en/s22161en.pdf) 2. Educational initiatives for medical and pharmacy students about drug promotion: an international cross-sectional survey. Geneva. World Health Organization, (92), (http://apps.who.int/medicinedocs/pdf/s8110e/s8110e.pdf) 3. Cross-border Advertising, Promotion and Sale of Medical Products Using the Internet. WHA Resolution; Fifty-First World Health Assembly, WHA51.9, (93), (http://apps.who.int/medicinedocs/documents/s21471en/s21471en.pdf) 4. Alternative Regulatory Models for Pharmaceutical Promotions Involving Civil Society and Other Non-Government Stakeholders, Medicines Transparency Alliance, (96), (http://apps.who.int/medicinedocs/documents/s22327en/s22327en.pdf) 5. Ethical Criteria for Medicinal Drug Promotion, World Health Organization, 1988, (13), (http://apps.who.int/medicinedocs/documents/whozip08e/whozip08e.pdf) 6. CIOMS/WHO Meeting on Ethical Criteria for Medicinal Drug Promotion. Essential Drugs Monitor No. 017, 1994, (90), (http://apps.who.int/medicinedocs/documents/s21142en/s21142en.pdf) 7. Drug Promotion: Push, Promote or Educate? Essential Drugs Monitor, No. 020, 1995, World Health Organization (WHO), (91), (http://apps.who.int/medicinedocs/documents/s21265en/s21265en.pdf) 8. Drug Promotion - What We Know, What We Have Yet to Learn - Reviews of Materials in the WHO/HAI Database on Drug Promotion, World Health Organization (WHO), (89), (http://apps.who.int/medicinedocs/pdf/s8109e/s8109e.pdf)
Framework:	Process
Rating Scale:	➜ NOT IMPLEMENTED (NI): There are no documented procedures in the NRA for regulation of promotion and advertisement of medical products. ➜ ONGOING IMPLEMENTATION (OI): The NRA has taken some steps to establish procedures for regulation of promotion and advertisement of medical products; however no results exist so far. ➜ PARTIALLY IMPLEMENTED (PI): Documented procedures in the NRA for regulation of promotion and advertisement of medical products were recently established; however the procedures are recently implemented and no results associated with this sub-indicator are documented yet. ➜ IMPLEMENTED (I): There are documented procedures in the NRA for regulation of promotion and advertisement of medical products, and these procedures are actually implemented.
Limitations and remarks:	▪ Procedures and documentation relating to the approval of promotion and advertisement applications might not exist if the NRA does not have the mandate to pre-approve such applications. In case no pre-approval system is in place the assessor should verify the existence of an alternative approach (e.g., active surveillance of promotional materials, rather than proactive approval) which satisfies the adequate control of promotion and advertisement activities. ▪ Scoring this sub-indicator as "not applicable NA" is excluded (i.e. this sub-indicator will always apply for all benchmarked NRAs).
Sub Indicator:	**MC04.03: Documented and implemented procedures for active monitoring of the promotion and advertisement of medical products**
Maturity Level:	4
Scope:	1. Medicines 2. Vaccines
Description:	The assessor should verify the availability of documented standard procedures within the NRA to actively monitor promotion and advertisement of medical products. These procedures should include screening mechanisms to identify false or misleading

	information contained in promotions and advertisements of medical products in the market. The monitoring and screening should include promotional materials on the internet. The assessor should also verify proper implementation of the procedures through checking of the relevant records and documentation. The records should include documentation of data collected, screening, review and regulatory decision- making, if any. Regulatory decisions should be scientifically justifiable.
Objective:	The objective of this sub-indicator is to ensure that the control of promotion and advertisement of medical products is an integral part of the overall market surveillance and control regulatory function. NRAs must have mechanisms in place to actively monitor these activities and take the necessary regulatory measures in case of misconduct.
Requirement:	Procedures along with the relevant records of regulatory decisions for monitoring the promotion and advertisement of medical products
Evidence to review:	The assessor should ask for and review: 1. SOPs that guide the active monitoring of the promotion and advertisement of medical products. 2. List of data collected from the market regarding the promotion and advertisement of medical products received over a wide range of time (e.g., 6 months or 1 year) 3. Example records and documentation of regulatory decisions, if any.
References:	1. Ethical Criteria for the Promotion, Advertisement, and Publicity of Medicines - PANDRH Series Technical Document No 12 (Pan American Network for Drug Regulatory Harmonization), (94), (http://apps.who.int/medicinedocs/documents/s22161en/s22161en.pdf) 2. Educational initiatives for medical and pharmacy students about drug promotion: an international cross-sectional survey. Geneva. World Health Organization, (92), (http://apps.who.int/medicinedocs/pdf/s8110e/s8110e.pdf) 3. Cross-border Advertising, Promotion and Sale of Medical Products Using the Internet. WHA Resolution; Fifty-First World Health Assembly, WHA51.9, (93), (http://apps.who.int/medicinedocs/documents/s21471en/s21471en.pdf) 4. Alternative Regulatory Models for Pharmaceutical Promotions Involving Civil Society and Other Non-Government Stakeholders, Medicines Transparency Alliance, (96), (http://apps.who.int/medicinedocs/documents/s22327en/s22327en.pdf) 5. Ethical Criteria for Medicinal Drug Promotion, World Health Organization, 1988, (13), (http://apps.who.int/medicinedocs/documents/whozip08e/whozip08e.pdf) 6. CIOMS/WHO Meeting on Ethical Criteria for Medicinal Drug Promotion. Essential Drugs Monitor No. 017, 1994, (90), (http://apps.who.int/medicinedocs/documents/s21142en/s21142en.pdf) 7. Drug Promotion: Push, Promote or Educate? Essential Drugs Monitor, No. 020, 1995, World Health Organization (WHO), (91), (http://apps.who.int/medicinedocs/documents/s21265en/s21265en.pdf) 8. Drug Promotion - What We Know, What We Have Yet to Learn - Reviews of Materials in the WHO/HAI Database on Drug Promotion, World Health Organization (WHO), (89), (http://apps.who.int/medicinedocs/pdf/s8109e/s8109e.pdf)
Framework:	Process
Rating Scale:	➜ NOT IMPLEMENTED (NI): There are no documented procedures in the NRA for active monitoring of the promotion and advertisement of medical products. ➜ ONGOING IMPLEMENTATION (OI): The NRA has taken some steps to establish procedures for active monitoring of the promotion and advertisement of medical products; however no results exist so far. ➜ PARTIALLY IMPLEMENTED (PI): Documented procedures in the NRA for active monitoring of the promotion and advertisement of medical products were recently established; however the procedures are recently implemented and no results associated with this sub-indicator are documented yet. ➜ IMPLEMENTED (I): There are documented procedures in the NRA for active monitoring of the promotion and advertisement of medical products and these procedures are actually implemented.

Limitations and remarks:	Scoring this sub-indicator as "not applicable NA" is excluded (i.e. this sub-indicator will always apply for all benchmarked NRAs).
Sub Indicator:	**MC04.04: Documented and implemented procedures exist for risk-based sampling of medical products from different points of the supply chain.**
Maturity Level:	3
Scope:	1. Medicines 2. Vaccines
Description:	The assessor should verify the availability within the NRA of a structured programme, with documented standard procedures, to carry out a medical products sampling and quality surveillance programme. The programme should be risk based with consideration of different risk factors (e.g. nature and category of products, location within the territory, manufacturer, product quality history, previous complaints, vigilance data, and any other relevant information). The quality surveillance programme should be extended to cover all points across the supply chain with emphasis on the terminal point and last stages of the chain (e.g., points of sale, handling or administration). The programme should include laboratory testing of the quality of the medical products. The assessor should also verify that procedures specify any follow up and regulatory actions to be undertaken in the event that SF medical products (i.e., products failing the quality surveillance) are detected. Ideally, the follow-up actions should include regulatory inspection when necessary.
Objective:	The objective of this sub-indicator is to ensure that risk based sampling and quality surveillance of medical products are implemented as a means for confirming quality of medical products in the market and throughout the supply chain. Additionally, a surveillance program may significantly contribute to detection of SF medical products.
Requirement:	Procedure along with relevant records for risk-based sampling of medical products on the market.
Evidence to review:	The assessor should ask for and review: 1. SOPs that guide medical product sampling and quality surveillance across the supply chain. 2. Examples of relevant records and documentation of surveillance activities, including product sampling, requests for testing, and testing results. 3. Examples of relevant records and documentation for any follow up or regulatory actions taken in the event that medical product failures are detected during the quality surveillance.
References:	1. Report on Post-Market Surveillance of First Line Anti-Tuberculosis Medicines in Kenya. Kenya Ministry of Public health and sanitation, MSH and USAID. 2012, (98), (http://apps.who.int/medicinedocs/documents/s21945en/s21945en.pdf) 2. Guidelines on the conduct of surveys of the quality of medicines, World Health Organization (WHO), (86), (http://apps.who.int/medicinedocs/en/q/ and http://digicollection.org/whoqapharm/)
Framework:	Process
Rating Scale:	➜ NOT IMPLEMENTED (NI): There are no documented procedures for risk-based sampling of medical products from different points of the supply chain. ➜ ONGOING IMPLEMENTATION (OI): The NRA has taken some steps to establish procedures for risk-based sampling of medical products from different points of the supply chain; however no results exist so far. ➜ PARTIALLY IMPLEMENTED (PI): Documented procedures for risk- based sampling of medical products from different points of the supply chain were recently established; however the procedures are recently implemented and no results associated with this sub-indicator are documented yet. ➜ IMPLEMENTED (I): There are documented procedures for risk-based sampling of medical products from different points of the supply chain, and these procedures are actually implemented.

Limitations and remarks:	Scoring this sub-indicator as "not applicable NA" is excluded (i.e. this sub-indicator will always apply for all benchmarked NRAs).
Sub Indicator:	**MC04.05: Documented and implemented procedures exist to enable the public to report suspected SF medical products.**
Maturity Level:	3
Scope:	1. Medicines 2. Vaccines
Description:	The assessor should verify the availability and implementation of documented procedures for enabling the public to report medical products suspected to be SF. Ideally the reporting procedures should be simple, effective, easy to use and accessible to a majority of the people. The reporting should be two-way, enabling public reporting to the NRA as well as regulatory feedback to the informants about the outcome of the relevant investigation. When appropriate, a wider group may be targeted for the feedback (e.g., media, professional associations, and customer representatives).
Objective:	The objective of this sub-indicator is to ensure that the public is involved in the reporting of suspected SF medical products as an essential approach for detection and prevention of this problem. In addition, these activities contribute to building the public confidence and trust in the regulatory system.
Requirement:	Procedures along with their relevant records to enable the public to report SF medical products
Evidence to review:	The assessor should ask for and review: 1. SOPs for enabling the public to report suspected SF medical products. 2. Examples of relevant records and documentation, including reporting forms, referral procedures, and reports of actions taken or regulatory decisions made, if any. 3. Examples of feedback to the informants.
References:	1. SF- Frequently asked questions. Scope, scale and harm. How big is the problem of SF medical products?, (87), (https://www.who.int/medicines/regulation/ssffc/faq-ssffc_1-10/en/) 2. Addressing the barriers to effective monitoring, reporting and containment of spurious/ substandard/falsely-labelled/ falsified/counterfeit medical products. A report prepared for the Medicines Transparency Alliance, Philippines: 2016, (88), (http://apps.who.int/ medicinedocs/documents/s22331en/s22331en.pdf) 3. Recommendations for health authorities to detect and deal with actions, activities and behaviors that result in substandard/spurious/falsely-labelled/falsified/counterfeit medical products, A68/33, annex 1, (129), (http://apps.who.int/gb/ebwha/pdf_files/WHA68/ A68_33-en.pdf) 4. Guidance on developing a national plan for preventing, detecting and responding to actions, activities and behaviors that result in SF medical products. WHO (document A70/23), (130), (https://www.who.int/medicines/regulation/ssffc/mechanism/A70_23-en6-14.pdf)
Framework:	Process
Rating Scale:	➜ NOT IMPLEMENTED (NI): There are no documented procedures to enable the public to report suspected SF medical products. ➜ ONGOING IMPLEMENTATION (OI): The NRA has taken some steps to establish procedures to enable the public to report suspected SF medical products; however no results exist so far. ➜ PARTIALLY IMPLEMENTED (PI): Documented procedures to enable the public to report suspected SF medical products were recently established; however such procedures are recently implemented and no results associated with this sub-indicator are documented yet. ➜ IMPLEMENTED (I): There are documented procedures to enable the public to report suspected SF medical products, and these procedures are actually implemented.

Limitations and remarks:	Scoring this sub-indicator as "not applicable NA" is excluded (i.e. this sub-indicator will always apply for all benchmarked NRAs).
Sub Indicator:	**MC04.06: Documented and implemented procedures exist in the NRA to review any complaints or market reports received.**
Maturity Level:	3
Scope:	1. Medicines 2. Vaccines
Description:	The assessor should verify the availability of documented procedures within the NRA to receive, review and respond to any complaints or reports related to medical products. These may include complaints and reports related to: (1) quality, safety or efficacy of medical products, (2) suspected cases of SF medical products, and (3) misconduct in promotion or advertising, including via the internet. Complaints and reports could be related to any medical product or company. The assessor should verify actual and proper implementation of the procedures through review of the relevant records and documentations. The records should include documentation of investigations of complaints and any subsequent regulatory decisions. Complaints and reports may come from consumers, health professionals, health institutions, and participants in the supply chain.
Objective:	The objective of this sub-indicator is to ensure that complaints and reports, as a major feedback mechanism about market control activities, are properly received and handled following well-established procedures in order to ensure consistency and effectiveness in the responses to these cases.
Requirement:	Procedures along with relevant records of regulatory decisions on complaints and reports received.
Evidence to review:	The assessor should ask for and review: 1. SOPs that guide the handling of complaints and reports. 2. List of market complaints and reports over a wide range of time (e.g., 6 months or 1 year). 3. Examples of market complaints and reports along with associated records (e.g., reports of case investigations and any subsequent regulatory decisions).
References:	1. WHO good manufacturing practices for pharmaceutical products: main principles, (51), (http://digicollection.org/whoqapharm/p/about and http://apps.who.int/medicinedocs/en)
Framework:	Process
Rating Scale:	➜ NOT IMPLEMENTED (NI): There are no documented procedures in the NRA to review and respond to any complaints or market reports received. ➜ ONGOING IMPLEMENTATION (OI): The NRA has taken some steps to establish procedures to review and respond to any complaints or market reports received; however no results exist so far. ➜ PARTIALLY IMPLEMENTED (PI): Documented procedures in the NRA to review and respond to any complaints or market reports received were recently established; however such procedures are recently implemented and no results associated with this sub-indicator are documented yet. ➜ IMPLEMENTED (I): There are documented procedures in the NRA to review and respond to any complaints or market reports received, and these procedures are actually implemented.
Limitations and remarks:	Scoring this sub-indicator as "not applicable NA" is excluded (i.e. this sub-indicator will always apply for all benchmarked NRAs).

Sub Indicator:	**MC04.07: Documented and implemented procedures and mechanisms exist to prevent, detect and respond to SF medical products.**
Maturity Level:	3
Scope:	1. Medicines 2. Vaccines
Description:	The assessor should verify the availability of documented standard procedures and mechanisms within the NRA to prevent, detect and respond to SF products in the market, including products being distributed via the internet. These procedures and mechanisms should include various approaches. Examples of approaches for detection of SF medical products might include routine inspections, targeted risk-based surveys, or investigations of reports of complaints, suspicious observations, unexpected adverse events, or whistle-blower concerns. Similarly measures for prevention of SF medical products might include public education and awareness campaigns, as well as other measures to ensure access to and affordability of quality medical product. Actions for response to SF medical products might include rapid alerts, prosecutions, and recalls, quarantines, or withdrawals of affected products. The assessor should verify actual and proper implementation of the procedures through checking of the relevant records and documentation. The records should include relevant databases, evidence collected, investigation reports (including descriptions of any field procedures, inspections and intelligence activities that might have been carried out jointly or with the support of national and international stakeholders) and any follow-up regulatory decisions.
Objective:	The objective of this sub-indicator is to ensure that well established procedures or mechanisms are implemented for the prevention, detection, and response to SF medical products.
Requirement:	Procedures along with the relevant records for prevention, detection and response to SF medical products
Evidence to review:	The assessor should ask for and review: 1. SOPs and other mechanisms to prevent, detect and respond to SF medical products. 2. Example records and documentation of prevention, detection and response to SF medical products.
References:	1. Addressing the barriers to effective monitoring, reporting and containment of spurious/ substandard/falsely-labelled/ falsified/counterfeit medical products. A report prepared for the Medicines Transparency Alliance, Philippines: 2016, (88), (http://apps.who.int/medicinedocs/documents/s22331en/s22331en.pdf) 2. SF- Frequently asked questions. Scope, scale and harm. How big is the problem of SF medical products?, (87), (https://www.who.int/medicines/regulation/ssffc/faq-ssffc_1-10/en/) 3. WHO Member State Mechanism on substandard/spurious/falsely-labelled/falsified/counterfeit medical products, A70/23, appendix 3, Working Definitions, (128), (https://www.who.int/medicines/regulation/ssffc/A70_23-en1.pdf) 4. Recommendations for health authorities to detect and deal with actions, activities and behaviors that result in substandard/spurious/falsely-labelled/falsified/counterfeit medical products, A68/33, annex 1, (129), (http://apps.who.int/gb/ebwha/pdf_files/WHA68/A68_33-en.pdf) 5. Guidance on developing a national plan for preventing, detecting and responding to actions, activities and behaviors that result in SF medical products. WHO (document A70/23), (130), (https://www.who.int/medicines/regulation/ssffc/mechanism/A70_23-en6-14.pdf)
Framework:	Process
Rating Scale:	➔ NOT IMPLEMENTED (NI): There are no documented procedures or mechanisms, in the NRA, for prevention, detection and response to SF medical products.

	➔ ONGOING IMPLEMENTATION (OI): The NRA has taken some steps to establish procedures and mechanisms for prevention, detection and response to SF medical products; however no results exist so far. ➔ PARTIALLY IMPLEMENTED (PI): Documented procedures and mechanisms for prevention, detection and response to SF medical products were recently established in the NRA; however such procedures are recently implemented and no results associated with this sub-indicator are documented yet. ➔ IMPLEMENTED (I): There are documented procedures and mechanisms, in the NRA, for prevention, detection and response to SF medical products, and these procedures are actually implemented.
Limitations and remarks:	Scoring this sub-indicator as "not applicable NA" is excluded (i.e. this sub-indicator will always apply for all benchmarked NRAs).
Sub Indicator:	**MC04.08: Documented and implemented procedures exist to ensure safe storage and disposal of detected SF medical products.**
Maturity Level:	3
Scope:	1. Medicines 2. Vaccines
Description:	The assessor should verify the availability of documented standard procedures within the NRA for safe storage and disposal of detected SF medical products. Safe storage and disposal provides assurance that detected SF medical products are not re-introduced to the market and that the best practices were employed to avoid or minimize adverse effects of this disposal on the people and environment. The assessor should also verify actual and proper implementation of the procedures through review of the relevant records and documentation. The records should include proof of storage and disposal along with documentation for the reconciliation between the recovered quantities versus the disposed ones.
Objective:	The objective of this sub-indicator is to ensure the control of detected SF medical products. Therefore, a national policy and strategy, combined with procedures to ensure safe storage and disposal of detected SF medical products, are essential to avoid re-introduction of these products to the market.
Requirement:	Procedures along with their relevant records for safe storage and disposal of SF medical products
Evidence to review:	The assessor should ask for and review: 1. SOPs for storage and disposal of SF medical products. 2. Example records and documentation of SF medical products storage and disposal including reconciliation of quantities (i.e., quantities detected, recovered, or recalled vs. quantities disposed).
References:	1. Guidelines for Safe Disposal of Unwanted Pharmaceuticals in and after Emergencies, (97), (http://apps.who.int/medicinedocs/pdf/whozip51e/whozip51e.pdf) 2. WHO good manufacturing practices for pharmaceutical products: main principles, (51), (http://digicollection.org/whoqapharm/p/about and http://apps.who.int/medicinedocs/en)
Framework:	Process
Rating Scale:	➔ NOT IMPLEMENTED (NI): There are no documented procedures, in the NRA, to ensure safe storage and disposal of detected SF medical products. ➔ ONGOING IMPLEMENTATION (OI): The NRA has taken some steps to establish procedures to ensure safe storage and disposal of detected SF medical products; however no results exist so far.

	➔ PARTIALLY IMPLEMENTED (PI): Documented procedures to ensure safe storage and disposal of detected SF medical products were recently established; however such procedures are recently implemented and no results associated with this sub-indicator are documented yet. ➔ IMPLEMENTED (I): There are documented procedures to ensure safe storage and disposal of detected SF medical products, and these procedures are actually implemented.
Limitations and remarks:	Scoring this sub-indicator as "not applicable NA" is excluded (i.e. this sub-indicator will always apply for all benchmarked NRAs).
Indicator:	**MC05 Mechanism in place to monitor regulatory performance and output.**
Objective:	The objective of this indicator is to ensure that mechanisms are in place to track regulatory effectiveness of the market surveillance and control activities, to measure relevant progress in the programme, and to establish, implement and regularly verify performance indicators.
Category:	09. Monitoring progress and assessing outcomes & impact
Sub Indicator:	**MC05.01: Database exists of approved and refused promotional and advertising materials along with the supporting documentation.**
Maturity Level:	4
Scope:	1. Medicines 2. Vaccines
Description:	The assessor should verify the establishment of a database of approved as well as refused marketing, promotional and advertising materials, along with documentation that supports the decisions taken. The database should not be limited to listing of approved and rejected materials. Instead, the database should also include the applications, the supporting documentation submitted by applicants, and records of the regulatory review, assessment, and final decision-making for these applications.
Objective:	The objective of this sub-indicator is to ensure that a database of applications for marketing, promotional and advertising materials is established for storing, consolidating and analyzing relevant information. The database also serves as a basis for further follow up and enforcement actions. Thus tracing relevant regulatory activities and decisions for the sake of institutional memory is ensured. Furthermore, analyses of the data would contribute to optimization of the performance of the regulatory program.
Requirement:	Database of promotional, marketing and advertising materials applications, documentations and regulatory decisions
Evidence to review:	The assessor should ask for and review: 1. Database of applications and supporting documentation of marketing, promotional and advertising materials. 2. Database of regulatory reviews and assessments of marketing, promotional and advertising materials.
References:	
Framework:	Output
Rating Scale:	➔ NOT IMPLEMENTED (NI): There is no database for approved and refused promotional materials along with their supporting documentation. ➔ ONGOING IMPLEMENTATION (OI): The NRA is preparing to establish a database, but there is no evidence of results from such activities.

	➔ PARTIALLY IMPLEMENTED (PI): There is evidence that the NRA has the elements (i.e., procedures, documentation, management systems, and related information.) and the capacity to perform the processes mentioned in the indicator; however it has only limited experience or a limited number of documented events. ➔ IMPLEMENTED (I): There is a database for approved and refused promotional materials along with their supporting documentation
Limitations and remarks:	This sub-indicator is applicable only to the countries where there are pre-approval activities related to medical products promotion and advertising. In case there is no NRA pre-approval system is in place, the assessor should verify the existence of an alternative approach which provides adequate control of promotional, marketing and advertising activities.
Sub Indicator:	**MC05.02: Database for product batches that have undergone surveillance along with their relevant testing results and regulatory actions is established and periodically reviewed.**
Maturity Level:	4
Scope:	1. Medicines 2. Vaccines
Description:	The assessor should verify the establishment and maintenance of a database of product batches that have been included in the market surveillance program (i.e., batches that have been sampled or tested). The database should include relevant findings, test results, and regulatory decisions. Importantly, this database should include information about SF medical products. The database should not only include a listing of the relevant information, but also provide data analyses designed to optimize the surveillance program, identify repeated violations and trends, and guide regulatory measures to prevent, detect and respond to SF medical products. Also, such database makes it possible to compile the information needed for similar actions at the global and international level.
Objective:	The objective of this sub-indicator is to ensure the establishment of a database of product batches that have been included in the surveillance program. The database should store, consolidate and analyze information from the market surveillance program. Thus tracing relevant regulatory activities and decisions for the sake of institutional memory is ensured. Furthermore, analyses of the data would contribute to optimization of the performance of the regulatory program.
Requirement:	Database of product batches that have been included in the market surveillance program, their relevant testing results and regulatory decisions or actions, if any
Evidence to review:	The assessor should ask for and review: 1. Database of product batches that have been included in the market surveillance program along with their results and regulatory actions, if any. 2. Updated analyses of the data along with consequent optimization, if any.
References:	
Framework:	Output
Rating Scale:	➔ NOT IMPLEMENTED (NI): There is no database within for NRA for product batches that have undergone surveillance along with their regulatory actions. ➔ ONGOING IMPLEMENTATION (OI): The NRA is preparing to establish a database, but there is no evidence of results from such activities. ➔ PARTIALLY IMPLEMENTED (PI): There is evidence that the NRA has the elements (i.e., procedures, documentation, management systems, and related information) and the capacity to perform the processes mentioned in the indicator; however it has only limited experience or a limited number of documented events.

	➔ IMPLEMENTED (I): There is a database within the NRA for product batches that have undergone surveillance along with their regulatory actions. Also, this database is regularly updated.
Limitations and remarks:	Scoring this sub-indicator as "not applicable NA" is excluded (i.e. this sub-indicator will always apply for all benchmarked NRAs).
Sub Indicator:	**MC05.03: Performance indicators for market surveillance and control activities are established and implemented**
Maturity Level:	4
Scope:	1. Medicines 2. Vaccines
Description:	The assessor should verify the existence and implementation of performance indicators for different activities included under the market surveillance and control functions. Specifically, the system should define key performance indicators (KPIs) along the entire market surveillance and control activity chain and all indicators should be adequately In addition, the assessor should verify measured indicators are analyzed to identify trends or abnormalities. Justifications for any identified abnormalities should be provided; when necessary, process optimizations should be introduced to avoid recurrence. justified. For the purpose of clarity and consistency, established KPIs should be supported with guidelines for monitoring and maintenance of the KPIs. The guidelines in turn should be supported by SOPs and tools that define the procedures to be used for monitoring and evaluating the performance indicators and that define procedures and timelines for reviewing and revising the indicators. For market surveillance and control activities, the performance indicators should cover the four themes: (1) control of import activities, (2) preventing, detecting and responding to SF medical products, (3) market surveillance program for monitoring the quality of medical products, and (4) control of promotional, marketing and advertising activities. Examples of indicators include, but are not limited to: number of product batches sampled as part of market surveillance program, number of approvals and refusals of promotional materials, and number of detected SF medical products (with sub- categorization). Established KPIs might be qualitative, quantitative or combination of both. In general, quantitative indicators are preferred to avoid bias or misinterpretation. However, qualitative indicators are also accepted. Qualitative indicators may or may not include scoring or scaling to render them semi-quantitative and thus more informative. The assessor should ensure that indicators are measured on a regular basis to monitor progress and advancement.
Objective:	The objective of this sub-indicator is to ensure that a system, mechanism, or procedure exists to require the NRA to establish performance indicators along the entire market surveillance and control chain. Additionally, the objective is to ensure that KPIs are actually contributing to monitoring of regulatory performance, to measuring effectiveness of market surveillance and control regulatory activities, and to making any necessary adjustments or optimizations.
Requirement:	KPIs for market surveillance and control activities
Evidence to review:	The assessor should ask for and review: 1. Documents supporting the system, mechanism, or procedure compelling the NRA to establish and implement performance indicators along the entire market surveillance and control activity chain. 2. Evidence that the performance indicators have been established and implemented, and that the members of staff involved in the market surveillance and control function are aware of the indicators and the guidelines and SOPs used for monitoring and evaluating their performance. 3. The current performance indicators for market surveillance and control activities. KPIs should cover the four themes listed in Description column.

	4. Analyses of the measured indicators along with the investigations done to identify trends or abnormalities. 5. Documentation for follow-up of any observed abnormalities, including justifications for any identified abnormalities as well as any process optimizations introduced to avoid recurrence.
References:	1. Quality management -- Quality of an organization -- Guidance to achieve sustained success, ISO 9004:2018, International Organization for Standardization (ISO), (115), (https://www.iso.org/standard/70397.html) 2. World Health Organization. European Observatory on Health Systems and Policies. Performance measurement for health system improvement: experiences, challenges and Prospects, (125), (http://www.who.int/management/district/performance/PerformanceMeasurementHealthSystemImprovement2.pdf) 3. World Health Organization. European Observatory on Health Systems and Policies. Health System Performance Comparison: an agenda for policy, information and research, (126), (http://www.euro.who.int/__data/assets/pdf_file/0009/244836/Health-System-Performance-Comparison.pdf)
Framework:	Output
Rating Scale:	➜ NOT IMPLEMENTED (NI): There are no KPIs for market surveillance and control activities. ➜ ONGOING IMPLEMENTATION (OI): The NRA has recently drafted KPIs for market surveillance and control activities but they have not yet been reported. ➜ PARTIALLY IMPLEMENTED (PI): The NRA has developed KPIs for market surveillance and control activities and has been applying them for less than two year or they have not covered all critical steps. ➜ IMPLEMENTED (I): The NRA has established and implemented KPIs for market surveillance and control activities. The indicators are reviewed regularly, and appropriate actions are taken and decisions made.
Limitations and remarks:	▪ When they refer to outcomes, indicators may be ambiguous and difficult to interpret, as outcomes are the result of many factors that are difficult to disentangle. When they refer to processes, indicators are often too specific, as they may focus on a particular intervention or condition or they may quickly become outdated as business models develop. ▪ Different methodologies are used to measure the NRAs performance on market surveillance and control activities. In this case, the assessor should verify that adequate supporting documents are available. The assessor should consider that developed performance indicators should be Specific, Measurable, Achievable, Realistic, and Time-bound (i.e., "SMART"). ▪ Scoring this sub-indicator as "not applicable NA" is excluded (i.e. this sub-indicator will always apply for all benchmarked NRAs).
Indicator:	**MC06 Mechanism exists to promote transparency, accountability and communication.**
Objective:	The objective of this indicator is to ensure that mechanisms are in place that promote effective communication of market surveillance and control activities and related information within the NRA, that promote transparency and outreach to the public, and that establish milestones that encourage accountability of the NRA to its mandate. Additionally these activities contribute to mutual understanding and involvement of all stakeholders relevant to market surveillance and control activities. Consequently, confidence in the regulatory system is raised.
Category:	08. Transparency, accountability and communication
Sub Indicator:	**MC06.01: Market surveillance and control activities are appropriately communicated within the NRA.**
Maturity Level:	3

Scope:	1. Medicines 2. Vaccines
Description:	The assessor should verify that market surveillance and control activities are properly communicated among different institutions, departments, and entities of the NRA (e.g. laboratory, inspection and enforcement departments). These internal communications should be guided by appropriate policies or procedures and supported by mechanisms for implementation.
Objective:	The objective of this sub-indicator is to ensure that communication of market surveillance and control activities within the NRA is well established as a best practice to promote regulatory effectiveness. In addition, such communication increases awareness and encourages internal understanding and cooperation among all relevant entities and departments within the NRA.
Requirement:	Communication within the NRA of the market surveillance and control activities
Evidence to review:	The assessor should ask for and review: 1. Documentation of guidelines, policies, procedures or mechanisms for communicating market surveillance and control activities within the NRA. 2. Records of communication (i.e., paper based or electronic) proving communication of information within the NRA.
References:	1. MDS-3: Managing Access to Medicines and Health Technologies (Third Edition), MSH, 2012, (99), (http://apps.who.int/medicinedocs/documents/s19577en/s19577en.pdf) 2. Guidelines on the conduct of surveys of the quality of medicines, World Health Organization (WHO), (86), (http://apps.who.int/medicinedocs/en/q/ and http://digicollection.org/whoqapharm/) 3. Recommendations for health authorities to detect and deal with actions, activities and behaviors that result in substandard/spurious/falsely-labelled/falsified/counterfeit medical products, A68/33, annex 1, (129), (http://apps.who.int/gb/ebwha/pdf_files/WHA68/A68_33-en.pdf) 4. Guidance on developing a national plan for preventing, detecting and responding to actions, activities and behaviors that result in SF medical products. WHO (document A70/23), (130), (https://www.who.int/medicines/regulation/ssffc/mechanism/A70_23-en6-14.pdf)
Framework:	Output
Rating Scale:	➜ NOT IMPLEMENTED (NI): Market surveillance and control activities are not communicated within the NRA. ➜ ONGOING IMPLEMENTATION (OI): The NRA is preparing to establish mechanisms for communication of market surveillance and control activities, but there is no evidence of results from such activities. ➜ PARTIALLY IMPLEMENTED (PI): There is evidence that the NRA has the elements (i.e., procedures, documentation, management systems, and relevant information) and the capacity to perform the processes mentioned in the indicator; however it has only limited experience or a limited number of documented events. ➜ IMPLEMENTED (I): Market surveillance and control activities are appropriately communicated within the NRA, and documentation is available to support that communication within the NRA is well-established.
Limitations and remarks:	Scoring this sub-indicator as "not applicable NA" is excluded (i.e. this sub-indicator will always apply for all benchmarked NRAs).
Sub Indicator:	**MC06.02: Findings and regulatory decisions of market surveillance and control activities are appropriately communicated to all national stakeholders including the general public.**
Maturity Level:	3

Scope:	1. Medicines 2. Vaccines
Description:	The assessor should verify that market surveillance and control activities are properly communicated to all relevant national stakeholders. For this activity, the intended stakeholders include, but are not limited to, governmental agencies (e.g., police and judicial authorities), non-governmental organizations, professional associations, customer representative associations, and the public community.
Objective:	The objective of this sub-indicator is to ensure that market surveillance and control activities are actively communicated among all relevant stakeholders. These communications, in turn, ensure regulatory effectiveness through involvement of these key players. In addition, such communication increases awareness, encourages mutual understanding and cooperation, and builds confidence and trust among all stakeholders, including public trust in the regulatory system.
Requirement:	Communication to different stakeholders including the community of market surveillance and control activities.
Evidence to review:	The assessor should ask for and review: 1. Records of communication (i.e., paper based or electronic) proving communication of market surveillance and control activities with other relevant stakeholders.
References:	1. Terms of reference for the Global Focal Point Network for SF medical products. WHO (document A69/41), (131), (https://www.who.int/medicines/regulation/ssffc/mechanism/A69_41-en6-8.pdf) 2. Recommendations for health authorities to detect and deal with actions, activities and behaviors that result in substandard/spurious/falsely-labelled/falsified/counterfeit medical products, A68/33, annex 1, (129), (http://apps.who.int/gb/ebwha/pdf_files/WHA68/A68_33-en.pdf) 3. Guidance on developing a national plan for preventing, detecting and responding to actions, activities and behaviors that result in SF medical products. WHO (document A70/23), (130), (https://www.who.int/medicines/regulation/ssffc/mechanism/A70_23-en6-14.pdf)
Framework:	Output
Rating Scale:	➜ NOT IMPLEMENTED (NI): Market surveillance and control activities are not communicated to national stakeholders or the public. ➜ ONGOING IMPLEMENTATION (OI): The NRA is preparing to establish mechanisms for communication of market surveillance and control activities to national stakeholders and the public, but there is no evidence of results from such activities. ➜ PARTIALLY IMPLEMENTED (PI): There is evidence that the NRA has the elements (i.e., procedures, documentation, management systems, and other relevant information) and the capacity to perform the processes mentioned in the indicator; however, it has only limited experience or a limited number of documented events. ➜ IMPLEMENTED (I): Market surveillance and control activities are communicated to national stakeholders and the public.
Limitations and remarks:	Scoring this sub-indicator as "not applicable NA" is excluded (i.e. this sub-indicator will always apply for all benchmarked NRAs).
Sub Indicator:	**MC06.03: Findings and regulatory decisions of market surveillance and control activities of common interest are appropriately communicated and shared with other countries and regional and international organizations.**
Maturity Level:	3
Scope:	1. Medicines 2. Vaccines

Description:	The assessor should verify that findings and regulatory decisions of market surveillance and control programme of common interest are shared with other countries, regional networks and international organizations (e.g. Rapid Alert Notifications and WHO Global Surveillance and Monitoring System for SF medical products). The assessor should verify that the relevant information is shared with external partners in a timely manner so that the information remains valuable and has the potential to minimize adverse events in locations outside the country.
Objective:	The objective of this sub-indicator is to ensure that those findings and regulatory decisions that are related to the market surveillance and control programme and that are of common interest, are shared with other countries, regional networks and international organizations. Sharing of market surveillance and control information, including decisions, is essential for ensuring coordinated global efforts for access to medical products of reliable quality.
Requirement:	Sharing of market surveillance and control information of interest with other countries and regional and international organizations.
Evidence to review:	The assessor should ask for and review: 1. Agreements, MOUs and other documentation reflecting cooperation between the NRA and other foreign entities for the purpose of sharing findings, data and decisions of market surveillance and control programme. 2. Examples of communication with foreign entities for the purpose of sharing findings, data and decisions of market surveillance and control programme.
References:	1. Recommendations for health authorities to detect and deal with actions, activities and behaviors that result in substandard/spurious/falsely-labelled/falsified/counterfeit medical products, A68/33, annex 1, (129), (http://apps.who.int/gb/ebwha/pdf_files/WHA68/A68_33-en.pdf) 2. Terms of reference for the Global Focal Point Network for SF medical products. WHO (document A69/41), (131), (https://www.who.int/medicines/regulation/ssffc/mechanism/A69_41-en6-8.pdf) 3. Guidance on developing a national plan for preventing, detecting and responding to actions, activities and behaviors that result in SF medical products. WHO (document A70/23), (130), (https://www.who.int/medicines/regulation/ssffc/mechanism/A70_23-en6-14.pdf)
Framework:	Output
Rating Scale:	➜ NOT IMPLEMENTED (NI): Market surveillance and control activities are not communicated or shared with other countries or regional or international organizations. ➜ ONGOING IMPLEMENTATION (OI): The NRA is preparing to establish mechanisms for communication of market surveillance and control activities with other countries and regional and international organizations, but there is no evidence of results from such activities. ➜ PARTIALLY IMPLEMENTED (PI): There is evidence that the NRA has the elements (i.e., procedures, documentation, management systems, and other related information) and the capacity to perform the processes mentioned in the indicator; however, it has only limited experience or a limited number of documented events. ➜ IMPLEMENTED (I): Market surveillance and control activities are communicated and shared with other countries and regional and international organizations.
Limitations and remarks:	Scoring this sub-indicator as "not applicable NA" is excluded (i.e. this sub-indicator will always apply for all benchmarked NRAs).

05

Licensing Establishments (LI): Indicators and Fact Sheets

WHO Global Benchmarking Tool (GBT) for Evaluation of National Regulatory System of Medical Products

05. Licensing Establishments (LI): Indicators and Fact Sheets

Function:	05 — LICENSING ESTABLISHMENTS (LI)
Description:	In order to protect public health, licensing activities are of outstanding importance and are considered fundamental, together with inspections activities, for guaranteeing the quality, safety and efficacy of medical products used within or exported out of the country. The National Regulatory Authority (NRA) is responsible for coordinating licensing activities and should be supported by published and readily available legal provisions, regulations and guidelines which ensure that licensing of facilities throughout the supply chain is based on compliance with Good Practices (GXP) and that the NRA is empowered to issue, suspend or revoke licenses for premises and establishments. Premises, facilities, establishments and companies throughout the supply chain should possess a license to operate issued by the NRA. These facilities include, but are not limited to, manufacturers, distributors, wholesalers, importers, exporters and retailers. The process of issuing licenses should be based on the implementation of and compliance with quality standards of GXP. An inspection for confirmation of compliance with GXP is required in order to grant or re-grant a license or approval of a substantial modification. An updated list or database of all licensed facilities should be published and publicly available. The GXPs considered most relevant for this function are good manufacturing practices and good distribution practices, including good cold chain management practices. Good clinical practices and good vigilance practices, which are generally excluded from this function, are addressed, however, in other functions. A general limitation to this function occurs when there is no domestic manufacturing of medical products. In this case, the function cannot apply to manufacturers, because none exist in the country. Nevertheless, the function will always apply to distribution practices, including wholesaling. Another general limitation applies to those countries that depend on the regulatory inspection function, without licensing, to ensure compliance to GXPs at the premises, facilities, establishments and companies throughout the supply chain. In the latter case, the whole function might not apply; however, the assessor of this establishment licensing function should liaise with the assessor of the regulatory inspection function to verify that proper and appropriate controls are in place despite the absence of any licensing activities in the country.
Indicator:	**LI01 Legal provisions, regulations and guidelines required to define framework for licensing activities.**
Objective:	The objective of this indicator is to ensure that licensing activities are supported by a comprehensive set of legal provisions, regulations and guidelines which provide the necessary mandate to implement all activities related to this regulatory function. There should be a legal basis to establish the licensing system for the facilities throughout the supply chain and to authorize the responsible entities to take the necessary actions. The legislation should also provide a mandate that allows for adequate and proportional sanctions, penalties and prosecutions for violations of the applicable legislation. (Please refer to regulatory inspection function for further information on the regulatory enforcement and compliance activities).
Category:	01. Legal provisions, regulations and guidelines

Sub Indicator:	**LI01.01: There are legal provisions for licensing of facilities throughout the supply chain and based on Good Practices (GXPs) compliance.**
Maturity Level:	1
Scope:	1. Medicines 2. Vaccines
Description:	The assessor should verify that legislation establishes fundamental functions in the regulatory authority appointed to license different type of facilities across the supply chain (e.g., manufacturer, re-packager, re-labeller, distributor, wholesaler and retailer). The assessor should ensure that, for the purpose of being licensed, legal provisions require the responsible entity to conduct a GXP inspection prior to taking related decision.
Objective:	The objective of this sub-indicator is to ensure the existence of legislation that requires premises, facilities, establishments and companies throughout the supply chain (including, but not limited to, manufactures, distributors, wholesalers, importers, exporters and retailers) hold a license to operate that is issued by the National Regulatory Authority (NRA).
Requirement:	Legal provisions, regulations and guidelines for licensing facilities
Evidence to review:	The assessor should ask for and review: 1. Published legal provisions establishing the licensing of facilities throughout the supply chain; 2. Relevant public information available from the website, official bulletins or other legal publications; 3. Legal provisions authorizing the NRA to conduct GXP inspections; 4. Guidelines, procedures, forms, and instructions for applicants; 5. Guidance to applicants defining the circumstances that would warrant an application for a new license or for renewal, expansion, or modification to an existing license.
References:	1. National drug regulatory legislation: guiding principles for small drug regulatory authorities. In: WHO Expert Committee on Specifications for Pharmaceutical Preparations: thirty-fifth report. Geneva: World Health Organization; 1999: Annex 8 (WHO Technical Report Series, No. 885), (1), (http://apps.who.int/medicinedocs/documents/s21964en/s21964en.pdf) 2. Guiding principles for small national drug regulatory authorities. In: WHO Expert Committee on Specifications for Pharmaceutical Preparations: thirty-first report. Geneva: World Health Organization; 1990: Annex 6 (WHO Technical Report Series, No. 790), (5), (http://apps.who.int/medicinedocs/documents/s21964en/s21964en.pdf) 3. Regulation and licensing of biological products in countries with newly developing regulatory authorities. In: WHO Expert Committee on Biological Standardization: forty-fifth report. Geneva: World Health Organization; 1995: Annex 1 (WHO Technical Report Series, No. 858), (3), (http://www.who.int/bloodproducts/publications/WHO_TRS_858_A1.pdf) 4. Effective drug regulation: A multicounty study. Geneva: World Health Organization; 2002, (7), (http://apps.who.int/medicinedocs/pdf/s2300e/s2300e.pdf) 5. Guidelines for national authorities on quality assurance for biological products. In: WHO Expert Committee on Biological Standardization: forty-second report. Geneva. World Health Organization; 1992: Annex 2 (WHO Technical Report Series, No. 822), (2), (http://www.who.int/biologicals/publications/trs/areas/biological_products/WHO_TRS_822_A2.pdf) 6. Guidelines on import procedures for pharmaceutical products, World Health Organization (WHO), (22), (http://digicollection.org/whoqapharm/p/about and http://apps.who.int/medicinedocs/en)
Framework:	Structure/Foundation/Inpu
Rating Scale:	➔ NOT IMPLEMENTED (NI): There is no legal basis for the indicator. ➔ ONGOING IMPLEMENTATION (OI): The NRA is preparing to establish a legal basis for this requirement, but there is no evidence of any results from those preparations.

	➔ PARTIALLY IMPLEMENTED (PI): The legal basis was established recently (less than one year ago) and it is at the implementation stage, so this practice is not yet consolidated. ➔ IMPLEMENTED (I): The NRA has legal provisions in place requiring premises, facilities, establishments and companies throughout the supply chain including, but not limited to, manufactures, distributors, wholesalers, importers, exporters and retailers, to hold a license to operate issued by the NRA.
Limitations and remarks:	▪ A general limitation to this function occurs when there is no domestic manufacturing of medical products. In this case, the function cannot apply to manufacturers, because none exist in the country. Nevertheless, the function will always apply to distribution, including wholesaling, practices. Another general limitation applies to those countries that depend on the regulatory inspection function, without licensing, to ensure compliance to GXP at the premises, facilities, establishments and companies throughout the supply chain. In the latter case, the whole function might not apply; however, the assessor of this establishment licensing function should liaise with the assessor of the regulatory inspection function to verify that proper and appropriate controls are in place despite the absence of any licensing activities in the country. ▪ Scoring this sub-indicator as "not applicable NA" is excluded (i.e. this sub-indicator will always apply for all benchmarked NRAs).
Sub Indicator:	**LI01.02: There are legal provisions to empower the NRA to issue, suspend or revoke licenses for establishments.**
Maturity Level:	1
Scope:	1. Medicines 2. Vaccines
Description:	The assessor should verify existing legislation establishes a requirement for compliance with and respect for the quality standards of GXPs on the part of manufacturers of pharmaceutical products and for the quality standards of Good Distribution Practice on the part of wholesale companies. Compliance with these quality standards is essential for ensuring that licensing establishments meet the requirements recommended by the World Health Organization (WHO) to safeguard the quality, safety, and effectiveness of their products. The NRA must verify a manufacturer's adherence to Good Manufacturing Practices before and after production starts. Therefore, it is imperative that the NRA is empowered by legislation to both issue licenses to such establishments and to suspend them when critical risks associated with lack of compliance with GXP are identified. The assessor should confirm the existence of laws, decrees and provisions related to licensing and verify that the legislation empowers the NRA to suspend or revoke licenses for establishments.
Objective:	The objective of this sub-indicator is to ensure that legislation empowers the NRA to not only issue licenses, but also to suspend or revoke licenses for establishments.
Requirement:	Legal provisions, regulations and guidelines on issuance, suspension, withdrawal or cancellation of licenses.
Evidence to review:	The assessor should ask for and review: 1. Legal provisions authorizing the NRA to suspend or revoke a license in case requirements are not met; 2. Relevant public information available from the website, official bulletins, or other legal publications.
References:	1. Effective drug regulation: A multicounty study. Geneva: World Health Organization; 2002, (7), (http://apps.who.int/medicinedocs/pdf/s2300e/s2300e.pdf) 2. National drug regulatory legislation: guiding principles for small drug regulatory authorities.

	In: WHO Expert Committee on Specifications for Pharmaceutical Preparations: thirty-fifth report. Geneva: World Health Organization; 1999: Annex 8 (WHO Technical Report Series, No. 885), (1), (http://apps.who.int/medicinedocs/documents/s21964en/s21964en.pdf) 3. Guiding principles for small national drug regulatory authorities. In: WHO Expert Committee on Specifications for Pharmaceutical Preparations: thirty-first report. Geneva: World Health Organization; 1990: Annex 6 (WHO Technical Report Series, No. 790), (5), (http://apps.who.int/medicinedocs/documents/s21964en/s21964en.pdf)
Framework:	Structure/Foundation/Input
Rating Scale:	➜ NOT IMPLEMENTED (NI): There are no legal provisions empowering the NRA to issue licenses and to suspend or halt production. ➜ ONGOING IMPLEMENTATION (OI): The NRA is preparing to establish a legal basis for this indicator, but there is no evidence of any results from such activities. ➜ PARTIALLY IMPLEMENTED (PI): The legal basis was established recently (less than one year ago) and it is at the implementation stage, so this practice is not yet consolidated; or the NRA carries out these actions, but legal provisions do not explicitly empower it to do so. ➜ IMPLEMENTED (I): The NRA has the legal bases and also consistently maintains documentation of the results of related activities over time. The legal provisions explicitly indicate that the NRA grants licenses and may revoke them or apply health sanctions, as the case may be, for any noncompliance it finds. There is evidence that the NRA is following through on these actions.
Limitations and remarks:	▪ In some cases, license revocation is not the responsibility of the NRA. Instead, other institutions may have that responsibility (e.g., police authorities). In any case, the inspectors should have the authority to halt production. ▪ Scoring this sub-indicator as "not applicable NA" is excluded (i.e. this sub-indicator will always apply for all benchmarked NRAs).
Sub Indicator:	**LI01.03: There are legal provisions that require that the NRA to be informed, for the purpose of notification or approval, in case post-licensure changes or variations are made.**
Maturity Level:	3
Scope:	1. Medicines 2. Vaccines
Description:	The assessor should verify the existence of legal provisions that require a responsible person from the establishment inform the NRA for notification or approval of any changes or variations to the conditions under which the initial license was issued. This provision applies to any change or variation which may affect the quality, safety or efficacy of medical products. Establishments may make changes at their facilities (e.g. introduce a new manufacturing line or new product). However, because such changes may create new risk factors that might impact the quality, safety, or efficacy of the products being manufactured, the NRA must assess the situation to decide whether to approve such changes and include them in the corresponding manufacturing license.
Objective:	The objective of this sub-indicator is to ensure that legal provisions or regulations provide the necessary mandate for the NRA to require that a responsible person from the establishment inform the NRA, for purpose of notification or approval, of any changes or variations to the conditions under which the initial license was issued.
Requirement:	Legal provisions, regulations and guidelines on post-licensure changes or variations
Evidence to review:	The assessor should ask for and review: 1. Published legal provisions regarding the obligation to report changes or variations to the original license;

	2. Relevant published guidelines, procedures, forms, and instructions for applicants; 3. Evidence of approved and rejected amendments.
References:	1. Effective drug regulation: A multicounty study. Geneva: World Health Organization; 2002, (7), (http://apps.who.int/medicinedocs/pdf/s2300e/s2300e.pdf) 2. National drug regulatory legislation: guiding principles for small drug regulatory authorities. In: WHO Expert Committee on Specifications for Pharmaceutical Preparations: thirty-fifth report. Geneva: World Health Organization; 1999: Annex 8 (WHO Technical Report Series, No. 885), (1), (http://apps.who.int/medicinedocs/documents/s21964en/s21964en.pdf) 3. Guiding principles for small national drug regulatory authorities. In: WHO Expert Committee on Specifications for Pharmaceutical Preparations: thirty-first report. Geneva: World Health Organization; 1990: Annex 6 (WHO Technical Report Series, No. 790), (5), (http://apps.who.int/medicinedocs/documents/s21964en/s21964en.pdf)
Framework:	Structure/Foundation/Input
Rating Scale:	➜ NOT IMPLEMENTED (NI): There is no legal basis for the indicator. ➜ ONGOING IMPLEMENTATION (OI): The NRA is preparing to establish the legal basis, but there is no evidence of results associated with such activities. ➜ PARTIALLY IMPLEMENTED (PI): The legal basis was established recently, and it is at the implementation stage, so this practice is not yet consolidated. ➜ IMPLEMENTED (I): The NRA has such legal bases and also consistently maintains documentation of the results of related activities over time. There is a legal provision requiring notification, and there are records that both license holders and the NRA are adhering to this legal provision.
Limitations and remarks:	Scoring this sub-indicator as "not applicable NA" is excluded (i.e. this sub-indicator will always apply for all benchmarked NRAs).
Sub Indicator:	**LI01.04: There are guidelines on the procedures to apply for a license and on content and format of the license application.**
Maturity Level:	3
Scope:	1. Medicines 2. Vaccines
Description:	The assessor should verify the existence of published guidance that specifies the content of the application, the forms that are required and the procedures to follow when submitting a license application. In order to ensure proper interpretation and complete compliance, it is important to verify that: 1. the instructions regarding the content and format of license application are clear; 2. the instructions that describe the procedure to follow when submitting an application license are clear; 3. the NRA has evidence, preferably public, that states that the guidelines are to be followed; 4. the requirements state that products at the stage of research and development also are included; 5. The guidelines clearly establish that the licensing requirements apply to domestic, foreign, public, and private manufacturers, distributers, wholesalers, importers, exporters and retailers; 6. the NRA applies these requirements consistently, and has documentary evidence, preferably public, to demonstrate this. Furthermore, the assessor should verify the guidelines are available, intelligible and properly communicated to the target audience. For these communications, a push rather than a pull approach should be employed.
Objective:	The objective of this sub-indicator is to ensure that guidelines for submitting an application for a license are available to those governed by the regulations. These guidelines should address the content of the application and its format. Availability of such guidelines will

	contribute to proficiency in all aspects of GXP covered by the legislation and to proper interpretation and implementation of the guidelines. Availability of guidelines also will help the NRA to be consistent in application of this requirement. Assessor should note that the publication and communication of these guidelines to the target audience is as critical as the guidelines themselves. For these communications, a push rather than a pull approach should be employed.
Requirement:	Guidelines on content and format of the application and on procedure to follow when submitting a license application.
Evidence to review:	The assessor should ask for and review: 1. Published guidelines for licensing applications, including instructions or guidelines for applicants. 2. Evidence that administrative instructions exist and that they are all available to establishments applying for licenses. 3. Official requirements for the submission of licensing applications; 4. Documented evidence from the NRA demonstrating that this indicator is implemented (if no publicly-available evidence is available)
References:	1. Effective drug regulation: A multicounty study. Geneva: World Health Organization; 2002, (7), (http://apps.who.int/medicinedocs/pdf/s2300e/s2300e.pdf) 2. National drug regulatory legislation: guiding principles for small drug regulatory authorities. In: WHO Expert Committee on Specifications for Pharmaceutical Preparations: thirty-fifth report. Geneva: World Health Organization; 1999: Annex 8 (WHO Technical Report Series, No. 885), (1), (http://apps.who.int/medicinedocs/documents/s21964en/s21964en.pdf) 3. Guiding principles for small national drug regulatory authorities. In: WHO Expert Committee on Specifications for Pharmaceutical Preparations: thirty-first report. Geneva: World Health Organization; 1990: Annex 6 (WHO Technical Report Series, No. 790), (5), (http://apps.who.int/medicinedocs/documents/s21964en/s21964en.pdf)
Framework:	Structure/Foundation/Input
Rating Scale:	➜ NOT IMPLEMENTED (NI): There are no guidelines for the content and format of the license application. ➜ ONGOING IMPLEMENTATION (OI): The NRA is preparing to establish such guidelines, but there is no evidence of results associated with such activities, or the guidelines are available within the NRA however they are not available, intelligible or communicated to the target audience. ➜ PARTIALLY IMPLEMENTED (PI): The guidelines were established recently and it is at the early implementation stage, so this practice is not yet consolidated. ➜ IMPLEMENTED (I): The NRA has guidelines for producers on the content of the application and its format, and on the procedures to follow when submitting an application for a production license in accordance with WHO standards. The NRA also consistently maintains documentation of the results of related activities over time.
Limitations and remarks:	Scoring this sub-indicator as "not applicable NA" is excluded (i.e. this sub-indicator will always apply for all benchmarked NRAs).
Sub Indicator:	**LI01.05: There are legal provisions that require manufacturers to inform the NRA about the appointed qualified and authorized person for the purpose of acknowledgment or approval.**
Maturity Level:	3
Scope:	1. Medicines 2. Vaccines
Description:	The assessor should verify that legal provisions or regulations exist to obligate the manufacturer to designate a qualified and authorized person.

Objective:	The objective of this sub-indicator is to ensure the existence of legal provisions or regulations that provide necessary mandate to the NRA to obligate the manufacturers to designate a qualified and authorized person.
Requirement:	Legal provisions, regulations and guidelines on the qualified and authorized person
Evidence to review:	The assessor should ask for and review: 1. Legal provisions or regulations authorizing the NRA to approve or acknowledge the qualified and authorized person appointed by the manufacturer;
References:	1. Effective drug regulation: A multicounty study. Geneva: World Health Organization; 2002, (7), (http://apps.who.int/medicinedocs/pdf/s2300e/s2300e.pdf) 2. National drug regulatory legislation: guiding principles for small drug regulatory authorities. In: WHO Expert Committee on Specifications for Pharmaceutical Preparations: thirty-fifth report. Geneva: World Health Organization; 1999: Annex 8 (WHO Technical Report Series, No. 885), (1), (http://apps.who.int/medicinedocs/documents/s21964en/s21964en.pdf) 3. Guiding principles for small national drug regulatory authorities. In: WHO Expert Committee on Specifications for Pharmaceutical Preparations: thirty-first report. Geneva: World Health Organization; 1990: Annex 6 (WHO Technical Report Series, No. 790), (5), (http://apps.who.int/medicinedocs/documents/s21964en/s21964en.pdf)
Framework:	Structure/Foundation/Input
Rating Scale:	➜ NOT IMPLEMENTED (NI): There is no legal basis for the indicator. ➜ ONGOING IMPLEMENTATION (OI): The NRA is preparing to establish a legal basis for this requirement, but there is no evidence of any results from those preparations. ➜ PARTIALLY IMPLEMENTED (PI): The legal basis was established recently (less than one year ago) and it is at the implementation stage, so this practice is not yet consolidated. ➜ IMPLEMENTED (I): The NRA has legal provisions in place requiring manufacturers to designate a qualified and authorized person and to inform the NRA of this for notification and approval purposes.
Limitations and remarks:	Scoring this sub-indicator as "not applicable NA" is excluded (i.e. this sub-indicator will always apply for all benchmarked NRAs).
Indicator:	**LI02 Arrangement for effective organization and good governance.**
Objective:	The objective of this indicator is to ensure the implementation of effective organization and good governance practices at the organizational structures in charge of establishment licensing activities.
Category:	02. Organization and governance
Sub Indicator:	**LI02.01: There is a defined structure with clear responsibilities to conduct establishments licensing activities.**
Maturity Level:	2
Scope:	1. Medicines 2. Vaccines
Description:	The assessor should identify the organization designated to establish, implement or maintain the licensing regulatory function, as well as the specific organizational structures taking on the different relevant activities. Responsibilities, duties and roles of these structures should be clearly defined and documented. If more than one structure is involved, the assessor should check the ways and approaches by which coordination between these structures is taking place.

Objective:	The objective of this sub-indicator is to ensure effective organization and good governance of establishment licensing activities and to ensure that these licensing activities are taken over by defined organizational structures with clear roles and responsibilities.
Requirement:	Roles and responsibilities of the structures in charge of establishment licensing activities.
Evidence to review:	The assessor should ask for and review: 1. Organization chart of the organization responsible for the implementation of licensing activities along with identification of the specific structures implementing the function. 2. Documentation clarifying roles and responsibilities of the organizational structures implementing licensing activities. This may include administrative decrees, terms of reference, or other relevant documents
References:	1. Effective drug regulation: A multicounty study. Geneva: World Health Organization; 2002, (7), (http://apps.who.int/medicinedocs/pdf/s2300e/s2300e.pdf) 2. National drug regulatory legislation: guiding principles for small drug regulatory authorities. In: WHO Expert Committee on Specifications for Pharmaceutical Preparations: thirty-fifth report. Geneva: World Health Organization; 1999: Annex 8 (WHO Technical Report Series, No. 885), (1), (http://apps.who.int/medicinedocs/documents/s21964en/s21964en.pdf) 3. Guiding principles for small national drug regulatory authorities. In: WHO Expert Committee on Specifications for Pharmaceutical Preparations: thirty-first report. Geneva: World Health Organization; 1990: Annex 6 (WHO Technical Report Series, No. 790), (5), (http://apps.who.int/medicinedocs/documents/s21964en/s21964en.pdf)
Framework:	Structure/Foundation/Input
Rating Scale:	➜ NOT IMPLEMENTED (NI): There is no defined structure in charge of establishment licensing activities. ➜ ONGOING IMPLEMENTATION (OI): A mandate to establish a structure in charge of licensing activities is available however the structure itself is not yet established. ➜ PARTIALLY IMPLEMENTED (PI): Structure in charge of licensing activities is newly established and mandated however the regular work and practice of this structure is not yet consolidated. ➜ IMPLEMENTED (I): There is a defined structure in charge of establishment licensing activities with clear and well-documented roles and responsibilities.
Limitations and remarks:	Scoring this sub-indicator as "not applicable NA" is excluded (i.e. this sub-indicator will always apply for all benchmarked NRAs).
Sub Indicator:	**LI02.02: Documented procedures and mechanisms are implemented to ensure the involvement and communication between all stakeholders relevant to establishments licensing activities.**
Maturity Level:	3
Scope:	1. Medicines 2. Vaccines
Description:	The assessor should verify that documented procedures and mechanisms are implemented to ensure the involvement and communication between different entities and departments relevant to licensing activities. These entities may be inside or outside the NRA (e.g., laboratory, inspection and enforcement departments, police authorities, and professional associations). In case of a decentralized establishment licensing function, an information exchange system, mechanism or platform must be established and used so that appropriate communication between the central and peripheral structures is ensured. As one example, the decentralized entity can receive requests or guidance from the central authority and report back to it. The availability of such communication mechanisms will also encourage consistency among different peripheral structures.

Objective:	The objective of this sub-indicator is to ensure the existence and implementation of documented procedures and mechanisms to guide the involvement and communication among the different entities and departments. These activities will encourage appropriate organization and good governance of the function.
Requirement:	Organization and governance
Evidence to review:	The assessor should ask for and review: 1. Guidelines or standard operating procedures (SOPs) that are related to external and internal communications; 2. Documentation of paths of communication and reporting; 3. Platforms for information sharing and exchange.
References:	1. National drug regulatory legislation: guiding principles for small drug regulatory authorities. In: WHO Expert Committee on Specifications for Pharmaceutical Preparations: thirty-fifth report. Geneva: World Health Organization; 1999: Annex 8 (WHO Technical Report Series, No. 885), (1), (http://apps.who.int/medicinedocs/documents/s21964en/s21964en.pdf) 2. Guiding principles for small national drug regulatory authorities. In: WHO Expert Committee on Specifications for Pharmaceutical Preparations: thirty-first report. Geneva: World Health Organization; 1990: Annex 6 (WHO Technical Report Series, No. 790), (5), (http://apps.who.int/medicinedocs/documents/s21964en/s21964en.pdf) 3. Effective drug regulation: A multicounty study. Geneva: World Health Organization; 2002, (7), (http://apps.who.int/medicinedocs/pdf/s2300e/s2300e.pdf) 4. Quality systems requirements for national good manufacturing practice inspectorates. In: WHO Expert Committee on Specifications for Pharmaceutical Preparations: thirty-sixth report. Geneva: World Health Organization; 2002: Annex 8 (WHO Technical Report Series, No. 902), (8), (http://apps.who.int/medicinedocs/documents/s22112en/s22112en.pdf)
Framework:	Structure/Foundation/Input
Rating Scale:	➔ NOT IMPLEMENTED (NI): There are no information exchange procedures or mechanisms among different stakeholders of the licensing function or between the central authority and the decentralized entities. ➔ ONGOING IMPLEMENTATION (OI): The NRA is developing an information exchange mechanism, but it is not yet ready, or exchanges are being conducted without an established methodology. ➔ PARTIALLY IMPLEMENTED (PI): The NRA recently established an information exchange procedure and mechanism and it is at the implementation stage, so this practice is not yet consolidated. ➔ IMPLEMENTED (I): There are established, implemented and maintained information exchange procedures and mechanisms among different stakeholders of the licensing function and between the central authority and the decentralized entities.
Limitations and remarks:	▪ The scope of this sub-indicator is not confined only to routine activities, but also applies, most importantly, to regulatory decisions and actions. ▪ Scoring this sub-indicator as "not applicable NA" is excluded (i.e. this sub-indicator will always apply for all benchmarked NRAs).
Indicator:	**LI03 Human resources to perform licensing activities.**
Objective:	The objective of this indicator is to ensure that all entities within an NRA are adequately resourced with a trained, experienced and skilled workforce that is empowered to fully perform the licensing function. This will ensure that medical products licensing processes or activities are performed in accordance with international best practices. The objective of this indicator is to evaluate the human resource capacity of the entities with respect to the number of personnel, the skills and experience of the personnel, and the overall composition the workforce, with the goal of evaluating whether the workforce possesses the specific expertise required to perform the licensing function.

Category:	Resources (HR, FR, infrastructure and equipment)
Sub Indicator:	**LI03.01: Sufficient competent staff (i.e., education, training, skills and experience) are assigned to perform licensing activities.**
Maturity Level:	3
Scope:	1. Medicines 2. Vaccines
Description:	The assessor should verify that the human resources assigned to perform licensing activities should be sufficient with respect to numbers and competent with respect to the requisite skills, education, experience and training. There should be technical documents and SOPs that provide guidance on the required background for licensing activities and that consider the requirements for educational background, competencies, skills, experience, and training. The assessor should verify that the NRA estimated the number of staff required to effectively and efficiently perform licensing function and that the NRA actually recruited that number. In addition, the assessor should verify that these competency requirements are well-established and maintained by the NRA. Metrics and statistics on the different activities performed as well as performance indicators can be used for estimating the adequacy of the number of the assigned staff. The assessor should also verify that the competency of the assigned staff is built, maintained and improved through recruitment as well as continuous on- the-job training.
Objective:	The objective of this sub-indicator is to ensure the existing human resources for licensing is sufficient, in terms of numbers, experience, and specific competencies, to perform all the activities along the entire licensing chain.
Requirement:	Sufficient number of competent human resources in charge of licensing activities.
Evidence to review:	The assessor should ask for and review: 1. Evidence that the number of staff members involved in each of the documented activities along the entire licensing process flow is adequate. 2. Evidence that the systems and structures are in place to ensure appropriate placement of staff with respect to competence and skills. 3. Evidence that the system and structures have been implemented. The documentation should include the records to verify that the staff competence is appropriate for the job requirements. 4. Evidence that the professional profiles of the human resources engaged in licensing activities are appropriate with respect to education, skills, and expertise, to perform a particular function along the licensing chain. Documentation should include a list of the requisite skills and training for each position. 5. Recruitment plan.
References:	1. WHO good manufacturing practices for pharmaceutical products: main principles, (51), (http://digicollection.org/whoqapharm/p/about and http://apps.who.int/medicinedocs/en)
Framework:	Structure/Foundation/Input
Rating Scale:	➜ NOT IMPLEMENTED (NI): The NRA does not have enough competent staff (i.e., education, training, skills and experience) to perform licensing activities ➜ ONGOING IMPLEMENTATION (OI): The NRA has recently developed a plan to recruit adequate competent staff; however, the plan has not been implemented. ➜ PARTIALLY IMPLEMENTED (PI): The NRA has initiated the implementation of the human resources development plan; however, there is need to complete the competency profile. ➜ IMPLEMENTED (I): The NRA has a sustained number of competent staff (i.e., education, training, skills and experience) assigned to perform licensing activities.

Limitations and remarks:	▪ Assessment of the adequacy and appropriateness of the number of staff members is quite subjective and should be linked to some process or output indicators. When estimating staff adequacy, the assessor should consider the workload, backlog, and delays in delivery based on established timeframes. ▪ Scoring this sub-indicator as "not applicable NA" is excluded (i.e. this sub-indicator will always apply for all benchmarked NRAs).
Sub Indicator:	**LI03.02: Duties, functions, and responsibilities of the staff in charge of licensing activities are established and updated in the respective job descriptions.**
Maturity Level:	3
Scope:	1. Medicines 2. Vaccines
Description:	The assessor should verify that procedures are in place to maintain a current and updated structure for managing job descriptions for personnel participating in licensing activities. In addition, job descriptions should address current staff duties, responsibilities and the requisite competencies. A job description with this format and content should be established and implemented for all staff. The management of job descriptions should be supported by a guidance document that provides direction on when and how to update the information, and where the information should be kept for easy access. The guidance document should present the appropriate duties and responsibilities that are assigned to each member of the organization involved in licensing activities. Thus, the professional profiles of staff are reflected in their respective roles and responsibilities within the NRA. There should be procedures to guide responsible persons to document that duties, functions and responsibilities are revised and kept up to date. In addition, procedures should be available to guide the keeping and documenting of up to date work schedules and enforcing the implementation of the documented guidelines and procedures.
Objective:	The objective of this sub-indicator is to ensure that duties and responsibilities of the staff are clear and well defined, that job descriptions are kept up to date with current duties, functions and responsibilities, and that these activities are adequately documented.
Requirement:	Duties, roles and responsibilities of the staff relevant to licensing activities.
Evidence to review:	The assessor should ask for and review: 1. Procedure and guidelines that guide placement of staff members within the NRA; 2. The professional profiles of staff (i.e., job descriptions) and documentation that they are related to their current roles and duties; 3. The professional profiles of the external experts and documentation that the profiles provide a composition that is complete and consistent with that prescribed in the legal provisions; 4. Procedures to guide the documentation of up to date duties and work schedules, and to enforce the implementation of the documented guidelines and procedures; 5. Job descriptions for designated staff.
References:	1. National drug regulatory legislation: guiding principles for small drug regulatory authorities. In: WHO Expert Committee on Specifications for Pharmaceutical Preparations: thirty-fifth report. Geneva: World Health Organization; 1999: Annex 8 (WHO Technical Report Series, No. 885), (1), (http://apps.who.int/medicinedocs/documents/s21964en/s21964en.pdf) 2. Quality management systems — Requirements. International Standard ISO 9001:2015. Geneva. International Organization for Standardization, 2015, (4), (https://www.iso.org/iso-9001-quality-management.html) 3. Guiding principles for small national drug regulatory authorities. In: WHO Expert Committee on Specifications for Pharmaceutical Preparations: thirty-first report. Geneva: World Health Organization; 1990: Annex 6 (WHO Technical Report Series, No. 790), (5), (http://apps.who.int/medicinedocs/documents/s21964en/s21964en.pdf) 4. Effective drug regulation: A multicounty study. Geneva: World Health Organization; 2002, (7), (http://apps.who.int/medicinedocs/pdf/s2300e/s2300e.pdf)

Framework:	Structure/Foundation/Input
Rating Scale:	➔ NOT IMPLEMENTED (NI): There is no evidence of defined or established duties, functions, responsibilities, respective job descriptions and necessary required competencies. ➔ ONGOING IMPLEMENTATION (OI): The NRA has recently drafted or developed the role and responsibilities document but it has not yet been implemented. ➔ PARTIALLY IMPLEMENTED (PI): The NRA has initiated implementation of this requirement but it has not been defined or followed for all staff or the roles and responsibilities documents, including staff job descriptions, are not up to date. ➔ IMPLEMENTED (I): The NRA has defined and established all required duties, functions, and responsibilities, and respective job descriptions are up-to-date.
Limitations and remarks:	Scoring this sub-indicator as "not applicable NA" is excluded (i.e. this sub-indicator will always apply for all benchmarked NRAs).
Sub Indicator:	**LI03.03: Training plan developed, implemented and updated at least once a year for staff in charge of licensing activities.**
Maturity Level:	3
Scope:	1. Medicines 2. Vaccines
Description:	The assessor should verify that training plans are developed, implemented and updated at least once every year to reflect the current situation by considering education and experience of the staff. The training plan should be complemented with guidelines or similar documents that guide the development and implementation of training plans. The assessor should ensure that induction training for new staff as well as continued on- the-job for staff is planned and implemented. There should be procedures to approve the training plan and the budget allocated for implementing and updating the training plan. The plans should present clearly defined training goals and should include training in certain topics and skills to address identified deficiencies. Learning objectives, training methods and activities, evidence of learning, and evaluation and assessment of training should be documented. This documentation should confirm that the learning objectives were achieved and were designed to address weaknesses within the entities. Procedures should be in place to ensure that a training plan is developed, implemented and updated at least once every year. The assessor should verify that there is a system in place for monitoring the implementation and effectiveness of the training plan and for documenting the skills acquired in training activities for internal and external experts. The assessor should verify that inspectors in charge of Good Manufacturing Practices inspections associated with manufacturer licensing activities receive a minimum of ten (10) training days per year as recommended by the WHO and Pharmaceutical Inspection Cooperation Scheme guidelines.
Objective:	The objective of this sub-indicator is to ensure that a training plan for staff exists, and that it is implemented and updated annually. Through the training plan, NRA can be sure that competency of staff in charge of licensing activities is maintained and enhanced.
Requirement:	Implementation of training plan
Evidence to review:	The assessor should ask for and review: 1. Guidelines for development, implementation and annual update (i.e., at least once per year) of the training plan. Guidelines should also provide for a mechanism to measure effectiveness of training. 2. Documentation for the system or structures used to approve the training plan and to evaluate the adequacy of the budget allocated to the training activities. 3. The current or existing staff training plan (or matrix) for staff. The assessor should assess this in in relation to the respective individual job descriptions.

	4. SOP for developing and maintaining the training plan. 5. Evidence that the NRA has investigated and identified training needs. 6. List of trainings performed. 7. Example records for training activities.
References:	1. National drug regulatory legislation: guiding principles for small drug regulatory authorities. In: WHO Expert Committee on Specifications for Pharmaceutical Preparations: thirty-fifth report. Geneva: World Health Organization; 1999: Annex 8 (WHO Technical Report Series, No. 885), (1), (http://apps.who.int/medicinedocs/documents/s21964en/s21964en.pdf) 2. Quality management systems — Requirements. International Standard ISO 9001:2015. Geneva. International Organization for Standardization, 2015, (4), (https://www.iso.org/iso-9001-quality-management.html) 3. Guiding principles for small national drug regulatory authorities. In: WHO Expert Committee on Specifications for Pharmaceutical Preparations: thirty-first report. Geneva: World Health Organization; 1990: Annex 6 (WHO Technical Report Series, No. 790), (5), (http://apps.who.int/medicinedocs/documents/s21964en/s21964en.pdf) 4. Effective drug regulation: A multicounty study. Geneva: World Health Organization; 2002, (7), (http://apps.who.int/medicinedocs/pdf/s2300e/s2300e.pdf) 5. Quality systems requirements for national good manufacturing practice inspectorates. In: WHO Expert Committee on Specifications for Pharmaceutical Preparations: thirty-sixth report. Geneva: World Health Organization; 2002: Annex 8 (WHO Technical Report Series, No. 902), (8), (http://apps.who.int/medicinedocs/documents/s22112en/s22112en.pdf)
Framework:	Process
Rating Scale:	➜ NOT IMPLEMENTED (NI): There is no systematic training program including training plan (or matrix). ➜ ONGOING IMPLEMENTATION (OI): The NRA has recently drafted or developed the training plan but there is no evidence of implementation. ➜ PARTIALLY IMPLEMENTED (PI): The NRA has developed and initiated the training plan implementation. However, the NRA has not fulfilled all required planed training or has been applying the plan for less than two years. ➜ IMPLEMENTED (I): The NRA has an updated training plan developed that is supported by adequate records to demonstrate effective plan implementation, including induction training for new staff and routine on-the-job training for recruited staff.
Limitations and remarks:	▪ Training plans must be updated regularly; ideally on an annual basis, but not less frequently that once every two years. ▪ Some regulatory functions may include many training activities that are not incorporated in the institutional training programme. Such training normally is offered by invitation. In this case, the assessor should recognize reports from non-routine licensing -relevant training not included in the NRA training plan. ▪ Scoring this sub-indicator as "not applicable NA" is excluded (i.e. this sub-indicator will always apply for all benchmarked NRAs).
Sub Indicator:	**LI03.04: The NRA generates and maintains records of staff training activities and training effectiveness verification.**
Maturity Level:	3
Scope:	1. Medicines 2. Vaccines
Description:	The assessor should verify that records of staff training that is performed or organized by the NRA are generated, maintained, regularly updated. This activity should be supported by guidelines that direct the NRA to generate and maintain records of staff training activities. Procedures should be in place to document and propose staff training needs and to

	allocate a budget for continuous staff capacity building and development. The assessor should check that there is an evaluation or assessment mechanism to verify the quality of learning, and to confirm that learning objectives are achieved. Documentation should include an inventory (i.e., soft and/or hard) system that records all impactful and non-impactful trainings and identifies all staff members who participated. A system to measure or estimate impact of trainings should be established.
Objective:	The objective of this sub-indicator is to ensure that training organized by the NRA or responsible regulatory authority is adequately documented and that the training records are adequately maintained and kept. Staff training records are considered an integral part of staff file and are a tool for measuring and tracking staff competency, development and adequacy.
Requirement:	Training records
Evidence to review:	The assessor should ask for and review: 1. Guidelines or similar documents that guide the NRA to generate and maintain records of staff training activities; 2. Evaluations of training effectiveness; 3. The training inventory, and procedures for completing the inventory; 4. Examples of archived records of staff training, and procedures for the archiving system.
References:	1. National drug regulatory legislation: guiding principles for small drug regulatory authorities. In: WHO Expert Committee on Specifications for Pharmaceutical Preparations: thirty-fifth report. Geneva: World Health Organization; 1999: Annex 8 (WHO Technical Report Series, No. 885), (1), (http://apps.who.int/medicinedocs/documents/s21964en/s21964en.pdf) 2. Quality management systems — Requirements. International Standard ISO 9001:2015. Geneva. International Organization for Standardization, 2015, (4), (https://www.iso.org/iso-9001-quality-management.html) 3. Guiding principles for small national drug regulatory authorities. In: WHO Expert Committee on Specifications for Pharmaceutical Preparations: thirty-first report. Geneva: World Health Organization; 1990: Annex 6 (WHO Technical Report Series, No. 790), (5), (http://apps.who.int/medicinedocs/documents/s21964en/s21964en.pdf) 4. Effective drug regulation: A multicounty study. Geneva: World Health Organization; 2002, (7), (http://apps.who.int/medicinedocs/pdf/s2300e/s2300e.pdf)
Framework:	Output
Rating Scale:	➜ NOT IMPLEMENTED (NI): There is no evidence that the NRA generates and maintains records of staff training activities. ➜ ONGOING IMPLEMENTATION (OI): The NRA has recently initiated plans to generate, document and keep records of staff training activities, however they are not yet followed. ➜ PARTIALLY IMPLEMENTED (PI): The NRA has recently initiated plans to generate, document and keep records of staff training activities but they are not fully followed for all training activities or they have been established for less than two years. ➜ IMPLEMENTED (I): The NRA generates and maintains records of staff training activities
Limitations and remarks:	▪ The assessor should note that some NRAs out-source training including staff capacity development activities. In this case the assessor should request the identity of the provider, as well as evaluations of the provider. The assessor may request the professional profiles of tutors or resource persons used to offer training. The assessor may also request records covering the archiving systems in place. ▪ Scoring this sub-indicator as "not applicable NA" is excluded (i.e. this sub-indicator will always apply for all benchmarked NRAs).

Indicator:	**LI04 Procedures established and implemented to perform licensing activities.**
Objective:	The objective of this indicator is to ensure that the NRA, when supported by appropriate mandates, effective organization and governance, and essential resources, is actually able to perform the licensing activities. These activities are performed through standard procedures and work instructions in order to ensure consistency, effectiveness, efficiency, impartiality and proportionality of the activities. There should be written procedures that define how relevant data are routinely shared among key personnel engaged in licensing activities and on how any actions taken are reviewed for appropriateness. Documented evidence to be assessed include procedures for review and sharing of relevant data between key players, for review of reports of notifications, investigations, data analyses, and committee meetings, and for taking appropriate actions.
Category:	Regulatory process
Sub Indicator:	**LI04.01: Procedures for assessment of applications for licensing activities, including license issuance, renewal, modification or revocation, are established and documented.**
Maturity Level:	3
Scope:	1. Medicines 2. Vaccines
Description:	The assessor should verify that different phases of licensing activities, including application receiving, screening, processing, assessing, and decision-making (e.g., issue, renew, amend, modify, suspend or revoke) are well established and documented. With particular emphasis on license renewals, amendments and modifications, the relevant procedures and mechanisms should ideally be based on Quality Risk Management principles. When applicable, the validity of the establishment license should be stated in the respective certificate in order to clarify status and to avoid misunderstandings.
Objective:	The objective of this sub-indicator is to ensure consistency and standardization of licensing activities through established and documented procedures and mechanisms that are complemented with the necessary tools.
Requirement:	Regulatory process
Evidence to review:	The assessor should ask for and review: 1. SOPs, checklists and records for different licensing activities (e.g. issuance, renewal, modification, and revocation); 2. Evaluation reports provided by the NRA and other documented evidence of decisions that were based on the procedures.
References:	1. National drug regulatory legislation: guiding principles for small drug regulatory authorities. In: WHO Expert Committee on Specifications for Pharmaceutical Preparations: thirty-fifth report. Geneva: World Health Organization; 1999: Annex 8 (WHO Technical Report Series, No. 885), (1), (http://apps.who.int/medicinedocs/documents/s21964en/s21964en.pdf) 2. Quality management systems — Requirements. International Standard ISO 9001:2015. Geneva. International Organization for Standardization, 2015, (4), (https://www.iso.org/iso-9001-quality-management.html) 3. Guiding principles for small national drug regulatory authorities. In: WHO Expert Committee on Specifications for Pharmaceutical Preparations: thirty-first report. Geneva: World Health Organization; 1990: Annex 6 (WHO Technical Report Series, No. 790), (5), (http://apps.who.int/medicinedocs/documents/s21964en/s21964en.pdf) 4. Effective drug regulation: A multicounty study. Geneva: World Health Organization; 2002, (7), (http://apps.who.int/medicinedocs/pdf/s2300e/s2300e.pdf)

Framework:	Process
Rating Scale:	➔ NOT IMPLEMENTED (NI): There are no procedures for making decisions on license issuance, renewal, modification, or revocation. ➔ ONGOING IMPLEMENTATION (OI): The NRA is preparing procedures for making decisions on licensing activities, but they are not completed so there is no evidence of results from such activities. ➔ PARTIALLY IMPLEMENTED (PI): Procedures for different licensing activities are newly established and at the implementation stage, so this practice is not yet consolidated. ➔ IMPLEMENTED (I): The NRA has procedures for making decisions on license issuance, renewal, modification, or revocation; the NRA applies the procedures consistently, and reliably maintains documentation of the results of related activities over time.
Limitations and remarks:	▪ In some countries, license renewal might not be applicable. Rather the license is maintained based on regular inspections for compliance with GXPs. In this case, the requirement to document license renewals will not apply provided the assessor confirms the proper implementation of regular regulatory inspections. ▪ Scoring this sub-indicator as "not applicable NA" is excluded (i.e. this sub-indicator will always apply for all benchmarked NRAs).
Sub Indicator:	**LI04.02: Inspection is required for granting or re-granting a license or approval of a substantial modification.**
Maturity Level:	3
Scope:	1. Medicines 2. Vaccines
Description:	The assessor should verify the existence and implementation of standard procedures for the inspection process that is required before granting or re-granting a license or approval of a substantial modification. The inspection should be carried out in accordance with the official guidelines and in accordance with a formal inspection plan.
Objective:	The objective of this sub-indicator is to ensure that the inspectorate has established procedures and other mechanisms to consistently perform inspections before granting or re-granting a license or an approval of a substantial modification. Also, the objective is to ensure consistency of licensing and inspection procedures and to ensure regulatory compliance of establishments. These activities will promote the ultimate goal of protecting public health.
Requirement:	Regulatory process
Evidence to review:	The assessor should ask for and review: 1. Procedures for the inspection process. 2. SOPs, checklists and records for different licensing activities (e.g. issuance, renewal, modification, or revocation. 3. Examples of inspection reports done prior to license issuance, renewal, amendment or revocation. 4. Procedures for the NRA to conduct GXP inspections.
References:	1. Quality systems requirements for national good manufacturing practice inspectorates. In: WHO Expert Committee on Specifications for Pharmaceutical Preparations: thirty-sixth report. Geneva: World Health Organization; 2002: Annex 8 (WHO Technical Report Series, No. 902), (8), (http://apps.who.int/medicinedocs/documents/s22112en/s22112en.pdf) 2. Guiding principles for small national drug regulatory authorities. In: WHO Expert Committee on Specifications for Pharmaceutical Preparations: thirty-first report. Geneva: World Health Organization; 1990: Annex 6 (WHO Technical Report Series, No. 790), (5), (http://apps.who.int/medicinedocs/documents/s21964en/s21964en.pdf) 3. Quality management systems — Requirements. International Standard ISO 9001:2015.

	Geneva. International Organization for Standardization, 2015, (4), (https://www.iso.org/iso-9001-quality-management.html) 4. Effective drug regulation: A multicounty study. Geneva: World Health Organization; 2002, (7), (http://apps.who.int/medicinedocs/pdf/s2300e/s2300e.pdf) 5. National drug regulatory legislation: guiding principles for small drug regulatory authorities. In: WHO Expert Committee on Specifications for Pharmaceutical Preparations: thirty-fifth report. Geneva: World Health Organization; 1999: Annex 8 (WHO Technical Report Series, No. 885), (1), (http://apps.who.int/medicinedocs/documents/s21964en/s21964en.pdf)
Framework:	Process
Rating Scale:	➔ NOT IMPLEMENTED (NI): License issuances and renewals and approvals of substantial modification are never made in conjunction with GXP inspections. ➔ ONGOING IMPLEMENTATION (OI): License issuances and renewals and approvals of substantial modification are sometimes made in conjunction with GXP inspections. ➔ PARTIALLY IMPLEMENTED (PI): License issuances and renewals and approvals of substantial modification have been made in conjunction with GXP inspections for a short time (less than one year) so this practice is not yet consolidated. ➔ IMPLEMENTED (I): License issuances and renewal and approvals of substantial modification are always made in conjunction with GXP inspections.
Limitations and remarks:	▪ In some cases, a license or approval of a substantial modification may be granted without inspection. However, these should be seen as exceptional situations and need to be justified, well described and compatible with guidelines. Also, these activities are tightly linked to transparency. ▪ Scoring this sub-indicator as "not applicable NA" is excluded (i.e. this sub-indicator will always apply for all benchmarked NRAs)
Sub Indicator:	**LI04.03: There are clearly defined timelines for the assessment of applications.**
Maturity Level:	3
Scope:	1. Medicines 2. Vaccines
Description:	The assessor should verify that clear timelines have been defined for the different steps in the licensing process as well as for the different types of license applications, including new applications and applications for license renewals or modifications. These timelines should be clear and understandable to the target audience. The assessor should review examples of the processing of different applications and ensure that a proper monitoring system is in place to verify adherence to the stated timelines.
Objective:	The objective of this sub-indicator is to ensure the existence and implementation of standard procedures for defining clear timelines for the processing of license applications.
Requirement:	Regulatory process
Evidence to review:	The assessor should ask for and review: 1. Records of license processing that cover the steps from initial application up to issuance of final decision. Assessor review should focus on timelines. 2. Records from the timelines tracking system, if available.
References:	
Framework:	Process
Rating Scale:	➔ NOT IMPLEMENTED (NI): There are no timelines for different licensing activities.

	➔ ONGOING IMPLEMENTATION (OI): The NRA is drafting timelines for different licensing activities however these are not yet implemented and no results are yet achieved. ➔ PARTIALLY IMPLEMENTED (PI): The NRA recently established timelines for different licensing activities so this practice is not yet consolidated. ➔ IMPLEMENTED (I): There are clear timelines, which are tracked, for different licensing activities.
Limitations and remarks:	Scoring this sub-indicator as "not applicable NA" is excluded (i.e. this sub-indicator will always apply for all benchmarked NRAs).
Sub Indicator:	**LI04.04: The same criteria are used for the licensing of domestic, public and private establishments regardless of ownership.**
Maturity Level:	3
Scope:	1. Medicines 2. Vaccines
Description:	The assessor should verify that the conduct of licensing activities and application of the relevant standards, procedures, and GXPs is consistent and unbiased regardless of the source of production (e.g., domestic or foreign, public or private sector).
Objective:	The objective of this sub-indicator is to ensure consistent and unbiased conduct of licensing activities and application of relevant standards, procedures and GXPs.
Requirement:	Regulatory process
Evidence to review:	The assessor should ask for and review: 1. SOPs or similar documents that ensure that the same licensing criteria are used regardless of ownership of the establishment (e.g., domestic, foreign, public or private). 2. Sample licensing records for establishments from different ownership categories (e.g., domestic, foreign, public or private).
References:	1. National drug regulatory legislation: guiding principles for small drug regulatory authorities. In: WHO Expert Committee on Specifications for Pharmaceutical Preparations: thirty-fifth report. Geneva: World Health Organization; 1999: Annex 8 (WHO Technical Report Series, No. 885), (1), (http://apps.who.int/medicinedocs/documents/s21964en/s21964en.pdf) 2. Quality management systems — Requirements. International Standard ISO 9001:2015. Geneva. International Organization for Standardization, 2015, (4), (https://www.iso.org/iso-9001-quality-management.html) 3. Guiding principles for small national drug regulatory authorities. In: WHO Expert Committee on Specifications for Pharmaceutical Preparations: thirty-first report. Geneva: World Health Organization; 1990: Annex 6 (WHO Technical Report Series, No. 790), (5), (http://apps.who.int/medicinedocs/documents/s21964en/s21964en.pdf) 4. Effective drug regulation: A multicounty study. Geneva: World Health Organization; 2002, (7), (http://apps.who.int/medicinedocs/pdf/s2300e/s2300e.pdf)
Framework:	Process
Rating Scale:	➔ NOT IMPLEMENTED (NI): The NRA does not apply the same licensing criteria for domestic, public and private establishments, including for products at the research and development stage. ➔ ONGOING IMPLEMENTATION (OI): The NRA is preparing to establish procedures to apply the same criteria, regardless of ownership, for licensing of domestic, public and private establishments, including for products at the research and development stage. However, there is no evidence of any results associated with such activities.

- ➔ PARTIALLY IMPLEMENTED (PI): The NRA recently established procedures to apply the same criteria, regardless of ownership, for licensing of domestic, public and private establishments, including for products at the research and development stage. These are at the implementation stage, so these practices are not yet consolidated.
- ➔ IMPLEMENTED (I): The NRA applies the same criteria, regardless of ownership, for licensing of domestic, public and private establishments, including for products at the research and development stage. The NRA consistently maintains documentation of the results of related activities over time.

Limitations and remarks:	Scoring this sub-indicator as "not applicable NA" is excluded (i.e. this sub-indicator will always apply for all benchmarked NRAs).
Indicator:	**LI05 Mechanism in place to monitor regulatory performance and output.**
Objective:	The objective of this indicator is to ensure the existence and implementation of a system or mechanism for monitoring regulatory performance and output and for using that information to estimate the effectiveness and efficiency of the licensing function.
Category:	09. Monitoring progress and assessing outcomes and impact
Sub Indicator:	**LI05.01: A database is established and regularly updated that includes all licensing applications received, approved, refused, suspended or withdrawn, along with the essential documentation for each application.**
Maturity Level:	4
Scope:	1. Medicines 2. Vaccines
Description:	The assessor should verify that, within the NRA, there is a database of all the applications received, approved, refused, suspended or withdrawn. The database should also include the essential documentation for each application. At a minimum, documentation should include the applications received and records of assessments done, and regulatory decisions made.
Objective:	The objective of this sub-indicator is to ensure consistency and traceability of licensing activities through the establishment and maintenance of a database of all the applications received, approved, refused, suspended or withdrawn, along with the essential documentation for each application.
Requirement:	Monitoring progress and assessing outcomes and impact
Evidence to review:	The assessor should ask for and review: 1. The NRA internal database of the licensing applications along with the regulatory decisions made for each application (i.e., approved, rejected, denied, withdrawn, cancelled, or suspended).
References:	1. National drug regulatory legislation: guiding principles for small drug regulatory authorities. In: WHO Expert Committee on Specifications for Pharmaceutical Preparations: thirty-fifth report. Geneva: World Health Organization; 1999: Annex 8 (WHO Technical Report Series, No. 885), (1), (http://apps.who.int/medicinedocs/documents/s21964en/s21964en.pdf) 2. Effective drug regulation: A multicounty study. Geneva: World Health Organization; 2002, (7), (http://apps.who.int/medicinedocs/pdf/s2300e/s2300e.pdf) 3. Guiding principles for small national drug regulatory authorities. In: WHO Expert Committee on Specifications for Pharmaceutical Preparations: thirty-first report. Geneva: World Health Organization; 1990: Annex 6 (WHO Technical Report Series, No. 790), (5), (http://apps.who.int/medicinedocs/documents/s21964en/s21964en.pdf)

	4. Quality management systems — Requirements. International Standard ISO 9001:2015. Geneva. International Organization for Standardization, 2015, (4), (https://www.iso.org/iso-9001-quality-management.html)
Framework:	Output
Rating Scale:	➜ NOT IMPLEMENTED (NI): There is no internal database of licensing applications along with their regulatory decisions (i.e., approved, rejected, denied, withdrawn, cancelled, or suspended). ➜ ONGOING IMPLEMENTATION (OI): The NRA is working on the establishment of an internal database of licensing applications along with their regulatory decisions (i.e., approved, rejected, denied, withdrawn, cancelled, or suspended) however the database is not yet established. ➜ PARTIALLY IMPLEMENTED (PI): The NRA has recently established an internal database of licensing applications along with their regulatory decisions (i.e., approved, rejected, denied, withdrawn, cancelled, or suspended), however the outputs and outcomes of this practice are not yet documented. ➜ IMPLEMENTED (I): There is an implemented internal database of licensing applications along with their regulatory decisions (i.e., approved, rejected, denied, withdrawn, cancelled, or suspended).
Limitations and remarks:	Scoring this sub-indicator as "not applicable NA" is excluded (i.e. this sub-indicator will always apply for all benchmarked NRAs).
Sub Indicator:	**LI05.02: Performance indicators for licensing activities are established and implemented**
Maturity Level:	4
Scope:	1. Medicines 2. Vaccines
Description:	The assessor should verify the existence and implementation of performance indicators for different activities included under the licensing functions. Specifically, the system should define key performance indicators (KPIs) along the entire licensing activity chain and all indicators should be adequately justified. For the purpose of clarity and consistency, established KPIs should be supported with guidelines for monitoring and maintenance of the KPIs. The guidelines in turn should be supported by SOPs and tools that define the procedures to be used for monitoring and evaluating the performance indicators and that define procedures and timelines for reviewing and revising the indicators. Established KPIs might be qualitative, quantitative or combination of both. In general, quantitative indicators are preferred to avoid bias or misinterpretation. However, qualitative indicators are also accepted. Qualitative indicators may or may not include scoring or scaling to render them semi-quantitative and thus more informative. The assessor should ensure that indicators are measured on a regular basis to monitor progress and advancement. In addition, the assessor should verify measured indicators are analyzed to identify trends or abnormalities. Justifications for any identified abnormalities should be provided; when necessary, process optimizations should be introduced to avoid recurrence.
Objective:	The objective of this sub-indicator is to ensure that a system, mechanism, or procedure exists to require the NRA to establish performance indicators along the entire licensing chain. Additionally, the objective is to ensure that KPIs are actually contributing to monitoring of regulatory performance, to measuring effectiveness of licensing regulatory activities, and to making any necessary adjustments or optimizations.
Requirement:	KPIs for licensing activities

Evidence to review:	The assessor should ask for and review: 1. Documents supporting the system, mechanism, or procedure compelling the NRA to establish and implement performance indicators along the entire licensing activity chain. 2. Evidence that the performance indicators have been established and implemented, and that the members of staff involved in the licensing function are aware of the indicators and the guidelines and SOPs used for monitoring and evaluating their performance. 3. The current performance indicators for licensing activities 4. Analyses of the measured indicators along with the investigations done to identify trends or abnormalities. 5. Documentation for follow- up of any observed abnormalities, including justifications for any identified abnormalities as well as any process optimizations introduced to avoid recurrence.
References:	1. National drug regulatory legislation: guiding principles for small drug regulatory authorities. In: WHO Expert Committee on Specifications for Pharmaceutical Preparations: thirty-fifth report. Geneva: World Health Organization; 1999: Annex 8 (WHO Technical Report Series, No. 885), (1), (http://apps.who.int/medicinedocs/documents/s21964en/s21964en.pdf) 2. Effective drug regulation: A multicounty study. Geneva: World Health Organization; 2002, (7), (http://apps.who.int/medicinedocs/pdf/s2300e/s2300e.pdf) 3. Guiding principles for small national drug regulatory authorities. In: WHO Expert Committee on Specifications for Pharmaceutical Preparations: thirty-first report. Geneva: World Health Organization; 1990: Annex 6 (WHO Technical Report Series, No. 790), (5), (http://apps.who.int/medicinedocs/documents/s21964en/s21964en.pdf) 4. Quality management systems — Requirements. International Standard ISO 9001:2015. Geneva. International Organization for Standardization, 2015, (4), (https://www.iso.org/iso-9001-quality-management.html) 5. Quality management -- Quality of an organization -- Guidance to achieve sustained success, ISO 9004:2018, International Organization for Standardization (ISO), (115), (https://www.iso.org/standard/70397.html)
Framework:	Output
Rating Scale:	➔ NOT IMPLEMENTED (NI): There are no KPIs for licensing activities. ➔ ONGOING IMPLEMENTATION (OI): The NRA has recently drafted KPIs for licensing activities but they have not yet been reported. ➔ PARTIALLY IMPLEMENTED (PI): The NRA has developed KPIs for licensing activities and has been applying them for less than two year or they have not covered all critical steps. ➔ IMPLEMENTED (I): The NRA has established and implemented KPIs for licensing activities. The indicators are reviewed regularly, and appropriate actions are taken, and decisions made.
Limitations and remarks:	▪ When they refer to outcomes, indicators may be ambiguous and difficult to interpret, as outcomes are the result of many factors that are difficult to disentangle. When they refer to processes, indicators are often too specific, as they may focus on a particular intervention or condition or they may quickly become outdated as business models develop. ▪ Different methodologies are used to measure the NRAs performance on licensing activities. In this case, the assessor should verify that adequate supporting documents are available. The assessor should consider that developed performance indicators should be Specific, Measurable, Achievable, Realistic, and Time-bound (i.e., "SMART"). ▪ Scoring this sub-indicator as "not applicable NA" is excluded (i.e. this sub-indicator will always apply for all benchmarked NRAs).
Indicator:	**LI06 Mechanism exists to promote transparency, accountability and communication.**
Objective:	The objective of this indicator is to ensure that mechanisms are in place that promote effective communication inside and outside the NRA, that promote transparency and outreach to the public, and that establish milestones that encourage accountability of the NRA to its mandate. Additionally, these contribute to mutual understanding and

	involvement of all stakeholders relevant to licensing activities. Consequently, confidence in the regulatory system is raised.
Category:	08. Transparency, accountability and communication
Sub Indicator:	**LI06.01: An updated list or database of all licensing applications, along with the regulatory decision for each, is regularly published and publicly available.**
Maturity Level:	3
Scope:	1. Medicines 2. Vaccines
Description:	The assessor should verify the availability of a well-established mechanism or procedure to promote transparency, accountability and communication of licensing activities. The assessor should check the availability of an updated and complete list or database of licensed facilities throughout the supply chain, along with the regulatory decision for each application (i.e., whether the license was granted or not). The assessor should determine whether the list or database is published and can be accessed by the public. As a minimal requirement, the list or database of all manufacturing licenses approved should be publicly available on the NRA website or the official government record of each country. The list or database should be maintained and regularly updated. This information supports decision-making on other regulatory activities within the NRA and provides transparency for the general public on the status of the NRAs licensing activities. The publication of negative decisions (i.e. applications which were not granted or approved) is encouraged; however, priority should go to approved applications.
Objective:	The objective of this sub-indicator is to build confidence and accountability of the licensing process via enhanced transparency.
Requirement:	Transparency, accountability and communication
Evidence to review:	The assessor should ask for and review: 1. Databases of establishments licensed by the NRA containing information on licenses that were approved, withdrawn, canceled, or suspended; 2. Latest publicly available list of licensed establishments.
References:	1. Guidelines on the implementation of the WHO certification scheme on the quality of pharmaceutical products moving in international commerce. In WHO Expert Committee on Specifications for Pharmaceutical Preparations: thirty-fourth report. Geneva. World Health Organization; 1996: Annex 10 (WHO Technical Report Series, No. 863), (29), (http://apps.who.int/medicinedocs/pdf/s5516e/s5516e.pdf) 2. Quality systems requirements for national good manufacturing practice inspectorates. In: WHO Expert Committee on Specifications for Pharmaceutical Preparations: thirty-sixth report. Geneva: World Health Organization; 2002: Annex 8 (WHO Technical Report Series, No. 902), (8), (http://apps.who.int/medicinedocs/documents/s22112en/s22112en.pdf) 3. Guidelines on import procedures for pharmaceutical products, World Health Organization (WHO), (22), (http://digicollection.org/whoqapharm/p/about and http://apps.who.int/medicinedocs/en)
Framework:	Output
Rating Scale:	➜ NOT IMPLEMENTED (NI): There is no publicly available list or database of all establishment licenses along with their regulatory actions. ➜ ONGOING IMPLEMENTATION (OI): The NRA is preparing to establish a database on licensed establishments, but there is no evidence of results from such activities. ➜ PARTIALLY IMPLEMENTED (PI): There is evidence that the NRA has the elements (i.e., procedures, documentation, management systems, and other relevant information.) and the capacity to perform the processes mentioned in the indicator, however, it has only limited experience or a limited number of documented events.

	➔ IMPLEMENTED (I): There is a publicly available list or database of all establishment licenses along with their regulatory actions.
Limitations and remarks:	The legal provisions may not allow publication of the establishments that have been sanctioned or suspended.
Sub Indicator:	**LI06.02: Inspection reports or summaries (or excerpts) relevant to licensing activities are published and publicly available.**
Maturity Level:	4
Scope:	1. Medicines 2. Vaccines
Description:	For inspections relevant to licensing activities, the assessor should verify that reports of inspections performed are available for the general public. The information which can be shared with the public varies according to the national legislation. In some countries, full inspection reports, redacted or non-redacted, might be published. In other countries, only inspection summaries or excerpts might be publicly available.
Objective:	The objective of this sub-indicator is to build confidence and accountability in the licensing entity via enhanced transparency through publication of the licensing-related inspection data.
Requirement:	Transparency, accountability and communication
Evidence to review:	The assessor should ask for and review: 1. Procedures and processes for publishing the list of inspections performed; 2. List of inspections performed; 3. Examples of actual published Inspection reports or summaries (or excerpts)
References:	1. National drug regulatory legislation: guiding principles for small drug regulatory authorities. In: WHO Expert Committee on Specifications for Pharmaceutical Preparations: thirty-fifth report. Geneva: World Health Organization; 1999: Annex 8 (WHO Technical Report Series, No. 885), (1), (http://apps.who.int/medicinedocs/documents/s21964en/s21964en.pdf) 2. Effective drug regulation: A multicounty study. Geneva: World Health Organization; 2002, (7), (http://apps.who.int/medicinedocs/pdf/s2300e/s2300e.pdf) 3. Guiding principles for small national drug regulatory authorities. In: WHO Expert Committee on Specifications for Pharmaceutical Preparations: thirty-first report. Geneva: World Health Organization; 1990: Annex 6 (WHO Technical Report Series, No. 790), (5), (http://apps.who.int/medicinedocs/documents/s21964en/s21964en.pdf) 4. Quality management systems — Requirements. International Standard ISO 9001:2015. Geneva. International Organization for Standardization, 2015, (4), (https://www.iso.org/iso-9001-quality-management.html)
Framework:	Output
Rating Scale:	➔ NOT IMPLEMENTED (NI): Licensing relevant inspection reports or summaries (or excerpts) are not publicly available. ➔ ONGOING IMPLEMENTATION (OI): The NRA established a procedure or mechanism by which licensing- relevant inspection reports or summaries (or excerpts) could be publicly available, however, this is not yet implemented. ➔ PARTIALLY IMPLEMENTED (PI): Licensing-related inspection reports or summaries are publicly available, but only upon request (i.e., using a pull rather than push publication mechanism). ➔ IMPLEMENTED (I): Licensing relevant inspection report or summaries (or excerpts) are regularly and consistently published and publicly available.
Limitations and remarks:	Scoring this sub-indicator as "not applicable NA" is excluded (i.e. this sub-indicator will always apply for all benchmarked NRAs).

06

Regulatory Inspection (RI): Indicators and Fact Sheets

WHO Global Benchmarking Tool (GBT) for Evaluation of National Regulatory System of Medical Products

06. Regulatory Inspection (RI): Indicators and Fact Sheets

Function:	06 — REGULATORY INSPECTION (RI)
Description:	Inspection of establishments across the medical product supply chain is an essential regulatory function. The supply chain includes manufacturers, distributors, re-packagers, re-labelers, importers, agents, traders, wholesalers and retailers of medical products. The purpose of regulatory inspections is to ensure that operations at these establishments are carried out in accordance with approved standards, norms, and guidelines and are in compliance with the national medical products legislation and regulations. These, in turn, should be consistent with World Health Organization recommendations and other internationally recognized guidelines. The scope of the function applies to different Good Practices (GXPs) and is not limited to Good Manufacturing Practices (GMPs). Good Distribution Practices and Good Clinical Practices also come under the scope of this function. Good Vigilance Practices are not addressed in this function but are addressed under the vigilance function. National Regulatory Authorities (NRAs) should have the legal mandate to inspect and enforce GXPs throughout the supply chain, to make decisions concerning the issuance, suspension or withdrawal of establishment licenses, and to issue authorizations or certifications for the activities performed by these establishments. Additionally, the NRA should develop policies, regulatory actions and procedures on the handling of medical products with suspected quality defects and medical products identified as substandard and falsified. Commonly, inspectors perform several types of inspections: pre-licensing or post-licensing, pre-approval or post-approval, announced or unannounced, and domestic or overseas inspections. Inspection activities should be conducted based on a risk management approach. Inspections reveal weaknesses and deficiencies, as well as actual or potential errors in the production, quality control, storage or distribution of medical products. Therefore, inspection activities are fundamental for guaranteeing the quality, safety and efficacy of medical products used by the population. An appeal system that is independent of the body that made the initial decision should be available. The credibility of the inspection depends on the transparency and clarity of the process, on the absence of conflicts of interest, and on the availability of regulations, directives, guidelines and procedures related to the quality management and assurance system of the inspectorate. The system also is highly dependent on the technical competence and integrity of the inspectors. The inspectorate must also ensure confidentiality of the information obtained in the course of its inspection activities. Networking with other international bodies and NRAs is an important method for acquiring, sharing, and exchanging information relevant to the quality and safety of medical products; in turn, this information contributes to informed science-based decisions. The inspectorate of the NRA should follow uniform procedures incorporating quality system principles. A general limitation for this function exists in countries where no domestic manufacturing capacities exist. In this case, domestic regulatory inspections based on GMP are not applicable; however Good Distribution Practices would always apply. Similarly, Good Clinical Practices inspections might not apply in countries where no clinical trials are conducted. Even in the absence of a domestic pharmaceutical manufacturer, a GMP inspection function is needed. GMP compliance is always a requirement for granting marketing authorization for a medical product. In this case, GMP compliance can be assured through overseas inspections or desk assessments,

	which may or may not include verification of documentation. Thus, even if there is no domestic manufacturer, there will be a need for a function which can ensure the GMP compliance of foreign pharmaceutical manufacturers either by physical inspection or desk review (e.g., taking into consideration the GMP certificates from a stringent regulatory authority).
Indicator:	**RI01 Legal provisions, regulations and guidelines required to define regulatory framework of inspection and enforcement.**
Objective:	The objective of this indicator is to ensure that regulatory inspection activities are supported by a comprehensive set of legal provisions, regulations and guidelines which provide the necessary mandate to implement all activities related to this regulatory function. Furthermore, national GXP rules should be consistent with internationally recognized and accepted GXP guidelines such as those from the World Health Organization. The NRA should show evidence that laws, regulations, decrees, agreements, or other mandatory legal provisions are in place regarding inspections that evaluate compliance with best practices and that provide oversight of activities at the establishments. The legal provisions also should provide a mandate to inspect the establishments of marketing authorization holders, manufacturers, importers, exporters, and distributors for compliance with national standards and GXP guidelines.
Category:	01. Legal provisions, regulations and guidelines
Sub Indicator:	**RI01.01: Legal provisions authorize the inspectorate to inspect and enforce Good Practices (GXPs) throughout the supply chain.**
Maturity Level:	1
Scope:	1. Medicines 2. Vaccines
Description:	The assessor should verify that current legislation establishes fundamental functions in the regulatory authority that is appointed to verify compliance with laws, regulations, standards and GXPs. These include Good Manufacturing Practices (GMP) for manufacturers, Good Distribution Practices (GDP) for distributors, wholesalers and retailers, and Good Clinical Practices (GCP) for sites where clinical studies are conducted. The assessor should also verify that legislation provides the obligation for manufacturers and marketing authorization (MA) holders to inform the National Regulatory Authority (NRA) of: 1. any safety signal or any quality defect which could impact patient safety of a marketed product, and 2. any marketing or regulatory decisions made in the country of origin or in another country where the product is marketed. In line with these legal provisions, the assessor should review the relevant, approved guidelines that explain the reporting obligations and that describe how, when and what quality defects or safety issues have to be reported. Examples of the types of reports include recall notifications, reports of study results from ongoing or previous studies, and information on supervision of clinical trials. Similar obligations should also be in force for the MA holder for all products marketed in the country. The assessor should ensure the existence and the implementation of a set of enforcement actions in case of non-compliance. The enforcement actions should include, but are not limited to recall, suspension, withdrawal, sanction, and prosecution. The assessor should identify if the law gives the inspectorate the mandate, power and authority that is adequate to implement administrative measures such as suspending or stopping production or supply. To ensure the quality of marketed products, such actions would be required in case of violations of regulatory requirements or detection of confirmed quality defects (i.e., circumstances potentially leading to issuance of a rapid alert).

Objective:	The objective of this sub-indicator is to ensure that laws, regulations, decrees, agreements, or other mandatory legal provisions have been established that give authority to the inspectorate to inspect establishments (e.g., MA holders, manufacturers, importers, exporters, and distributors) to assess compliance with best practices and to provide oversight of activities. The regulatory authorities should have the mandate to evaluate compliance with national standards and GXP guidelines throughout the supply chain.
Requirement:	Legal provisions, regulations and guidelines
Evidence to review:	The assessor should ask for and review: 1. Published legal provisions (e.g., laws, acts, executive orders, or regulations) establishing the mandate for the inspectorate to inspect establishments and enforce regulations; 2. Legal provisions establishing the authority to inspect according to GXP throughout the supply chain.
References:	1. Guiding principles for small national drug regulatory authorities. In: WHO Expert Committee on Specifications for Pharmaceutical Preparations: thirty-first report. Geneva: World Health Organization; 1990: Annex 6 (WHO Technical Report Series, No. 790), (5), (http://apps.who.int/medicinedocs/documents/s21964en/s21964en.pdf) 2. Quality systems requirements for national good manufacturing practice inspectorates. In: WHO Expert Committee on Specifications for Pharmaceutical Preparations: thirty-sixth report. Geneva: World Health Organization; 2002: Annex 8 (WHO Technical Report Series, No. 902), (8), (http://apps.who.int/medicinedocs/documents/s22112en/s22112en.pdf) 3. National drug regulatory legislation: guiding principles for small drug regulatory authorities. In: WHO Expert Committee on Specifications for Pharmaceutical Preparations: thirty-fifth report. Geneva: World Health Organization; 1999: Annex 8 (WHO Technical Report Series, No. 885), (1), (http://apps.who.int/medicinedocs/documents/s21964en/s21964en.pdf) 4. Effective drug regulation: A multicounty study. Geneva: World Health Organization; 2002, (7), (http://apps.who.int/medicinedocs/pdf/s2300e/s2300e.pdf) 5. Quality management systems — Requirements. International Standard ISO 9001:2015. Geneva. International Organization for Standardization, 2015, (4), (https://www.iso.org/iso-9001-quality-management.html) 6. PIC/S Pre-Accession Procedure, related documents, PIC/S Audit Checklist, (138), (https://www.picscheme.org/en/pre-accession)
Framework:	Structure/Foundation/Input
Rating Scale:	➜ NOT IMPLEMENTED (NI): There are no legal provisions for mandating the NRA to inspect and enforce GXP. ➜ ONGOING IMPLEMENTATION (OI): The NRA is taking steps toward the establishment of legal provisions to allow for regulatory inspections however no formal mandate exists for the regulatory inspection function. ➜ PARTIALLY IMPLEMENTED (PI): The NRA has the legal provisions to conduct the regulatory inspection activities; however such activities are recently implemented and results associated with this sub-indicator are not yet documented. ➜ IMPLEMENTED (I): Legal provisions exist for mandating the NRA to inspect and enforce GXP.
Limitations and remarks:	Scoring this sub-indicator as "not applicable NA" is excluded (i.e. this sub-indicator will always apply for all benchmarked NRAs).
Sub Indicator:	**RI01.02: Legal provisions allow inspectors to enter facilities throughout the supply chain at any reasonable time and in any place.**
Maturity Level:	1

Scope:	1. Medicines 2. Vaccines
Description:	The assessor should verify that the legal provisions provide the mandate, the power and the authority for the inspectors to enter establishments throughout the supply chain at any reasonable time and in any place within those facilities. In this context, "any reasonable time" means any time within normal working hours of the establishment that is the subject of the inspection. For example, if the establishment operates during the night, then the legal provisions should ideally authorize the inspectors to have access at that time. On the other side, access to unlicensed or unauthorized establishments or access to establishments outside normal working hours may not be mandated by the respective legal provisions. In such cases, special approvals from judicial departments might be needed.
Objective:	The objective of this sub-indicator is to ensure that laws, regulations, decrees, agreements, or other mandatory legal provisions regarding inspections are actually providing the necessary mandate to allow inspectors to enter establishments throughout the supply chain at any reasonable time and in any place within those facilities. Such provisions should apply to regulatory inspections that evaluate compliance with best practices and provide other oversight activities. Additionally, these provisions significantly contribute to efficiency and effectiveness of inspection function.
Requirement:	Legal provisions, regulations and guidelines
Evidence to review:	The assessor should ask for and review: 1. Published legal provisions (e.g. laws, acts, executive orders, or regulations) 2. Examples of inspection records. Assessor should review inspection activities and select examples of records of unannounced or "for cause" inspections that were initiated either as a part of an investigation or in response to a complaint or quality issue.
References:	1. Guiding principles for small national drug regulatory authorities. In: WHO Expert Committee on Specifications for Pharmaceutical Preparations: thirty-first report. Geneva: World Health Organization; 1990: Annex 6 (WHO Technical Report Series, No. 790), (5), (http://apps.who.int/medicinedocs/documents/s21964en/s21964en.pdf) 2. Quality systems requirements for national good manufacturing practice inspectorates. In: WHO Expert Committee on Specifications for Pharmaceutical Preparations: thirty-sixth report. Geneva: World Health Organization; 2002: Annex 8 (WHO Technical Report Series, No. 902), (8), (http://apps.who.int/medicinedocs/documents/s22112en/s22112en.pdf) 3. National drug regulatory legislation: guiding principles for small drug regulatory authorities. In: WHO Expert Committee on Specifications for Pharmaceutical Preparations: thirty-fifth report. Geneva: World Health Organization; 1999: Annex 8 (WHO Technical Report Series, No. 885), (1), (http://apps.who.int/medicinedocs/documents/s21964en/s21964en.pdf) 4. Effective drug regulation: A multicountry study. Geneva: World Health Organization; 2002, (7), (http://apps.who.int/medicinedocs/pdf/s2300e/s2300e.pdf) 5. PIC/S Pre-Accession Procedure, related documents, PIC/S Audit Checklist, (138), (https://www.picscheme.org/en/pre-accession)
Framework:	Structure/Foundation/Input
Rating Scale:	➜ NOT IMPLEMENTED (NI): There are no legal provisions allowing the inspectors to enter establishments throughout the supply chain at any reasonable time and in any place within the facilities. ➜ ONGOING IMPLEMENTATION (OI): The NRA is taking steps toward the establishment of legal provisions to allow inspectors to enter establishments throughout the supply chain at any reasonable time and in any place within the facilities; however, no results yet exist. ➜ PARTIALLY IMPLEMENTED (PI): Legal provisions allowing the inspectors to enter establishments throughout the supply chain at any reasonable time and in any place within facilities are recently established; however, the results of this practice are not yet documented.

	➔ IMPLEMENTED (I): There are legal provisions allowing the inspectors to enter establishments throughout the supply chain at any reasonable time and in any place within the facilities, and documented evidence exists to demonstrate that it happens.
Limitations and remarks:	Scoring this sub-indicator as "not applicable NA" is excluded (i.e. this sub-indicator will always apply for all benchmarked NRAs).
Sub Indicator:	**RI01.03: Legal provisions allow inspectors to collect relevant evidence, including samples, during GXP inspections.**
Maturity Level:	2
Scope:	1. Medicines 2. Vaccines
Description:	The assessor should verify that inspectors have the power and authority to collect any important evidence during their inspection and investigation activities. Examples of evidence include copies of documents, photos, videos and samples. As part of compliance verification, the designated inspectors should also be able to collect product samples for testing by the national control laboratory at any phase of the production or supply chain.
Objective:	The objective of this sub-indicator is to ensure that the respective laws, regulations, decrees, or other mandatory legal provisions allow inspectors to collect relevant evidence, including samples, during GXP inspections. Samples can also be used to check adulteration which might appear during the supply chain.
Requirement:	Legal provisions, regulations and guidelines
Evidence to review:	The assessor should ask for and review: 1. Published legal provisions (e.g. laws, acts, executive orders, or regulations) 2. Examples of inspection records. Assessor should review inspection reports and the evidence (e.g., documents or materials) or samples collected during inspection activities. 3. Records of laboratory results for samples and decisions based on those results.
References:	1. WHO good practices for pharmaceutical quality control laboratories, (35), (http://digicollection.org/whoqapharm/p/about and http://apps.who.int/medicinedocs/en) 2. WHO good manufacturing practices for pharmaceutical products: main principles, (51), (http://digicollection.org/whoqapharm/p/about and http://apps.who.int/medicinedocs/en) 3. Guidelines on heating, ventilation and air-conditioning systems for non-sterile pharmaceutical products, World Health Organization (WHO), (60), (http://apps.who.int/medicinedocs/en/q/ and http://digicollection.org/whoqapharm/) 4. WHO good manufacturing practices: water for pharmaceutical use, World Health Organization (WHO), (58), (http://apps.who.int/medicinedocs/en/q/ and http://digicollection.org/whoqapharm/) 5. WHO good manufacturing practices for sterile pharmaceutical products, World Health Organization (WHO), (61), (http://apps.who.int/medicinedocs/en/q/ and http://digicollection.org/whoqapharm/) 6. WHO guidelines for drafting a site master file, World Health Organization (WHO), (64), (http://apps.who.int/medicinedocs/en/q/ and http://digicollection.org/whoqapharm/) 7. WHO good manufacturing practices for active pharmaceutical ingredients, World Health Organization (WHO), (67), (http://apps.who.int/medicinedocs/en/q/ and http://digicollection.org/whoqapharm/) 8. Guidelines on packaging for pharmaceutical products, World Health Organization (WHO), (80), (http://apps.who.int/medicinedocs/en/q/ and http://digicollection.org/whoqapharm/) 9. WHO good distribution practices for pharmaceutical products, World Health

	Organization (WHO), (27), (http://digicollection.org/whoqapharm/p/about and http://apps.who.int/medicinedocs/en) 10. Guidelines for good clinical practice (GCP) for trials on pharmaceutical products, (40), (http://apps.who.int/medicinedocs/en) 11. National drug regulatory legislation: guiding principles for small drug regulatory authorities. In: WHO Expert Committee on Specifications for Pharmaceutical Preparations: thirty-fifth report. Geneva: World Health Organization; 1999: Annex 8 (WHO Technical Report Series, No. 885), (1), (http://apps.who.int/medicinedocs/documents/s21964en/s21964en.pdf) 12. WHO guidelines for sampling of pharmaceutical products and related materials, World Health Organization (WHO), (31), (http://digicollection.org/whoqapharm/p/about and http://apps.who.int/medicinedocs/en) 13. Quality management systems — Requirements. International Standard ISO 9001:2015. Geneva. International Organization for Standardization, 2015, (4), (https://www.iso.org/iso-9001-quality-management.html) 14. Guidance on developing a national plan for preventing, detecting and responding to actions, activities and behaviors that result in SF medical products. WHO (document A70/23), (130), (https://www.who.int/medicines/regulation/ssffc/mechanism/A70_23-en6-14.pdf) 15. Guiding principles for small national drug regulatory authorities. In: WHO Expert Committee on Specifications for Pharmaceutical Preparations: thirty-first report. Geneva: World Health Organization; 1990: Annex 6 (WHO Technical Report Series, No. 790), (5), (http://apps.who.int/medicinedocs/documents/s21964en/s21964en.pdf) 16. WHO guidelines for sampling of pharmaceutical products and related materials, World Health Organization (WHO), (31), (http://digicollection.org/whoqapharm/p/about and http://apps.who.int/medicinedocs/en) 17. PIC/S Pre-Accession Procedure, related documents, PIC/S Audit Checklist, (138), (https://www.picscheme.org/en/pre-accession)
Framework:	Structure/Foundation/Input
Rating Scale:	➜ NOT IMPLEMENTED (NI): There are no legal provisions allowing the inspectors to collect relevant evidence, including samples, during GXP inspections. ➜ ONGOING IMPLEMENTATION (OI): The NRA is taking steps toward the establishment of legal provisions to allow inspectors to collect relevant evidence, including samples, during GXP inspections however this has not yet been carried out. ➜ PARTIALLY IMPLEMENTED (PI): There is evidence that the NRA has the legal basis, elements, and capacity to perform the processes mentioned in the indicator, but the NRA has only limited, recent experience with it. ➜ IMPLEMENTED (I): There are legal provisions allowing the inspectors to collect relevant evidence, including samples, during GXP inspections and the implementation of this activity is documented.
Limitations and remarks:	Scoring this sub-indicator as "not applicable NA" is excluded (i.e. this sub-indicator will always apply for all benchmarked NRAs).
Sub Indicator:	**RI01.04: Updated national GXP regulations, norms or guidelines are mandatory.**
Maturity Level:	3
Scope:	1. Medicines 2. Vaccines
Description:	The assessor should review the GXP regulations and guidelines which should be updated, published and available to all stakeholders. Also, the assessor should verify that the guidance is consistent with World Health Organization (WHO) or other internationally recognized guidance. If applicable, differences should be identified. The assessor should verify that the national regulations are mandatory and actually implemented.

Objective:	The objective of this sub-indicator is to ensure that national GXP regulations, norms and guidelines are available and their implementation is mandatory for the establishments subjected to regulatory inspections.
Requirement:	Legal provisions, regulations and guidelines
Evidence to review:	The assessor should ask for and review: 1. Published GXP regulations, norms and guidelines (e.g. GMP, GDP, GCP, and Good Cold Chain Management Practices) 2. Evidence that the guidelines are implemented and enforceable by the NRA.
References:	1. National drug regulatory legislation: guiding principles for small drug regulatory authorities. In: WHO Expert Committee on Specifications for Pharmaceutical Preparations: thirty-fifth report. Geneva: World Health Organization; 1999: Annex 8 (WHO Technical Report Series, No. 885), (1), (http://apps.who.int/medicinedocs/documents/s21964en/s21964en.pdf) 2. Quality management systems — Requirements. International Standard ISO 9001:2015. Geneva. International Organization for Standardization, 2015, (4), (https://www.iso.org/iso-9001-quality-management.html) 3. Effective drug regulation: A multicountry study. Geneva: World Health Organization; 2002, (7), (http://apps.who.int/medicinedocs/pdf/s2300e/s2300e.pdf) 4. Quality systems requirements for national good manufacturing practice inspectorates. In: WHO Expert Committee on Specifications for Pharmaceutical Preparations: thirty-sixth report. Geneva: World Health Organization; 2002: Annex 8 (WHO Technical Report Series, No. 902), (8), (http://apps.who.int/medicinedocs/documents/s22112en/s22112en.pdf) 5. WHO good distribution practices for pharmaceutical products, World Health Organization (WHO), (27), (http://digicollection.org/whoqapharm/p/about and http://apps.who.int/medicinedocs/en) 6. WHO good practices for pharmaceutical quality control laboratories, (35), (http://digicollection.org/whoqapharm/p/about and http://apps.who.int/medicinedocs/en) 7. WHO good manufacturing practices for pharmaceutical products: main principles, (51), (http://digicollection.org/whoqapharm/p/about and http://apps.who.int/medicinedocs/en) 13. Guiding principles for small national drug regulatory authorities. In: WHO Expert Committee on Specifications for Pharmaceutical Preparations: thirty-first report. Geneva: World Health Organization; 1990: Annex 6 (WHO Technical Report Series, No. 790), (5), (http://apps.who.int/medicinedocs/documents/s21964en/s21964en.pdf) 14. PIC/S Pre-Accession Procedure, related documents, PIC/S Audit Checklist, (138), (https://www.picscheme.org/en/pre-accession) 8. WHO good manufacturing practices: water for pharmaceutical use, World Health Organization (WHO), (58), (http://apps.who.int/medicinedocs/en/q/ and http://digicollection.org/whoqapharm/) 9. Guidelines on heating, ventilation and air-conditioning systems for non-sterile pharmaceutical products, World Health Organization (WHO), (60), (http://apps.who.int/medicinedocs/en/q/ and http://digicollection.org/whoqapharm/) 10. WHO good manufacturing practices for sterile pharmaceutical products, World Health Organization (WHO), (61), (http://apps.who.int/medicinedocs/en/q/ and http://digicollection.org/whoqapharm/) 11. WHO good manufacturing practices for active pharmaceutical ingredients, World Health Organization (WHO), (67), (http://apps.who.int/medicinedocs/en/q/ and http://digicollection.org/whoqapharm/) 12. Guidelines on packaging for pharmaceutical products, World Health Organization (WHO), (80), (http://apps.who.int/medicinedocs/en/q/ and http://digicollection.org/whoqapharm/)
Framework:	Structure/Foundation/Input
Rating Scale:	➜ NOT IMPLEMENTED (NI): National GXP guidelines do not exist or are not mandatory.

	➜ ONGOING IMPLEMENTATION (OI): The NRA is taking steps towards establishment of national GXP guidelines however none of these guidelines (e.g., GMP, GDP, and GCP) is yet established. ➜ PARTIALLY IMPLEMENTED (PI): Some national GXP guidelines (e.g., GMP, GDP or GCP) are established while others are not. ➜ IMPLEMENTED (I): National GXP regulations, norms and guidelines exist and are mandatory.
Limitations and remarks:	Scoring this sub-indicator as "not applicable NA" is excluded (i.e. this sub-indicator will always apply for all benchmarked NRAs).
Sub Indicator:	**RI01.05: Legal provisions and regulations allow the recognition of and/or reliance on foreign NRA inspections and enforcement actions based on well- defined criteria.**
Maturity Level:	1
Scope:	1. Medicines 2. Vaccines
Description:	The assessor should review the legal provisions and regulations which should be available and published and verify that the guidance allows for the recognition of and/or reliance on foreign NRA inspections and enforcement actions based on well- defined criteria. While the criteria may vary significantly, the assessor must ensure the criteria are clear and supported by an appropriate rationale.
Objective:	The objective of this sub-indicator is to ensure that laws, regulations, or other mandatory legal provisions are actually providing the mandate for the recognition of and/or reliance on foreign NRA inspections and enforcement actions based on well-defined criteria.
Requirement:	Legal provisions, regulations and guidelines
Evidence to review:	The assessor should ask for and review: 1. Published legal provisions and regulations for recognition and/or reliance. 2. Examples of records demonstrating recognition of and/or reliance on foreign NRA inspections and enforcement actions.
References:	1. National drug regulatory legislation: guiding principles for small drug regulatory authorities. In: WHO Expert Committee on Specifications for Pharmaceutical Preparations: thirty-fifth report. Geneva: World Health Organization; 1999: Annex 8 (WHO Technical Report Series, No. 885), (1), (http://apps.who.int/medicinedocs/documents/s21964en/s21964en.pdf) 2. Quality systems requirements for national good manufacturing practice inspectorates. In: WHO Expert Committee on Specifications for Pharmaceutical Preparations: thirty-sixth report. Geneva: World Health Organization; 2002: Annex 8 (WHO Technical Report Series, No. 902), (8), (http://apps.who.int/medicinedocs/documents/s22112en/s22112en.pdf) 3. Guiding principles for small national drug regulatory authorities. In: WHO Expert Committee on Specifications for Pharmaceutical Preparations: thirty-first report. Geneva: World Health Organization; 1990: Annex 6 (WHO Technical Report Series, No. 790), (5), (http://apps.who.int/medicinedocs/documents/s21964en/s21964en.pdf) 4. Effective drug regulation: A multicountry study. Geneva: World Health Organization; 2002, (7), (http://apps.who.int/medicinedocs/pdf/s2300e/s2300e.pdf) 5. Quality management systems — Requirements. International Standard ISO 9001:2015. Geneva. International Organization for Standardization, 2015, (4), (https://www.iso.org/iso-9001-quality-management.html)
Framework:	Structure/Foundation/Input

Rating Scale:	➔ NOT IMPLEMENTED (NI): There are no legal provisions or regulations allowing the recognition of and/or reliance on foreign NRA inspections and enforcement actions. ➔ ONGOING IMPLEMENTATION (OI): The NRA is taking steps toward the establishment of legal provisions and regulations allowing the recognition of and/or reliance on foreign NRA inspections and enforcement actions however this has not yet been carried out in practice. ➔ PARTIALLY IMPLEMENTED (PI): Legal provisions or regulations allowing the recognition of and/or reliance on foreign NRA inspections and enforcement actions are recently established, but there is only limited, recent experience (less than two years) with the implementation of the same. ➔ IMPLEMENTED (I): There are legal provisions or regulations allowing the recognition of and/or reliance on foreign NRA inspections and enforcement actions.
Limitations and remarks:	In some countries neither recognition nor reliance are permitted. In this case, the assessor can score the sub-indicator as NOT APPLICABLE if evidence is provided to show effective and efficient regulatory inspection function without recognition or reliance.
Indicator:	**RI02 Arrangement for effective organization and good governance.**
Objective:	The objective of this indicator is to ensure the implementation of effective organization and good governance practices at the entities in charge of establishments licensing activities, which in turn contributes to effective and efficient functioning of the regulatory inspection activities.
Category:	2. Organization and good governance
Sub Indicator:	**RI02.01: There is a defined organizational structure with clear responsibilities to conduct regulatory inspection activities.**
Maturity Level:	2
Scope:	1. Medicines 2. Vaccines
Description:	The assessor should identify the organization designated to establish, implement or maintain the regulatory inspection function, as well as the specific organizational structures taking on the different relevant activities. Responsibilities, duties and roles of these structures should be clearly defined and documented. If more than one structure is involved, the assessor should check the ways and approaches by which coordination among these structures takes place.
Objective:	The objective of this sub-indicator is to ensure effective organization and good governance of regulatory inspection activities and to ensure that these activities are taken over by defined structures with clear roles and responsibilities.
Requirement:	Roles and responsibilities of the structures in charge of establishments licensing activities.
Evidence to review:	The assessor should ask for and review: 1. Organization chart of the organization responsible for the implementation of inspection activities along with identification of the particular structures implementing the function. 2. Documentation clarifying roles and responsibilities of the organizational structures implementing inspection activities. This may include administrative decrees, terms of reference, and other relevant documents. 3. Documentation identifying established mechanisms of coordination (e.g.,

	committees, internal and work-sharing) among organizational structures, if any, which take part in regulatory inspection activities.
References:	1. National drug regulatory legislation: guiding principles for small drug regulatory authorities. In: WHO Expert Committee on Specifications for Pharmaceutical Preparations: thirty-fifth report. Geneva: World Health Organization; 1999: Annex 8 (WHO Technical Report Series, No. 885), (1), (http://apps.who.int/medicinedocs/documents/s21964en/s21964en.pdf) 2. Quality systems requirements for national good manufacturing practice inspectorates. In: WHO Expert Committee on Specifications for Pharmaceutical Preparations: thirty-sixth report. Geneva: World Health Organization; 2002: Annex 8 (WHO Technical Report Series, No. 902), (8), (http://apps.who.int/medicinedocs/documents/s22112en/s22112en.pdf) 3. Guiding principles for small national drug regulatory authorities. In: WHO Expert Committee on Specifications for Pharmaceutical Preparations: thirty-first report. Geneva: World Health Organization; 1990: Annex 6 (WHO Technical Report Series, No. 790), (5), (http://apps.who.int/medicinedocs/documents/s21964en/s21964en.pdf) 4. Effective drug regulation: A multicountry study. Geneva: World Health Organization; 2002, (7), (http://apps.who.int/medicinedocs/pdf/s2300e/s2300e.pdf) 5. Quality management systems — Requirements. International Standard ISO 9001:2015. Geneva. International Organization for Standardization, 2015, (4), (https://www.iso.org/iso-9001-quality-management.html)
Framework:	Structure/Foundation/Input
Rating Scale:	➜ NOT IMPLEMENTED (NI): There is no defined organizational structure in charge of regulatory inspection activities. ➜ ONGOING IMPLEMENTATION (OI): A mandate to establish a structure in charge of regulatory inspection activities is available however the structure itself is not yet established. ➜ PARTIALLY IMPLEMENTED (PI): A structure in charge of regulatory inspection activities is newly established and mandated however the regular work and practice of this structure is not yet consolidated. ➜ IMPLEMENTED (I): There is a defined organizational structure in charge of regulatory inspection activities with clear and well-documented roles and responsibilities.
Limitations and remarks:	Scoring this sub-indicator as "not applicable NA" is excluded (i.e. this sub-indicator will always apply for all benchmarked NRAs).
Sub Indicator:	**RI02.02: Documented procedures and mechanisms are implemented to ensure the involvement and communication among all stakeholders relevant to regulatory inspection activities.**
Maturity Level:	3
Scope:	1. Medicines 2. Vaccines
Description:	The assessor should verify that documented procedures and mechanisms are implemented to ensure the involvement and communication among different entities and departments relevant to regulatory inspection activities. These entities may be inside or outside the NRA (e.g. National Control Laboratory, NRA departments involved in vigilance or MA activities, police, customs authorities, judicial offices, professional associations, manufacturers, and other industrial organizations). In case of a decentralized establishment licensing function, an information exchange system, mechanism or platform must be established and used so that appropriate communication between the central and peripheral structures is ensured. As one example, the decentralized entity can receive requests or guidance from the central

	authority and report back to it. The availability of such communication mechanisms will also encourage consistency among different peripheral structures.
Objective:	The objective of this sub-indicator is to ensure the existence and implementation of documented procedures and mechanisms to guide the involvement and communication among the different entities and departments. These activities will encourage appropriate organization and good governance of the function.
Requirement:	Agreements, memoranda of understanding and procedures for ensuring involvement of and communication among stakeholders relevant to regulatory inspection function.
Evidence to review:	The assessor should ask for and review: 1. Guidelines or Standard Operating Procedures (SOPs) that are related to external and internal communications. 2. Examples of records of communication and collaborations providing evidence for implementation of the above-mentioned procedures. 3. Documented evidence for regular formal and official communications and meetings among above mentioned key players. Assessor should verify that these are systematic and well-established processes. 4. Documentation for paths of communication and reporting. 5. Platforms for information sharing and exchange.
References:	1. National drug regulatory legislation: guiding principles for small drug regulatory authorities. In: WHO Expert Committee on Specifications for Pharmaceutical Preparations: thirty-fifth report. Geneva: World Health Organization; 1999: Annex 8 (WHO Technical Report Series, No. 885), (1), (http://apps.who.int/medicinedocs/documents/s21964en/s21964en.pdf) 2. Quality systems requirements for national good manufacturing practice inspectorates. In: WHO Expert Committee on Specifications for Pharmaceutical Preparations: thirty-sixth report. Geneva: World Health Organization; 2002: Annex 8 (WHO Technical Report Series, No. 902), (8), (http://apps.who.int/medicinedocs/documents/s22112en/s22112en.pdf) 3. Guiding principles for small national drug regulatory authorities. In: WHO Expert Committee on Specifications for Pharmaceutical Preparations: thirty-first report. Geneva: World Health Organization; 1990: Annex 6 (WHO Technical Report Series, No. 790), (5), (http://apps.who.int/medicinedocs/documents/s21964en/s21964en.pdf) 4. Effective drug regulation: A multicountry study. Geneva: World Health Organization; 2002, (7), (http://apps.who.int/medicinedocs/pdf/s2300e/s2300e.pdf) 5. Quality management systems — Requirements. International Standard ISO 9001:2015. Geneva. International Organization for Standardization, 2015, (4), (https://www.iso.org/iso-9001-quality-management.html)
Framework:	Structure/Foundation/Input
Rating Scale:	➔ NOT IMPLEMENTED (NI): There are no information exchange procedures or mechanisms among different stakeholders of the regulatory inspection function or between the central authority and the decentralized entities. ➔ ONGOING IMPLEMENTATION (OI): The NRA is developing an information exchange mechanism, but it is not yet ready, or exchanges are being conducted without an established methodology. ➔ PARTIALLY IMPLEMENTED (PI): The NRA recently established an information exchange procedure or mechanism and it is at the early implementation stage, so this practice is not yet consolidated. ➔ IMPLEMENTED (I): There are established, implemented and maintained information exchange procedures and mechanisms among different stakeholders of the regulatory inspection function and between the central authority and the decentralized entities.
Limitations and remarks:	Scoring this sub-indicator as "not applicable NA" is excluded (i.e. this sub-indicator will always apply for all benchmarked NRAs).

Indicator:	**RI03 Human resources to perform regulatory inspection activities.**
Objective:	The objective of this indicator is to ensure to that all entities within an NRA are adequately resourced with a trained, experienced and skilled workforce that is empowered to fully perform the regulatory inspection function. This will ensure that regulatory inspection activities are performed in accordance with international best practices.
Category:	06. Resources (HR, FR, infrastructure and equipment)
Sub Indicator:	**RI03.01: Sufficient competent staff (i.e., education, training, skills and experience) are assigned to perform regulatory inspection activities**
Maturity Level:	3
Scope:	1. Medicines 2. Vaccines
Description:	The assessor should verify that the human resources assigned to perform regulatory inspection activities should be sufficient with respect to numbers and competent with respect to the requisite skills, education, experience and training. There should be technical documents and SOPs that provide guidance on the required background for regulatory inspection activities and that consider the requirements for educational background, competencies, skills, experience, and training. The assessor should verify that the NRA estimated the number of staff required to effectively and efficiently perform regulatory inspection function and that the NRA actually recruited that number. In addition, the assessor should verify that these competency requirements are well-established and maintained by the NRA. Metrics and statistics on the different activities performed as well as performance indicators can be used for estimating the adequacy of the number of the assigned staff. The assessor should also verify that the competency of the assigned staff is built, maintained and improved through recruitment as well as continuous on-the-job training.
Objective:	The objective of this sub-indicator is to ensure the existing human resources for regulatory inspection is sufficient, in terms of numbers, experience, and specific competencies, to perform all the activities along the entire regulatory inspection chain.
Requirement:	Sufficient number of competent human resources in charge of regulatory inspection activities.
Evidence to review:	The assessor should ask for and review: 1. Evidence that the number of staff members involved in each of the documented activities along the entire regulatory inspection process flow is adequate. 2. Evidence that the systems and structures are in place to ensure appropriate placement of staff with respect to competence and skills. 3. Evidence that the system and structures have been implemented. The documentation should include the records to verify that the staff competence is appropriate for the job requirements. 4. Evidence that the professional profiles of the human resources engaged in regulatory inspection activities are appropriate with respect to education, skills, and expertise, to perform a particular function along the regulatory inspection chain. Documentation should include a list of the requisite skills and training for each position. 5. Recruitment plan.
References:	1. National drug regulatory legislation: guiding principles for small drug regulatory authorities. In: WHO Expert Committee on Specifications for Pharmaceutical Preparations: thirty-fifth report. Geneva: World Health Organization; 1999: Annex 8 (WHO Technical Report Series, No. 885), (1), (http://apps.who.int/medicinedocs/documents/s21964en/s21964en.pdf)

	2. Quality systems requirements for national good manufacturing practice inspectorates. In: WHO Expert Committee on Specifications for Pharmaceutical Preparations: thirty-sixth report. Geneva: World Health Organization; 2002: Annex 8 (WHO Technical Report Series, No. 902), (8), (http://apps.who.int/medicinedocs/documents/s22112en/s22112en.pdf) 3. Guiding principles for small national drug regulatory authorities. In: WHO Expert Committee on Specifications for Pharmaceutical Preparations: thirty-first report. Geneva: World Health Organization; 1990: Annex 6 (WHO Technical Report Series, No. 790), (5), (http://apps.who.int/medicinedocs/documents/s21964en/s21964en.pdf) 4. Effective drug regulation: A multicountry study. Geneva: World Health Organization; 2002, (7), (http://apps.who.int/medicinedocs/pdf/s2300e/s2300e.pdf) 5. Quality management systems — Requirements. International Standard ISO 9001:2015. Geneva. International Organization for Standardization, 2015, (4), (https://www.iso.org/iso-9001-quality-management.html) 6. PIC/S Pre-Accession Procedure, related documents, PIC/S Audit Checklist, (138), (https://www.picscheme.org/en/pre-accession)
Framework:	Process
Rating Scale:	➔ NOT IMPLEMENTED (NI): The NRA does not have enough competent staff (i.e., education, training, skills and experience) to perform regulatory inspection activities ➔ ONGOING IMPLEMENTATION (OI): The NRA has recently developed a plan to recruit adequate competent staff; however, the plan has not been implemented. ➔ PARTIALLY IMPLEMENTED (PI): The NRA has initiated the implementation of the human resources development plan; however, there is need to complete the competency profile. ➔ IMPLEMENTED (I): The NRA has a sustained number of competent staff (i.e., education, training, skills and experience) assigned to perform regulatory inspection activities.
Limitations and remarks:	▪ Assessment of the adequacy and appropriateness of the number of staff members is quite subjective and should be linked to some process or output indicators. When estimating staff adequacy, the assessor should consider the workload, backlog, and delays in delivery based on established timeframes. ▪ Scoring this sub-indicator as "not applicable NA" is excluded (i.e. this sub-indicator will always apply for all benchmarked NRAs).
Sub Indicator:	**RI03.02: Duties, functions, and responsibilities of the staff in charge of regulatory inspection activities are established and updated in the respective job descriptions**
Maturity Level:	3
Scope:	1. Medicines 2. Vaccines
Description:	The assessor should verify that procedures are in place to maintain a current and updated structure for managing job descriptions for personnel participating in regulatory inspection activities. In addition, job descriptions should address current staff duties, responsibilities and the requisite competencies. A job description with this format and content should be established and implemented for all staff. When inspection activities are subcontracted, liability of third party inspectors should be clearly defined in an agreement or contract. The management of job descriptions should be supported by a guidance document that provides direction on when and how to update the information, and where the information should be kept for easy access. The guidance document should present the appropriate duties and responsibilities that are assigned to each member of the organization involved in regulatory inspection activities. Thus, the professional profiles of staff are reflected in their respective roles and responsibilities within the NRA. There should be procedures to guide responsible persons to document

	that duties, functions and responsibilities are revised and kept up to date. In addition, procedures should be available to guide the keeping and documenting of up to date work schedules and enforcing the implementation of the documented guidelines and procedures.
Objective:	The objective of this sub-indicator is to ensure that duties and responsibilities of the staff are clear and well defined, that job descriptions are kept up to date with current duties, functions and responsibilities, and that these activities are adequately documented.
Requirement:	Duties, roles and responsibilities of the staff relevant to regulatory inspection activities.
Evidence to review:	The assessor should ask for and review: 1. Procedure and guidelines that guide placement of staff members within the NRA; 2. The professional profiles of staff (i.e., job descriptions) and documentation that they are related to their current roles and duties; 3. The professional profiles of any external experts and documentation that the profiles provide a composition that is complete and consistent with that prescribed in the legal provisions; 4. Procedures to guide the documentation of up to date duties and work schedules, and to enforce the implementation of the documented guidelines and procedures; 5. Job descriptions for designated staff.
References:	1. National drug regulatory legislation: guiding principles for small drug regulatory authorities. In: WHO Expert Committee on Specifications for Pharmaceutical Preparations: thirty-fifth report. Geneva: World Health Organization; 1999: Annex 8 (WHO Technical Report Series, No. 885), (1), (http://apps.who.int/medicinedocs/documents/s21964en/s21964en.pdf) 2. Quality systems requirements for national good manufacturing practice inspectorates. In: WHO Expert Committee on Specifications for Pharmaceutical Preparations: thirty-sixth report. Geneva: World Health Organization; 2002: Annex 8 (WHO Technical Report Series, No. 902), (8), (http://apps.who.int/medicinedocs/documents/s22112en/s22112en.pdf) 3. Guiding principles for small national drug regulatory authorities. In: WHO Expert Committee on Specifications for Pharmaceutical Preparations: thirty-first report. Geneva: World Health Organization; 1990: Annex 6 (WHO Technical Report Series, No. 790), (5), (http://apps.who.int/medicinedocs/documents/s21964en/s21964en.pdf) 4. Effective drug regulation: A multicountry study. Geneva: World Health Organization; 2002, (7), (http://apps.who.int/medicinedocs/pdf/s2300e/s2300e.pdf) 5. Quality management systems — Requirements. International Standard ISO 9001:2015. Geneva. International Organization for Standardization, 2015, (4), (https://www.iso.org/iso-9001-quality-management.html)
Framework:	Process
Rating Scale:	➜ NOT IMPLEMENTED (NI): There is no evidence of defined or established duties, functions, responsibilities, respective job descriptions and necessary required competencies. ➜ ONGOING IMPLEMENTATION (OI): The NRA has recently drafted or developed the role and responsibilities document but it has not yet been implemented. ➜ PARTIALLY IMPLEMENTED (PI): The NRA has initiated implementation of this requirement but it has not been defined or followed for all staff or the roles and responsibilities documents, including staff job descriptions, are not up to date. ➜ IMPLEMENTED (I): The NRA has defined and established all required duties, functions, and responsibilities, and respective job descriptions are up-to-date.
Limitations and remarks:	Scoring this sub-indicator as "not applicable NA" is excluded (i.e. this sub-indicator will always apply for all benchmarked NRAs).

Sub Indicator:	**RI03.03: Training plan developed, implemented and updated at least once a year for staff in charge of regulatory inspection activities.**
Maturity Level:	3
Scope:	1. Medicines 2. Vaccines
Description:	The assessor should verify that training plans are developed, implemented and updated at least once every year to reflect the current situation by considering education and experience of the staff. The training plan should be complemented with guidelines or similar documents that guide the development and implementation of training plans. The assessor should ensure that induction training for new staff as well as continued on- the-job for staff is planned and implemented. There should be procedures to approve the training plan and the budget allocated for implementing and updating the training plan. The plans should present clearly defined training goals and should include training in certain topics and skills to address identified deficiencies. Learning objectives, training methods and activities, evidence of learning, and evaluation and assessment of training should be documented. This documentation should confirm that the learning objectives were achieved and were designed to address weaknesses within the entities. Procedures should be in place to ensure that a training plan is developed, implemented and updated at least once every year. The assessor should verify that there is a system in place for monitoring the implementation and effectiveness of the training plan and for documenting the skills acquired in training activities for internal and external experts. The assessor should verify that inspectors in charge of GMP inspections receive a minimum of ten (10) training days per year as recommended by the WHO and Pharmaceutical Inspection Cooperation Scheme guidelines. Furthermore, the NRA should establish the minimum number of days that an inspector must spend on inspections in order to retain competence.
Objective:	The objective of this sub-indicator is to ensure that a training plan for staff exists, and that it is implemented and updated annually. Through the training plan, NRA can be sure that competency of staff in charge of regulatory inspection activities is maintained and enhanced.
Requirement:	Implementation of training plan
Evidence to review:	The assessor should ask for and review: 1. Guidelines for development, implementation and annual update (i.e., at least once per year) of the training plan. Guidelines should also provide for a mechanism to measure effectiveness of training. 2. Documentation for the system or structures used to approve the training plan and to evaluate the adequacy of the budget allocated to the training activities. 3. The current or existing staff training plan (or matrix) for staff. The assessor should assess this in in relation to the respective individual job descriptions. 4. SOP for developing and maintaining the training plan. 5. Evidence that the NRA has investigated and identified training needs. 6. List of trainings performed. 7. Example records for training activities. 8. Documentation of the number of training days per inspector as well as average number of training days for staff. 9. Number of days spent on site for inspections per inspector as well as average number of days spent on inspection.
References:	1. National drug regulatory legislation: guiding principles for small drug regulatory authorities. In: WHO Expert Committee on Specifications for Pharmaceutical Preparations: thirty-fifth report. Geneva: World Health Organization; 1999: Annex 8 (WHO Technical Report Series, No. 885), (1), (http://apps.who.int/medicinedocs/documents/s21964en/s21964en.pdf)

	2. Quality systems requirements for national good manufacturing practice inspectorates. In: WHO Expert Committee on Specifications for Pharmaceutical Preparations: thirty-sixth report. Geneva: World Health Organization; 2002: Annex 8 (WHO Technical Report Series, No. 902), (8), (http://apps.who.int/medicinedocs/documents/s22112en/s22112en.pdf) 3. Guiding principles for small national drug regulatory authorities. In: WHO Expert Committee on Specifications for Pharmaceutical Preparations: thirty-first report. Geneva: World Health Organization; 1990: Annex 6 (WHO Technical Report Series, No. 790), (5), (http://apps.who.int/medicinedocs/documents/s21964en/s21964en.pdf) 4. Effective drug regulation: A multicountry study. Geneva: World Health Organization; 2002, (7), (http://apps.who.int/medicinedocs/pdf/s2300e/s2300e.pdf) 5. Quality management systems — Requirements. International Standard ISO 9001:2015. Geneva. International Organization for Standardization, 2015, (4), (https://www.iso.org/iso-9001-quality-management.html) 6. PIC/S Pre-Accession Procedure, related documents, PIC/S Audit Checklist, (138), (https://www.picscheme.org/en/pre-accession)
Framework:	Process
Rating Scale:	➔ NOT IMPLEMENTED (NI): There is no systematic training program including training plan (or matrix). ➔ ONGOING IMPLEMENTATION (OI): The NRA has recently drafted or developed the training plan but there is no evidence of implementation. ➔ PARTIALLY IMPLEMENTED (PI): The NRA has developed and initiated the training plan implementation. However, the NRA has not fulfilled all required planned training or has been applying the plan for less than two years. ➔ IMPLEMENTED (I): The NRA has an updated training plan developed that is supported by adequate records to demonstrate effective plan implementation, including induction training for new staff and routine on-the-job training for recruited staff.
Limitations and remarks:	▪ Training plans must be updated regularly; ideally on an annual basis, but not less frequently that once every two years. ▪ Some regulatory functions may include many training activities that are not incorporated in the institutional training programme. Such training normally is offered by invitation. In this case, the assessor should recognize reports from non-routine regulatory inspection -relevant training not included in the NRA training plan. ▪ Scoring this sub-indicator as "not applicable NA" is excluded (i.e. this sub-indicator will always apply for all benchmarked NRAs).
Sub Indicator:	**RI03.04: The NRA generates and maintains records of staff training activities and training effectiveness verification.**
Maturity Level:	3
Scope:	1. Medicines 2. Vaccines
Description:	The assessor should verify that records of staff training that is performed or organized by the NRA are generated, maintained, regularly updated. This activity should be supported by guidelines that direct the NRA to generate and maintain records of staff training activities. Procedures should be in place to document and propose staff training needs and to allocate a budget for continuous staff capacity building and development. The assessor should check that there is an evaluation or assessment mechanism to verify the quality of learning, and to confirm that learning objectives are achieved. Documentation should include an inventory (i.e., soft and/or hard) system that records all impactful and non-impactful trainings and identifies all staff members who participated. A system to measure or estimate impact of trainings should be established.

Objective:	The objective of this sub-indicator is to ensure that training organized by the NRA or responsible regulatory authority is adequately documented and that the training records are adequately maintained and kept. Staff training records are considered an integral part of staff file and are a tool for measuring and tracking staff competency, development and adequacy.
Requirement:	Training records
Evidence to review:	The assessor should ask for and review: 1. Guidelines or similar documents that guide the NRA to generate and maintain records of staff training activities; 2. Evaluations of training effectiveness; 3. The training inventory, and procedures for completing the inventory; 4. Examples of archived records of staff training, and procedures for the archiving system.
References:	1. National drug regulatory legislation: guiding principles for small drug regulatory authorities. In: WHO Expert Committee on Specifications for Pharmaceutical Preparations: thirty-fifth report. Geneva: World Health Organization; 1999: Annex 8 (WHO Technical Report Series, No. 885), (1), (http://apps.who.int/medicinedocs/documents/s21964en/s21964en.pdf) 2. Quality systems requirements for national good manufacturing practice inspectorates. In: WHO Expert Committee on Specifications for Pharmaceutical Preparations: thirty-sixth report. Geneva: World Health Organization; 2002: Annex 8 (WHO Technical Report Series, No. 902), (8), (http://apps.who.int/medicinedocs/documents/s22112en/s22112en.pdf) 3. Guiding principles for small national drug regulatory authorities. In: WHO Expert Committee on Specifications for Pharmaceutical Preparations: thirty-first report. Geneva: World Health Organization; 1990: Annex 6 (WHO Technical Report Series, No. 790), (5), (http://apps.who.int/medicinedocs/documents/s21964en/s21964en.pdf) 4. Effective drug regulation: A multicountry study. Geneva: World Health Organization; 2002, (7), (http://apps.who.int/medicinedocs/pdf/s2300e/s2300e.pdf) 5. Quality management systems — Requirements. International Standard ISO 9001:2015. Geneva. International Organization for Standardization, 2015, (4), (https://www.iso.org/iso-9001-quality-management.html)
Framework:	Output
Rating Scale:	➜ NOT IMPLEMENTED (NI): There is no evidence that the NRA generates and maintains records of staff training activities. ➜ ONGOING IMPLEMENTATION (OI): The NRA has recently initiated plans to generate, document and keep records of staff training activities, however they are not yet followed. ➜ PARTIALLY IMPLEMENTED (PI): The NRA has recently initiated plans to generate, document and keep records of staff training activities but they are not fully followed for all training activities or they have been established for less than two years. ➜ IMPLEMENTED (I): The NRA generates and maintains records of staff training activities.
Limitations and remarks:	▪ The assessor should note that some NRAs out-source training including staff capacity development activities. In this case the assessor should request the identity of the provider, as well as evaluations of the provider. The assessor may request the professional profiles of tutors or resource persons used to offer training. The assessor may also request records covering the archiving systems in place. ▪ Scoring this sub-indicator as "not applicable NA" is excluded (i.e. this sub-indicator will always apply for all benchmarked NRAs).

Indicator:	**RI04 Procedures established and implemented to perform inspection and enforcement.**
Objective:	The objective of this indicator is to ensure the NRA or Inspectorate is supported by appropriate mandates, effective organization and governance, and essential resources. The regulatory inspection activities should be implemented through standard procedures and work instructions in order to ensure consistency, effectiveness, efficiency, impartiality and proportionality of the activities. The NRA should have established a system which allows the regular review of quality aspects of the authorized products on the market, and which includes processes to review and share relevant data between key players and to take appropriate action.
Category:	07. Regulatory process
Sub Indicator:	**RI04.01: The different inspection activities, including inspection preparation, conduct and reporting, are documented for GXP inspections.**
Maturity Level:	3
Scope:	1. Medicines 2. Vaccines
Description:	The assessor should verify the existence of procedures for efficiently working on planning, preparing, conducting, reporting and monitoring of activities for GXP inspections performed throughout the supply chain. The assessor should also confirm the existence of documented procedures and resources to enable regulatory GXP inspections to be carried out in accordance with official guidelines and national legislation and in accordance with a formal inspection plan. All relevant instructions, standards, written procedures, worksheets, check lists and reference data should be maintained up-to-date and be readily available to staff. As part of inspection processes and procedures, the assessor should verify that inspection reports are prepared in accordance with applicable national or other requirements. In addition, the assessor should verify that reports are prepared in approved format and signed and dated by the relevant inspector. Ideally, the report should follow a standard format which in, turn, is in compliance with the relevant WHO guidelines or other internationally recognized and accepted guidelines.
Objective:	The objective of this sub-indicator is to ensure that all pre-inspection, inspection and post-inspection activities are well-documented and follow written procedures. These activities include inspection planning, preparation (e.g., inspection announcement and designation of inspectors), conduct (e.g., opening meeting and evidence collection), and reporting (e.g., classification of findings, closing meeting, conclusions and recommendations). These procedures enable the regulatory inspections of manufacturing and distribution operations to be carried out in accordance with official guidelines and national legislation and in accordance with a formal inspection plan. Following these procedures will also ensure consistency, effectiveness, impartiality and proportionality of practices.
Requirement:	Regulatory process
Evidence to review:	The assessor should ask for and review: 1. SOPs and procedures for planning, conducting, and monitoring of GXP inspections, as well as records for performance of these activities; 2. GXP inspection reports and documentation of processes for inspection review and follow-up. The inspection process should be analyzed on a regular basis.; 3. Instructions, worksheets, check lists and reference data relevant to the different inspection activities.
References:	1. National drug regulatory legislation: guiding principles for small drug regulatory authorities. In: WHO Expert Committee on Specifications for Pharmaceutical

	Preparations: thirty-fifth report. Geneva: World Health Organization; 1999: Annex 8 (WHO Technical Report Series, No. 885), (1), (http://apps.who.int/medicinedocs/documents/s21964en/s21964en.pdf) 2. Quality systems requirements for national good manufacturing practice inspectorates. In: WHO Expert Committee on Specifications for Pharmaceutical Preparations: thirty-sixth report. Geneva: World Health Organization; 2002: Annex 8 (WHO Technical Report Series, No. 902), (8), (http://apps.who.int/medicinedocs/documents/s22112en/s22112en.pdf) 3. Guiding principles for small national drug regulatory authorities. In: WHO Expert Committee on Specifications for Pharmaceutical Preparations: thirty-first report. Geneva: World Health Organization; 1990: Annex 6 (WHO Technical Report Series, No. 790), (5), (http://apps.who.int/medicinedocs/documents/s21964en/s21964en.pdf) 4. Effective drug regulation: A multicountry study. Geneva: World Health Organization; 2002, (7), (http://apps.who.int/medicinedocs/pdf/s2300e/s2300e.pdf) 5. Quality management systems — Requirements. International Standard ISO 9001:2015. Geneva. International Organization for Standardization, 2015, (4), (https://www.iso.org/iso-9001-quality-management.html) 6. PIC/S Pre-Accession Procedure, related documents, PIC/S Audit Checklist, (138), (https://www.picscheme.org/en/pre-accession)
Framework:	Process
Rating Scale:	➜ NOT IMPLEMENTED (NI): There is no documentation for the different inspection activities that evaluate compliance with GXP, including inspection preparation, conduct and reporting. ➜ ONGOING IMPLEMENTATION (OI): The NRA is preparing to establish the procedures along with the associated documentation for the different inspection activities that check compliance with GXP, including inspection preparation, conduct and reporting; however these are not yet established. ➜ PARTIALLY IMPLEMENTED (PI): There is evidence that the NRA has the capacity to conduct the inspections mentioned in the indicator, with procedures and documentation in place; however, experience is limited or recent and therefore the relevant records are limited. ➜ IMPLEMENTED (I): The NRA has established procedures for the different inspection activities that check compliance with GXP, including inspection preparation, conduct and reporting, and the NRA consistently maintains documentation of the results of related activities over time.
Limitations and remarks:	Scoring this sub-indicator as "not applicable NA" is excluded (i.e. this sub-indicator will always apply for all benchmarked NRAs).
Sub Indicator:	**RI04.02: Regulatory inspection follow-up, decision-making (including certification) and enforcement activities are documented.**
Maturity Level:	3
Scope:	1. Medicines 2. Vaccines
Description:	The assessor should check the availability and implementation of procedures related to following up after the inspection, making of regulatory decisions (including certifications) and initiating enforcement actions. There should be written guidance, e.g., on how to follow up on identified deficiencies. The assessor should review documented evidence that actions were initiated when needed, e.g. with regard to product MAs or establishment licenses. The assessor should review examples of inspection reports, with special attention to findings and observations from the inspection and to deficiencies, recommendations, summaries and conclusions. The assessor should check and verify that relevant regulatory actions were taken to enforce compliance with GXP.

	Assessor should review that any corrective or preventive actions taken as a result of audits (or other reports of non-conformities) are implemented and documented, and that effectiveness of the actions is verified. The assessor should also verify the existence of internal procedures or mechanisms to ensure that GXP certifications (where applicable) are properly issued. Evidence that a system is in place for GXP certification should also be reviewed.
Objective:	The objective of this sub-indicator is to ensure the availability and implementation of procedures related to following up after the regulatory inspections, making of regulatory decisions (including certifications) and initiating enforcement actions. Assessor should review evidence that actions were initiated, when needed, e.g., with regard to product MAs or establishment licenses. Such documentation would in turn contribute to consistency and effectiveness of the regulatory inspection function.
Requirement:	Regulatory process
Evidence to review:	The assessor should ask for and review: 1. SOPs for GXP follow up 2. SOPs for GXP certification 3. SOPs for GXP enforcement 4. Examples of GXP certificates 5. Examples of GXP enforcement records.
References:	1. Effective drug regulation: A multicountry study. Geneva: World Health Organization; 2002 (7) (http://apps.who.int/medicinedocs/pdf/s2300e/s2300e.pdf) 2. Quality management systems — Requirements. International Standard ISO 9001:2015. Geneva. International Organization for Standardization, 2015, (4), (https://www.iso.org/iso-9001-quality-management.html) 3. Quality systems requirements for national good manufacturing practice inspectorates. In: WHO Expert Committee on Specifications for Pharmaceutical Preparations: thirty-sixth report. Geneva: World Health Organization; 2002: Annex 8 (WHO Technical Report Series, No. 902), (8), (http://apps.who.int/medicinedocs/documents/s22112en/s22112en.pdf) 4. Guiding principles for small national drug regulatory authorities. In: WHO Expert Committee on Specifications for Pharmaceutical Preparations: thirty-first report. Geneva: World Health Organization; 1990: Annex 6 (WHO Technical Report Series, No. 790), (5), (http://apps.who.int/medicinedocs/documents/s21964en/s21964en.pdf) 5. National drug regulatory legislation: guiding principles for small drug regulatory authorities. In: WHO Expert Committee on Specifications for Pharmaceutical Preparations: thirty-fifth report. Geneva: World Health Organization; 1999: Annex 8 (WHO Technical Report Series, No. 885), (1), (http://apps.who.int/medicinedocs/documents/s21964en/s21964en.pdf) 6. PIC/S Pre-Accession Procedure, related documents, PIC/S Audit Checklist, (138), (https://www.picscheme.org/en/pre-accession)
Framework:	Proces
Rating Scale:	There is no documentation of the regulatory inspection follow up, decision-making (including certification) or enforcement activities. ➜ ONGOING IMPLEMENTATION (OI): The NRA is preparing to establish procedures along with the associated documentation for regulatory inspection follow up, decision-making (including certification) and enforcement activities. ➜ PARTIALLY IMPLEMENTED (PI): There is evidence that the NRA has established the documentation relevant to regulatory inspection follow up, decision-making (including certification) and enforcement activities; however NRA experience with these activities is only recent or limited. ➜ IMPLEMENTED (I): The NRA demonstrates that all the regulatory inspection follow up, decision- making (including certification) and enforcement activities are in place, and that the NRA consistently maintains documentation of the results of related activities over time.

Limitations and remarks:	Scoring this sub-indicator as "not applicable NA" is excluded (i.e. this sub-indicator will always apply for all benchmarked NRAs).
Sub Indicator:	**RI04.03: Inspection planning is based on quality risk management (QRM).**
Maturity Level:	3
Scope:	1. Medicines 2. Vaccines
Description:	The assessor should verify the existence and implementation of QRM throughout the process of inspection planning. The scope of QRM includes: • Planning of routine GXP inspections by the inspectorates: • Inspections of Investigational Medicinal Product manufacturers; • Follow-up activities, such as assigning a new risk rating to the site following the receipt of new information about the site or its products. This normally occurs between inspections. Examples of the types of new information might include information on quality defects, product recalls, market surveillance or product testing. This review process requires a complete knowledge of the GXP compliance status. New sites should not be rated for their initial inspection in accordance with QRM principles, because the inspectorate in question probably will not have the necessary and complete knowledge about the site or products. Thus, QRM should not normally be applied until a full inspection has occurred. Important questions to be answered during the process of preparing for an inspection include: 1. The focus, depth, site and the duration of the inspection; 2. The required number of inspectors to be assigned; 3. Identification of any specific competency or expertise required on the inspection team. Applying QRM principles require the collection of relevant data during inspection preparation, and these data (e.g. vigilance, laboratory, and previous inspection data) are fundamental for risk-based planning. The preparation requires the inspectors to consider the following items before making their recommendations: 1. Specific areas in which deficiencies were identified during the most recent inspection at the site; 2. specific areas that were not inspected in recent inspections, 3. Any new information that may relate to the site, for example, new quality defect reports, MA variation applications affecting the site, product recall actions, non-conforming results from market surveillance testing, or any other general indicators of non-compliance (e.g., a failure to implement a MA variation on time). Ideally, a meaningful and robust inspection plan based on QRM should be developed in conjunction with data from other regulatory departments (e.g. vigilance data, quality control data, or market surveillance data).
Objective:	The objective of this sub-indicator is to ensure that planning of the frequency and scope of inspections is based on QRM for enhancement of the inspection programme effectiveness and efficiency. QRM is a methodology based upon the concept of rating sites on the basis of an estimated risk that they may pose to patients, consumers, animals and users of medicines. The Inspectorates should prioritize sites for inspection when planning the frequency and scope of GXP inspections.
Requirement:	Regulatory process
Evidence to review:	The assessor should ask for and review: 1. Procedures describing methodology for developing annual (i.e., routine) inspection plans along with examples of completed plans; 2. Documentation of GXP inspection plan review process along with any updates to the inspection plans (e.g., updates based on access to additional information).

References:	1. Quality management systems — Requirements. International Standard ISO 9001:2015. Geneva. International Organization for Standardization, 2015, (4), (https://www.iso.org/iso-9001-quality-management.html) 2. National drug regulatory legislation: guiding principles for small drug regulatory authorities. In: WHO Expert Committee on Specifications for Pharmaceutical Preparations: thirty-fifth report. Geneva: World Health Organization; 1999: Annex 8 (WHO Technical Report Series, No. 885), (1), (http://apps.who.int/medicinedocs/documents/s21964en/s21964en.pdf) 3. Guiding principles for small national drug regulatory authorities. In: WHO Expert Committee on Specifications for Pharmaceutical Preparations: thirty-first report. Geneva: World Health Organization; 1990: Annex 6 (WHO Technical Report Series, No. 790), (5), (http://apps.who.int/medicinedocs/documents/s21964en/s21964en.pdf) 4. Effective drug regulation: A multicountry study. Geneva: World Health Organization; 2002, (7), (http://apps.who.int/medicinedocs/pdf/s2300e/s2300e.pdf) 5. WHO guidelines on quality risk management, (55), (http://digicollection.org/whoqapharm/p/about and http://apps.who.int/medicinedocs/en) 6. Quality systems requirements for national good manufacturing practice inspectorates. In: WHO Expert Committee on Specifications for Pharmaceutical Preparations: thirty-sixth report. Geneva: World Health Organization; 2002: Annex 8 (WHO Technical Report Series, No. 902), (8), (http://apps.who.int/medicinedocs/documents/s22112en/s22112en.pdf) 7. Quality Risk Management, Q9, International Council for Harmonization (ICH), (123), (http://www.ich.org/products/guidelines/quality/quality-single/article/quality-risk-management.html) 8. A recommended model for risk-based inspection planning in the GMP environment, PIC/S. PI 037-1, Pharmaceutical Inspection Convention / Pharmaceutical Inspection Cooperation Scheme (PIC/S), (124), (https://www.picscheme.org/layout/document.php?id=160) 9. PIC/S Pre-Accession Procedure, related documents, PIC/S Audit Checklist, (138), (https://www.picscheme.org/en/pre-accession)
Framework:	Process
Rating Scale:	➜ NOT IMPLEMENTED (NI): There is no evidence of activities or documentation for this indicator. ➜ ONGOING IMPLEMENTATION (OI): The NRA is preparing to establish procedures to plan inspections based on risk management but no results yet exist. ➜ PARTIALLY IMPLEMENTED (PI): There is evidence that the NRA has procedures to plan inspections based on risk management, as well as the capacity to perform the procedures mentioned in the indicator; however NRA experience with this is only recent or limited. If inspection planning has only recently been established, the rating should be PI. ➜ IMPLEMENTED (I): The NRA demonstrates all the aforementioned elements and also consistently maintains documentation of the results of related activities over time.
Limitations and remarks:	Scoring this sub-indicator as "not applicable NA" is excluded (i.e. this sub-indicator will always apply for all benchmarked NRAs).
Sub Indicator:	**RI04.04: Multi-disciplinary teams are used to ensure proper expertise for inspection of specific medical products.**
Maturity Level:	3
Scope:	1. Medicines 2. Vaccines
Description:	The assessor should verify the existence and implementation of a system for defining the composition of the inspection team. The composition of the inspection team should be based on the skills and experience required for the type of inspection

	being performed. A lead inspector should be designated. This lead inspector has the responsibility to coordinate the entire inspection process (i.e., from the planning up to the evaluation of the corrective measures) in active collaboration with the other members of the inspection team. Assessor should note that a follow-up inspection would trigger a new inspection process. Sub-contracted personnel or experts may be employed as part of an inspection team to assist or to advise in a technical capacity; however, the team should normally be led by a GMP lead inspector. Sub-contracted personnel should be bound by the requirements of the quality system and there should be a written contractual agreement between the parties. Organizations, experts or other persons to whom inspection activities are contracted, should be free from any commercial or financial pressures which might affect their freedom to act. They should follow defined ethics rules to avoid conflict of interests. Senior management of the Pharmaceutical Inspectorate should ensure that these outside persons are appropriately qualified and experienced and that they are independent of any organizations which they might be asked to inspect. In case of specialized or highly sophisticated products (e.g. vaccines or advanced therapy medicinal products), experts may be asked to join the inspection team. However, it is important that designation of the necessary experts be based on QRM in order to ensure consistency, effectiveness, impartiality and proportionality of inspection process. The number of members of the inspection team is another aspect which should be considered for optimal work of the team throughout the inspection process.
Objective:	The objective of this sub-indicator is to ensure that optimal human resources are available for and involved in regulatory inspections. Optimal composition of inspection teams contributes to effective and efficient implementation of the function.
Requirement:	Regulatory process
Evidence to review:	The assessor should ask for and review: 1. Procedures for team inspections 2. Examples of inspection plans, including nominations for inspection teams. 3. Examples of inspection records.
References:	1. National drug regulatory legislation: guiding principles for small drug regulatory authorities. In: WHO Expert Committee on Specifications for Pharmaceutical Preparations: thirty-fifth report. Geneva: World Health Organization; 1999: Annex 8 (WHO Technical Report Series, No. 885), (1), (http://apps.who.int/medicinedocs/documents/s21964en/s21964en.pdf) 2. Quality systems requirements for national good manufacturing practice inspectorates. In: WHO Expert Committee on Specifications for Pharmaceutical Preparations: thirty-sixth report. Geneva: World Health Organization; 2002: Annex 8 (WHO Technical Report Series, No. 902), (8), (http://apps.who.int/medicinedocs/documents/s22112en/s22112en.pdf) 3. Guiding principles for small national drug regulatory authorities. In: WHO Expert Committee on Specifications for Pharmaceutical Preparations: thirty-first report. Geneva: World Health Organization; 1990: Annex 6 (WHO Technical Report Series, No. 790), (5), (http://apps.who.int/medicinedocs/documents/s21964en/s21964en.pdf) 4. Effective drug regulation: A multicountry study. Geneva: World Health Organization; 2002, (7), (http://apps.who.int/medicinedocs/pdf/s2300e/s2300e.pdf) 5. Quality management systems — Requirements. International Standard ISO 9001:2015. Geneva. International Organization for Standardization, 2015, (4), (https://www.iso.org/iso-9001-quality-management.html)
Framework:	Process
Rating Scale:	➜ NOT IMPLEMENTED (NI): The NRA does not use multi-disciplinary teams for inspection of specific medical products. ➜ ONGOING IMPLEMENTATION (OI): The NRA is taking steps to use multi-disciplinary teams for inspection of specific medical products but no results are yet available. ➜ PARTIALLY IMPLEMENTED (PI): The NRA recently established the practice of

	using multi-disciplinary teams for inspection of specific medical products however results of such practice are not yet documented. ➜ IMPLEMENTED (I): The NRA regularly and consistently uses multi-disciplinary teams for inspection of specific medical products.
Limitations and remarks:	▪ In order to ensure the access to certain specific expertise, the inspection team may include experts from the quality control laboratory or reviewers or other personnel external to the NRA. However, there is still a need for all members of the inspection team to be qualified as inspectors with at least a minimum of inspection training (e.g., techniques for asking questions or writing observations). ▪ Scoring this sub-indicator as "not applicable NA" is excluded (i.e. this sub-indicator will always apply for all benchmarked NRAs).
Sub Indicator:	**RI04.05: Inspection findings and observations are categorized according to QRM.**
Maturity Level:	3
Scope:	1. Medicines 2. Vaccines
Description:	The assessor should verify the existence and implementation of a quality system that covers the different inspection processes. The assessor should also verify that inspection findings and observations are categorized according to QRM following a systematic process consistent with WHO or other internationally-recognized guidelines (e.g., observations should be classified as critical, major, or other, according to their actual or potential impact on the patients and receivers).
Objective:	The objective of this sub-indicator is to ensure that QRM considerations include reporting and are not limited to inspection planning, preparation and conduct. Use of QRM for the reporting process would significantly contribute to efficiency and effectiveness of the inspection process, including the categorization of the findings and observations.
Requirement:	Regulatory process
Evidence to review:	The assessor should ask for and review: 1. Procedures for categorization of findings, including categorization criteria 2. Examples of reviews of inspection reports 3. Examples of findings reviews and categorizations. These should be compared to categorization procedures and criteria.
References:	1. Quality systems requirements for national good manufacturing practice inspectorates. In: WHO Expert Committee on Specifications for Pharmaceutical Preparations: thirty-sixth report. Geneva: World Health Organization; 2002: Annex 8 (WHO Technical Report Series, No. 902), (8), (http://apps.who.int/medicinedocs/documents/s22112en/s22112en.pdf) 2. Quality management systems — Requirements. International Standard ISO 9001:2015. Geneva. International Organization for Standardization, 2015, (4), (https://www.iso.org/iso-9001-quality-management.html) 3. WHO guidelines on quality risk management, (55), (http://digicollection.org/whoqapharm/p/about and http://apps.who.int/medicinedocs/en) 4. Effective drug regulation: A multicountry study. Geneva: World Health Organization; 2002, (7), (http://apps.who.int/medicinedocs/pdf/s2300e/s2300e.pdf) 5. National drug regulatory legislation: guiding principles for small drug regulatory authorities. In: WHO Expert Committee on Specifications for Pharmaceutical Preparations: thirty-fifth report. Geneva: World Health Organization; 1999: Annex 8 (WHO Technical Report Series, No. 885), (1), (http://apps.who.int/medicinedocs/documents/s21964en/s21964en.pdf) 6. Guiding principles for small national drug regulatory authorities. In: WHO Expert

	Committee on Specifications for Pharmaceutical Preparations: thirty-first report. Geneva: World Health Organization; 1990: Annex 6 (WHO Technical Report Series, No. 790), (5), (http://apps.who.int/medicinedocs/documents/s21964en/s21964en.pdf) 7. Quality Risk Management, Q9, International Council for Harmonization (ICH), (123), (http://www.ich.org/products/guidelines/quality/quality-single/article/quality-risk-management.html) 8. Guidance on Good Manufacturing Practices (GMP): inspection report, World Health Organization (WHO), (84), (http://apps.who.int/medicinedocs/en/q/ and http://digicollection.org/whoqapharm/)
Framework:	Process
Rating Scale:	➔ NOT IMPLEMENTED (NI): Inspection findings and observations are not categorized according to QRM. ➔ ONGOING IMPLEMENTATION (OI): The NRA is taking steps to categorize inspection findings and observations according to QRM, but no results are yet available. ➔ PARTIALLY IMPLEMENTED (PI): The NRA recently established the practice to categorize findings and observations according to QRM; however results of such practice are not yet documented. ➔ IMPLEMENTED (I): Inspection findings and observations are categorized according to QRM.
Limitations and remarks:	▪ As per WHO guidelines (WHO Technical Report Series 996, annex 4, Guidance on good manufacturing practices: inspection report), a "critical" deficiency may be defined as an observation that has produced, or may result in a significant risk of producing, a product that is harmful to the user. A "major" deficiency may be defined as a non-critical observation that: a) has produced or may produce a product that does not comply with its MA and/or prequalification application (including variations); b) indicates a major deviation from the GMP guide; c) indicates a failure to carry out satisfactory procedures for release of batches; d) indicates a failure of the person responsible for quality assurance or quality control to fulfill his or her duties; or e) consists of several other deficiencies, none of which on its own may be major, but which together may represent a major deficiency and should be explained and reported as such. A deficiency may be classified as "other" if it cannot be classified as either critical or major but indicates a departure from GMP. A deficiency may be classified as "other" either because it is judged as minor or because there is insufficient information to classify it as "major" or "critical". ▪ Scoring this sub-indicator as "not applicable NA" is excluded (i.e. this sub-indicator will always apply for all benchmarked NRAs).
Sub Indicator:	**RI04.06: The same criteria are used for the inspection of domestic, foreign, public and private facilities regardless of the ownership.**
Maturity Level:	3
Scope:	1. Medicines 2. Vaccines
Description:	The assessor should check that the same criteria are applied equally for all establishments, domestic, foreign, public, or private, regardless of ownership. In this case, the relevant criteria include regulatory requirements and actual inspection and enforcement actions. In the evaluation of this sub-indicator, the assessor is asked to perform a systematic review and comparison of inspection processes as applied to different types of facilities.
Objective:	The objective of this sub-indicator is to ensure that regulatory requirements are applied equally for all inspections (i.e., domestic, foreign, public, or private) regardless of ownership.
Requirement:	Regulatory process

Evidence to review:	The assessor should ask for and review: 1. Examples of inspection processes and reports from domestic, foreign, public, or private facilities. Assessor should review these to confirm that there are no differences in application of regulatory requirements, regardless of ownership.
References:	1. National drug regulatory legislation: guiding principles for small drug regulatory authorities. In: WHO Expert Committee on Specifications for Pharmaceutical Preparations: thirty-fifth report. Geneva: World Health Organization; 1999: Annex 8 (WHO Technical Report Series, No. 885), (1), (http://apps.who.int/medicinedocs/documents/s21964en/s21964en.pdf) 2. Effective drug regulation: A multicountry study. Geneva: World Health Organization; 2002, (7), (http://apps.who.int/medicinedocs/pdf/s2300e/s2300e.pdf) 3. Quality management systems — Requirements. International Standard ISO 9001:2015. Geneva. International Organization for Standardization, 2015, (4), (https://www.iso.org/iso-9001-quality-management.html) 4. Guiding principles for small national drug regulatory authorities. In: WHO Expert Committee on Specifications for Pharmaceutical Preparations: thirty-first report. Geneva: World Health Organization; 1990: Annex 6 (WHO Technical Report Series, No. 790), (5), (http://apps.who.int/medicinedocs/documents/s21964en/s21964en.pdf) 5. Quality systems requirements for national good manufacturing practice inspectorates. In: WHO Expert Committee on Specifications for Pharmaceutical Preparations: thirty-sixth report. Geneva: World Health Organization; 2002: Annex 8 (WHO Technical Report Series, No. 902), (8), (http://apps.who.int/medicinedocs/documents/s22112en/s22112en.pdf)
Framework:	Process
Rating Scale:	➜ NOT IMPLEMENTED (NI): There is no evidence that the inspectorate uses the same criteria for the inspection of domestic, foreign, public and private establishments regardless the ownership. ➜ ONGOING IMPLEMENTATION (OI): The NRA is working on ensuring that the same criteria are used for the inspection of domestic, foreign, public and private establishments regardless the ownership; however, no yet results are yet available. ➜ PARTIALLY IMPLEMENTED (PI): There is evidence that the NRA uses the same criteria for the inspection of domestic, foreign, public and private establishments regardless the ownership; however, it has only limited or recent experience with it. ➜ IMPLEMENTED (I): There is evidence that the NRA uses the same criteria for the inspection of domestic, foreign, public and private establishments regardless the ownership; and also consistently maintains documentation of the results of related activities over time.
Limitations and remarks:	Scoring this sub-indicator as "not applicable NA" is excluded (i.e. this sub-indicator will always apply for all benchmarked NRAs).
Indicator:	**RI05 Mechanism in place to monitor regulatory performance and output.**
Objective:	The objective of this indicator is to ensure the existence and implementation of a system or mechanism for monitoring regulatory performance and output and for using that information to estimate the effectiveness and efficiency of the regulatory inspection function.
Category:	09. Monitoring progress and assessing outcomes & impact
Sub Indicator:	**RI05.01: A database is established and regularly updated of all establishments which may be subject to inspection, along with their relevant regulatory decisions (certifications and/or enforcement activities).**
Maturity Level:	4

Scope:	1. Medicines 2. Vaccines
Description:	The assessor should verify the existence of an updated database of all facilities and premises subject to regulatory inspections throughout the supply chain. Clinical trial sites should also be included. The database should be comprehensive and should contain essential information for the inspected facility, as well as information from previous inspections (e.g., general information, conclusions, and relevant regulatory decisions such as certification or enforcement actions). Furthermore, the assessor should verify that the database is regularly updated in accordance with well-established procedures and mechanisms.
Objective:	The objective of this sub-indicator is to ensure consistency and traceability of regulatory inspection activities through the establishment and maintenance of a database of all the inspected establishments along with the regulatory decisions associated with each establishment (e.g., certifications and enforcement actions).
Requirement:	Monitoring progress and assessing outcomes and impact
Evidence to review:	The assessor should ask for and review: 1. Database of inspected facilities showing inventory of facilities along with regulatory decisions.
References:	1. Effective drug regulation: A multicountry study. Geneva: World Health Organization; 2002, (7), (http://apps.who.int/medicinedocs/pdf/s2300e/s2300e.pdf) 2. Quality management systems — Requirements. International Standard ISO 9001:2015. Geneva. International Organization for Standardization, 2015, (4), (https://www.iso.org/iso-9001-quality-management.html) 3. Quality systems requirements for national good manufacturing practice inspectorates. In: WHO Expert Committee on Specifications for Pharmaceutical Preparations: thirty-sixth report. Geneva: World Health Organization; 2002: Annex 8 (WHO Technical Report Series, No. 902), (8), (http://apps.who.int/medicinedocs/documents/s22112en/s22112en.pdf) 4. Guiding principles for small national drug regulatory authorities. In: WHO Expert Committee on Specifications for Pharmaceutical Preparations: thirty-first report. Geneva: World Health Organization; 1990: Annex 6 (WHO Technical Report Series, No. 790), (5), (http://apps.who.int/medicinedocs/documents/s21964en/s21964en.pdf) 5. National drug regulatory legislation: guiding principles for small drug regulatory authorities. In: WHO Expert Committee on Specifications for Pharmaceutical Preparations: thirty-fifth report. Geneva: World Health Organization; 1999: Annex 8 (WHO Technical Report Series, No. 885), (1), (http://apps.who.int/medicinedocs/documents/s21964en/s21964en.pdf)
Framework:	Output
Rating Scale:	➜ NOT IMPLEMENTED (NI): There is no list or database of all establishments that are subject to inspection along with their regulatory actions (certification and/or enforcement). ➜ ONGOING IMPLEMENTATION (OI): The NRA is preparing to establish a database, but there is no evidence of results from such activities. ➜ PARTIALLY IMPLEMENTED (PI): There is evidence that the NRA has the elements (i.e., procedures, documentation, management systems, and other relevant information) and the capacity to perform the processes mentioned in the indicator, however, it has only limited experience or a limited number of documented events. ➜ IMPLEMENTED (I): There is list or database of all establishments that are subject to inspection along with their regulatory actions (certification and/or enforcement). Also, this list or database is regularly updated.
Limitations and remarks:	▪ Some facilities may be subject to inspection without being licensed by the NRA (e.g. clinical trial sites). Although these sites may not be licensed by the NRA,

	ideally, they are licensed by another governmental institution. Integration and communication within the government is critical in the latter situation. ▪ Scoring this sub-indicator as "not applicable NA" is excluded (i.e. this sub-indicator will always apply for all benchmarked NRAs).
Sub Indicator:	**RI05.02: Inspection reports are well-archived and easily retrieved.**
Maturity Level:	3
Scope:	1. Medicines 2. Vaccines
Description:	The assessor should verify that reports of inspections are well-archived and easily retrieved. The assessor should review how all the information collected during the inspection process is managed and how inspection reports are registered and archived (e.g., in paper or electronic formats).
Objective:	The objective of this sub-indicator is to ensure that a mechanism or procedure is in place for defining a standard format for inspection reports and for setting up an archival system which is secure and can be reached only by authorized, competent personnel. Reports should be easily, securely, effectively and efficiently retrieved.
Requirement:	Monitoring progress and assessing outcomes and impact
Evidence to review:	The assessor should ask for and review: 1. SOPs for archiving and retrieval of inspection reports 2. Evidence for adequate space and suitability of the archive system 3. Documentation of the time needed to retrieve inspection reports.
References:	1. Effective drug regulation: A multicountry study. Geneva: World Health Organization; 2002, (7), (http://apps.who.int/medicinedocs/pdf/s2300e/s2300e.pdf) 2. Quality management systems — Requirements. International Standard ISO 9001:2015. Geneva. International Organization for Standardization, 2015, (4), (https://www.iso.org/iso-9001-quality-management.html) 3. Quality systems requirements for national good manufacturing practice inspectorates. In: WHO Expert Committee on Specifications for Pharmaceutical Preparations: thirty-sixth report. Geneva: World Health Organization; 2002: Annex 8 (WHO Technical Report Series, No. 902), (8), (http://apps.who.int/medicinedocs/documents/s22112en/s22112en.pdf) 4. Guiding principles for small national drug regulatory authorities. In: WHO Expert Committee on Specifications for Pharmaceutical Preparations: thirty-first report. Geneva: World Health Organization; 1990: Annex 6 (WHO Technical Report Series, No. 790), (5), (http://apps.who.int/medicinedocs/documents/s21964en/s21964en.pdf) 5. National drug regulatory legislation: guiding principles for small drug regulatory authorities. In: WHO Expert Committee on Specifications for Pharmaceutical Preparations: thirty-fifth report. Geneva: World Health Organization; 1999: Annex 8 (WHO Technical Report Series, No. 885), (1), (http://apps.who.int/medicinedocs/documents/s21964en/s21964en.pdf) 6. PIC/S Pre-Accession Procedure, related documents, PIC/S Audit Checklist, (138), (https://www.picscheme.org/en/pre-accession)
Framework:	Output
Rating Scale:	➔ NOT IMPLEMENTED (NI): Inspection reports are not properly archived and not easily retrieved. ➔ ONGOING IMPLEMENTATION (OI): The NRA is in the process of establishing an inspection archival system.

	➔ PARTIALLY IMPLEMENTED (PI): Inspection report archival system is recently established; however, consolidated documentation over time (at least two years) is not yet available. ➔ IMPLEMENTED (I): Inspection reports are properly archived and easily retrieved.
Limitations and remarks:	Scoring this sub-indicator as "not applicable NA" is excluded (i.e. this sub-indicator will always apply for all benchmarked NRAs).
Sub Indicator:	**RI05.03: Inspection reports are subjected to a regular and robust review by experts other than the designated inspection team.**
Maturity Level:	4
Scope:	1. Medicines 2. Vaccines
Description:	The assessor should check the existence of a process for systematic review of each inspection report by a group of experts other than the designated inspectors who performed the inspection and wrote the report. The reviewing experts or committee may be internal or external provided that the necessary confidentially and declaration of interest measures are followed as indicated in the transparency and communication indicator. The review process should be technically efficient, thorough and deep.
Objective:	The objective of this sub-indicator is to ensure the existence of a systematic review of each individual inspection report by a group of experts other than the designated inspectors who performed the inspection and wrote the report. This enhances objectivity and fairness and reduces bias.
Requirement:	Regulatory process
Evidence to review:	The assessor should ask for and review: 1. SOPs for review of GXP inspection reports 2. Examples of records of the review of GXP inspection reports.
References:	1. Guiding principles for small national drug regulatory authorities. In: WHO Expert Committee on Specifications for Pharmaceutical Preparations: thirty-first report. Geneva: World Health Organization; 1990: Annex 6 (WHO Technical Report Series, No. 790), (5), (http://apps.who.int/medicinedocs/documents/s21964en/s21964en.pdf) 2. Effective drug regulation: A multicountry study. Geneva: World Health Organization; 2002, (7), (http://apps.who.int/medicinedocs/pdf/s2300e/s2300e.pdf) 3. Guidance on Good Manufacturing Practices (GMP): inspection report, World Health Organization (WHO), (84), (http://apps.who.int/medicinedocs/en/q/ and http://digicollection.org/whoqapharm/) 4. National drug regulatory legislation: guiding principles for small drug regulatory authorities. In: WHO Expert Committee on Specifications for Pharmaceutical Preparations: thirty-fifth report. Geneva: World Health Organization; 1999: Annex 8 (WHO Technical Report Series, No. 885), (1), (http://apps.who.int/medicinedocs/documents/s21964en/s21964en.pdf) 5. Quality management systems — Requirements. International Standard ISO 9001:2015. Geneva. International Organization for Standardization, 2015, (4), (https://www.iso.org/iso-9001-quality-management.html) 6. Quality systems requirements for national good manufacturing practice inspectorates. In: WHO Expert Committee on Specifications for Pharmaceutical Preparations: thirty-sixth report. Geneva: World Health Organization; 2002: Annex 8 (WHO Technical Report Series, No. 902), (8), (http://apps.who.int/medicinedocs/documents/s22112en/s22112en.pdf)
Framework:	Process
Rating Scale:	➔ NOT IMPLEMENTED (NI): Inspection reports are not subjected to a regular and robust review by experts other than the designated inspection team.

	➔ ONGOING IMPLEMENTATION (OI): The NRA is in the process of establishing a regular and robust review by experts other than the designated inspection team; however, such a mechanism or process is not yet established. ➔ PARTIALLY IMPLEMENTED (PI): The NRA recently established a process for regular and robust review by experts other than the designated inspection team; however, it is at the implementation stage, so this practice is not yet consolidated. ➔ IMPLEMENTED (I): Inspection reports are subjected to a regular and robust review by experts other than the designated inspection team.
Limitations and remarks:	Scoring this sub-indicator as "not applicable NA" is excluded (i.e. this sub-indicator will always apply for all benchmarked NRAs).
Sub Indicator:	**RI05.04: Inspection data and outcomes are systematically evaluated or interpreted.**
Maturity Level:	4
Scope:	1. Medicines 2. Vaccines
Description:	The assessor should confirm that inspection reports and data, including inspection findings and outcomes, are collectively reviewed, analyzed, evaluated and interpreted in a systematic way to identify gaps, strengths, and trends. The output of this systematic review and analysis represents the body of inspection metrics. The availability of these inspection metrics enables the NRA to identify relevant guidelines that require developing or updating, to set up and amend inspection plans and resources, and to re- structure the format of inspection process.
Objective:	The objective of this sub-indicator is to ensure that a system is in place for checking and confirming the effectiveness of the regulatory inspection programme through the systematic review, analysis, evaluation and interpretation of the inspection reports.
Requirement:	Monitoring progress and assessing outcomes and impact
Evidence to review:	The assessor should ask for and review: 1. Documentation of available inspection data and analyses of outcomes (i.e., inspection metrics). 2. Documentation showing frequency of data analysis and review.
References:	1. Effective drug regulation: A multicountry study. Geneva: World Health Organization; 2002, (7), (http://apps.who.int/medicinedocs/pdf/s2300e/s2300e.pdf) 2. Quality management systems — Requirements. International Standard ISO 9001:2015. Geneva. International Organization for Standardization, 2015, (4), (https://www.iso.org/iso-9001-quality-management.html) 3. Quality systems requirements for national good manufacturing practice inspectorates. In: WHO Expert Committee on Specifications for Pharmaceutical Preparations: thirty-sixth report. Geneva: World Health Organization; 2002: Annex 8 (WHO Technical Report Series, No. 902), (8), (http://apps.who.int/medicinedocs/documents/s22112en/s22112en.pdf) 4. Guiding principles for small national drug regulatory authorities. In: WHO Expert Committee on Specifications for Pharmaceutical Preparations: thirty-first report. Geneva: World Health Organization; 1990: Annex 6 (WHO Technical Report Series, No. 790), (5), (http://apps.who.int/medicinedocs/documents/s21964en/s21964en.pdf) 5. National drug regulatory legislation: guiding principles for small drug regulatory authorities. In: WHO Expert Committee on Specifications for Pharmaceutical Preparations: thirty-fifth report. Geneva: World Health Organization; 1999: Annex 8 (WHO Technical Report Series, No. 885), (1), (http://apps.who.int/medicinedocs/documents/s21964en/s21964en.pdf)

Framework:	Output
Rating Scale:	➔ NOT IMPLEMENTED (NI): Inspection data are not systematically evaluated and interpreted. ➔ ONGOING IMPLEMENTATION (OI): The NRA is in the process of establishing a system for inspection data evaluation and interpretation. ➔ PARTIALLY IMPLEMENTED (PI): The NRA recently established a system for evaluation and interpretation of Inspection data; however, consolidated documentation over a time (at least two years) is not yet available. ➔ IMPLEMENTED (I): Inspection data are systematically evaluated and interpreted.
Limitations and remarks:	Scoring this sub-indicator as "not applicable NA" is excluded (i.e. this sub-indicator will always apply for all benchmarked NRAs).
Sub Indicator:	**RI05.05: Performance indicators for regulatory inspection activities are established and implemented**
Maturity Level:	4
Scope:	1. Medicines 2. Vaccines
Description:	The assessor should verify the existence and implementation of performance indicators for different activities included under the regulatory inspection functions. Specifically, the system should define key performance indicators (KPIs) along the entire regulatory inspection activity chain and all indicators should be adequately justified. For the purpose of clarity and consistency, established KPIs should be supported with guidelines for monitoring and maintenance of the KPIs. The guidelines in turn should be supported by SOPs and tools that define the procedures to be used for monitoring and evaluating the performance indicators and that define procedures and timelines for reviewing and revising the indicators. Established KPIs might be qualitative, quantitative or combination of both. In general, quantitative indicators are preferred to avoid bias or misinterpretation. However, qualitative indicators are also accepted. Qualitative indicators may or may not include scoring or scaling to render them semi-quantitative and thus more informative. The assessor should ensure that indicators are measured on a regular basis to monitor progress and advancement. In addition, the assessor should verify measured indicators are analyzed to identify trends or abnormalities. Justifications for any identified abnormalities should be provided; when necessary, process optimizations should be introduced to avoid recurrence.
Objective:	The objective of this sub-indicator is to ensure that a system, mechanism, or procedure exists to require the NRA to establish performance indicators along the entire regulatory inspection chain. Additionally, the objective is to ensure that KPIs are actually contributing to monitoring of regulatory performance, to measuring effectiveness of regulatory inspection regulatory activities, and to making any necessary adjustments or optimizations.
Requirement:	KPIs for regulatory inspection activities
Evidence to review:	The assessor should ask for and review: 1. Documents supporting the system, mechanism, or procedure compelling the NRA to establish and implement performance indicators along the entire regulatory inspection activity chain. 2. Evidence that the performance indicators have been established and implemented, and that the members of staff involved in the regulatory inspection function are aware of the indicators and the guidelines and SOPs used for monitoring and evaluating their performance. 3. The current performance indicators for regulatory inspection activities

	4. Analyses of the measured indicators along with the investigations done to identify trends or abnormalities. 5. Documentation for follow-up of any observed abnormalities, including justifications for any identified abnormalities as well as any process optimizations introduced to avoid recurrence.
References:	1. Effective drug regulation: A multicountry study. Geneva: World Health Organization; 2002, (7), (http://apps.who.int/medicinedocs/pdf/s2300e/s2300e.pdf) 2. Quality management systems — Requirements. International Standard ISO 9001:2015. Geneva. International Organization for Standardization, 2015, (4), (https://www.iso.org/iso-9001-quality-management.html) 3. Quality systems requirements for national good manufacturing practice inspectorates. In: WHO Expert Committee on Specifications for Pharmaceutical Preparations: thirty-sixth report. Geneva: World Health Organization; 2002: Annex 8 (WHO Technical Report Series, No. 902), (8), (http://apps.who.int/medicinedocs/documents/s22112en/s22112en.pdf) 4. Guiding principles for small national drug regulatory authorities. In: WHO Expert Committee on Specifications for Pharmaceutical Preparations: thirty-first report. Geneva: World Health Organization; 1990: Annex 6 (WHO Technical Report Series, No. 790), (5), (http://apps.who.int/medicinedocs/documents/s21964en/s21964en.pdf) 5. National drug regulatory legislation: guiding principles for small drug regulatory authorities. In: WHO Expert Committee on Specifications for Pharmaceutical Preparations: thirty-fifth report. Geneva: World Health Organization; 1999: Annex 8 (WHO Technical Report Series, No. 885), (1), (http://apps.who.int/medicinedocs/documents/s21964en/s21964en.pdf) 6. World Health Organization. European Observatory on Health Systems and Policies. Performance measurement for health system improvement: experiences, challenges and Prospects, (125), (https://www.who.int/management/district/performance/PerformanceMeasurementHealthSystemImprovement2.pdf) 7. World Health Organization. European Observatory on Health Systems and Policies. Health System Performance Comparison: an agenda for policy, information and research, (126), (http://www.euro.who.int/__data/assets/pdf_file/0009/244836/Health-System-Performance-Comparison.pdf) 8. Quality management -- Quality of an organization -- Guidance to achieve sustained success, ISO 9004:2018, International Organization for Standardization (ISO), (115), (https://www.iso.org/standard/70397.html)
Framework:	Output
Rating Scale:	➜ NOT IMPLEMENTED (NI): There are no KPIs for regulatory inspection activities. ➜ ONGOING IMPLEMENTATION (OI): The NRA has recently drafted KPIs for regulatory inspection activities but they have not yet been reported. ➜ PARTIALLY IMPLEMENTED (PI): The NRA has developed KPIs for regulatory inspection activities and has been applying them for less than two year or they have not covered all critical steps. ➜ IMPLEMENTED (I): The NRA has established and implemented KPIs for regulatory inspection activities. The indicators are reviewed regularly, and appropriate actions are taken, and decisions made.
Limitations and remarks:	▪ When they refer to outcomes, indicators may be ambiguous and difficult to interpret, as outcomes are the result of many factors that are difficult to disentangle. When they refer to processes, indicators are often too specific, as they may focus on a particular intervention or condition or they may quickly become outdated as business models develop. ▪ Different methodologies are used to measure the NRAs performance on regulatory inspection activities. In this case, the assessor should verify that adequate supporting documents are available. The assessor should consider that developed performance indicators should be Specific, Measurable, Achievable, Realistic, and Time- bound (i.e., “SMART”).

- Scoring this sub-indicator as "not applicable NA" is excluded (i.e. this sub-indicator will always apply for all benchmarked NRAs).

Indicator:	**RI06 Mechanism exists to promote transparency, accountability and communication.**
Objective:	The objective of this indicator is to ensure that mechanisms are in place that promote communication within and outside the NRA, that promote transparency and outreach to the public, and that establish milestones that reflect the accountability of the NRA to its mandate. Additionally, these contribute to mutual understanding and involvement of all stakeholders relevant to regulatory inspection activities. Consequently, confidence in the regulatory system is raised.
Category:	08. Transparency, accountability and communication
Sub Indicator:	**RI06.01: The list of inspectors is publicly available and the identity of the designated team for each inspection is communicated to the relevant institutions subject to inspections.**
Maturity Level:	4
Scope:	1. Medicines 2. Vaccines
Description:	The assessor should verify that a proper mechanism is available, enacted and used, together with internal procedures, to ensure that information related to the list and identity of the inspectors is publicly available. The assessor should also verify that the identity of the designated team for each inspection is provided to the institutions that are being inspected. The communications regarding information of designated inspectors may be done via public communication aids (e.g., website or national bulletin) or, for a specific inspection, via a letter of designation, a notification of inspection, or a similar approach.
Objective:	The objective of this sub-indicator is to ensure confidence building and accountability of the licensing structure via enhanced transparency, specifically, a mechanism to ensure the list and identity of inspectors is publicly available.
Requirement:	Transparency, accountability and communication
Evidence to review:	The assessor should ask for and review: 1. Procedures and processes for publishing the list of inspectors. 2. Documents comparing the current NRA list of inspectors to the publicly available list of inspectors. 3. Procedures and processes for communicating the identity of the designated team for each inspection to the relevant institution subject to inspection. 4. Examples of inspection notifications, letters of designation or similar communications using another mechanism.
References:	1. Effective drug regulation: A multicountry study. Geneva: World Health Organization; 2002, (7), (http://apps.who.int/medicinedocs/pdf/s2300e/s2300e.pdf) 2. Quality management systems — Requirements. International Standard ISO 9001:2015. Geneva. International Organization for Standardization, 2015, (4), (https://www.iso.org/iso-9001-quality-management.html) 3. Quality systems requirements for national good manufacturing practice inspectorates. In: WHO Expert Committee on Specifications for Pharmaceutical Preparations: thirty-sixth report. Geneva: World Health Organization; 2002: Annex 8 (WHO Technical Report Series, No. 902), (8), (http://apps.who.int/medicinedocs/documents/s22112en/s22112en.pdf) 4. Guiding principles for small national drug regulatory authorities. In: WHO Expert Committee on Specifications for Pharmaceutical Preparations: thirty-first report.

	Geneva: World Health Organization; 1990: Annex 6 (WHO Technical Report Series, No. 790), (5), (http://apps.who.int/medicinedocs/documents/s21964en/s21964en.pdf) 5. National drug regulatory legislation: guiding principles for small drug regulatory authorities. In: WHO Expert Committee on Specifications for Pharmaceutical Preparations: thirty-fifth report. Geneva: World Health Organization; 1999: Annex 8 (WHO Technical Report Series, No. 885), (1), (http://apps.who.int/medicinedocs/documents/s21964en/s21964en.pdf) 6. PIC/S Pre-Accession Procedure, related documents, PIC/S Audit Checklist, (138), (https://www.picscheme.org/en/pre-accession)
Framework:	Output
Rating Scale:	➔ NOT IMPLEMENTED (NI): The NRA is not notifying the inspectee of the designated inspection team and the list of the inspectors is not published ➔ ONGOING IMPLEMENTATION (OI): The NRA notifies the inspectee of the designated inspection; however, the list of inspectors is not established and is neither internally nor publicly available. ➔ PARTIALLY IMPLEMENTED (PI): The NRA notifies the inspectee of the designated inspection team; however, the list of inspectors is not published. ➔ IMPLEMENTED (I): The NRA publishes an updated list of inspectors and a procedure for notifying the inspectee of the designated inspection team is well-established.
Limitations and remarks:	Scoring this sub-indicator as "not applicable NA" is excluded (i.e. this sub-indicator will always apply for all benchmarked NRAs).
Sub Indicator:	**RI06.02: The updated list or database of all inspected facilities along their regulatory decisions, actions and enforcement activities, is regularly published and publicly available.**
Maturity Level:	4
Scope:	1. Medicines 2. Vaccines
Description:	The assessor should verify that a well-established system is in place to ensure that information related to inspections performed is available to the general public. This information includes a list of inspections performed, along with the following information for each inspection: conclusions, regulatory decisions, regulatory actions and enforcement actions (e.g., recalls, production suspensions, license suspensions or revocations, sanctions, or prosecutions). In addition, the assessor should make sure that urgent regulatory decisions (e.g., those related to quality, safety or efficacy of a medical product) and enforcement actions affecting the public health are immediately communicated to the public to ensure high level of public health protection.
Objective:	The objective of this sub-indicator is to build confidence and accountability of the licensing structure via enhanced transparency through making the information related to regulatory inspections available for the general public.
Requirement:	Transparency, accountability and communication
Evidence to review:	The assessor should ask for and review: 1. Latest publicly available list or database of inspected facilities along with their conclusions, regulatory decisions, regulatory actions and enforcements. 2. Earlier publicly available list of inspected facilities.
References:	1. Effective drug regulation: A multicountry study. Geneva: World Health Organization; 2002, (7), (http://apps.who.int/medicinedocs/pdf/s2300e/s2300e.pdf) 2. Quality management systems — Requirements. International Standard ISO

	9001:2015. Geneva. International Organization for Standardization, 2015, (4), (https://www.iso.org/iso-9001-quality-management.html) 3. Quality systems requirements for national good manufacturing practice inspectorates. In: WHO Expert Committee on Specifications for Pharmaceutical Preparations: thirty-sixth report. Geneva: World Health Organization; 2002: Annex 8 (WHO Technical Report Series, No. 902), (8), (http://apps.who.int/medicinedocs/documents/s22112en/s22112en.pdf) 4. Guiding principles for small national drug regulatory authorities. In: WHO Expert Committee on Specifications for Pharmaceutical Preparations: thirty-first report. Geneva: World Health Organization; 1990: Annex 6 (WHO Technical Report Series, No. 790), (5), (http://apps.who.int/medicinedocs/documents/s21964en/s21964en.pdf) 5. National drug regulatory legislation: guiding principles for small drug regulatory authorities. In: WHO Expert Committee on Specifications for Pharmaceutical Preparations: thirty-fifth report. Geneva: World Health Organization; 1999: Annex 8 (WHO Technical Report Series, No. 885), (1), (http://apps.who.int/medicinedocs/documents/s21964en/s21964en.pdf) 6. PIC/S Pre-Accession Procedure, related documents, PIC/S Audit Checklist, (138), (https://www.picscheme.org/en/pre-accession)
Framework:	Output
Rating Scale:	➔ NOT IMPLEMENTED (NI): There is no publicly available list or database of all inspections performed along with their conclusions, regulatory decisions, regulatory actions and enforcements. ➔ ONGOING IMPLEMENTATION (OI): The NRA is preparing to establish a publicly available list or database of all inspections performed along with their conclusions, regulatory decisions, regulatory actions and enforcements, but there is no evidence of results from such activities. ➔ PARTIALLY IMPLEMENTED (PI): There is evidence that the NRA has the elements (i.e., procedures, documentation, management systems, and other relevant information) and the capacity to perform the processes mentioned in the indicator, however, it has only limited experience or a limited number of documented events. ➔ IMPLEMENTED (I): There is a publicly available list or database of all inspections performed along with their conclusions, regulatory decisions, regulatory actions and enforcements.
Limitations and remarks:	Scoring this sub-indicator as "not applicable NA" is excluded (i.e. this sub-indicator will always apply for all benchmarked NRAs).
Sub Indicator:	**RI06.03: Inspection metrics are regularly published and publicly available.**
Maturity Level:	4
Scope:	1. Medicines 2. Vaccines
Description:	The assessor should check that a well-established and regularly updated system or mechanism is available to communicate to the public information related to inspection metrics or performance. The available quality metrics can be used as input in inspection models, but also can be used to predict possible drug shortages, to determine inspection schedules for a manufacturer, or to optimize the format of inspection processes. Some examples of possible inspection metrics include: total number inspections, relative proportion of each type of inspection (e.g., routine, cause- triggered, new product, new license, innovative pharma, or generics), number in each category of findings (i.e., critical, major or other), number of inspection findings for each inspection type, average number of findings reported for each type of inspection, average number of inspection findings over time, and the number of selected frequently occurring observations. Inspection

	metrics are always dependent on inspectorate mandate and activities planned. The above examples do not represent an exhaustive list of the possible metrics. Rather, other inspection metrics may be adopted based on multiple factors which include the objective, the relevance, and the ease of measurements.
Objective:	The objective of this sub-indicator is to ensure confidence building and accountability of the licensing structure via enhanced transparency provided by a system or mechanism in place to inform the general public of inspection metrics.
Requirement:	Transparency, accountability and communication
Evidence to review:	The assessor should ask for and review: 1. Procedures and processes addressing inspections metrics 2. Procedures and processes for publishing the inspection metrics and performance 3. Published inspection metrics.
References:	1. Effective drug regulation: A multicountry study. Geneva: World Health Organization; 2002, (7), (http://apps.who.int/medicinedocs/pdf/s2300e/s2300e.pdf) 2. Quality management systems — Requirements. International Standard ISO 9001:2015. Geneva. International Organization for Standardization, 2015, (4), (https://www.iso.org/iso-9001-quality-management.html) 3. Quality systems requirements for national good manufacturing practice inspectorates. In: WHO Expert Committee on Specifications for Pharmaceutical Preparations: thirty-sixth report. Geneva: World Health Organization; 2002: Annex 8 (WHO Technical Report Series, No. 902), (8), (http://apps.who.int/medicinedocs/documents/s22112en/s22112en.pdf) 4. Guiding principles for small national drug regulatory authorities. In: WHO Expert Committee on Specifications for Pharmaceutical Preparations: thirty-first report. Geneva: World Health Organization; 1990: Annex 6 (WHO Technical Report Series, No. 790), (5), (http://apps.who.int/medicinedocs/documents/s21964en/s21964en.pdf) 5. National drug regulatory legislation: guiding principles for small drug regulatory authorities. In: WHO Expert Committee on Specifications for Pharmaceutical Preparations: thirty-fifth report. Geneva: World Health Organization; 1999: Annex 8 (WHO Technical Report Series, No. 885), (1), (http://apps.who.int/medicinedocs/documents/s21964en/s21964en.pdf)
Framework:	Output
Rating Scale:	➜ NOT IMPLEMENTED (NI): Inspection metrics are not regularly published or publicly available. ➜ ONGOING IMPLEMENTATION (OI): The NRA is preparing to establish publicly available inspection metrics, but there is no evidence of results from such activities. ➜ PARTIALLY IMPLEMENTED (PI): There is evidence that the NRA has the elements (i.e., procedures, documentation, management systems, and other relevant information) and the capacity to perform the processes mentioned in the indicator, however, it has only limited experience or a limited number of documented events. ➜ IMPLEMENTED (I): Inspection metrics are not regularly published and publicly available.
Limitations and remarks:	Scoring this sub-indicator as "not applicable NA" is excluded (i.e. this sub-indicator will always apply for all benchmarked NRAs).
Sub Indicator:	**RI06.04: Information on inspections conducted is regularly published and publicly available in accordance with national confidentiality requirements.**
Maturity Level:	4
Scope:	1. Medicines 2. Vaccines

Description:	The assessor should check that the regulatory inspections performed, and reports for those inspections, are available for the general public. The information that may be shared with the public varies according to the national legislations. In some countries, full inspection reports (redacted or non-redacted) may be published. In other countries, only inspection summaries (or excerpts) may be publicly available. Both approaches are accepted; however, the earlier one is encouraged. It should be noted that publication of inspection reports or summaries would significantly contribute to regulatory reliance and recognition in the area of regulatory inspection.
Objective:	The objective of this sub-indicator is to build confidence and accountability of the licensing structure via enhanced transparency through public availability of information on inspections performed and reports from those inspections.
Requirement:	Transparency, accountability and communication
Evidence to review:	The assessor should ask for and review: 1. Procedures and processes for publishing the list of inspections performed 2. The list of inspections performed 3. Examples of actual published Inspection reports or summaries (or excerpts).
References:	1. Effective drug regulation: A multicountry study. Geneva: World Health Organization; 2002, (7), (http://apps.who.int/medicinedocs/pdf/s2300e/s2300e.pdf) 2. Quality management systems — Requirements. International Standard ISO 9001:2015. Geneva. International Organization for Standardization, 2015, (4), (https://www.iso.org/iso-9001-quality-management.html) 3. Quality systems requirements for national good manufacturing practice inspectorates. In: WHO Expert Committee on Specifications for Pharmaceutical Preparations: thirty-sixth report. Geneva: World Health Organization; 2002: Annex 8 (WHO Technical Report Series, No. 902), (8), (http://apps.who.int/medicinedocs/documents/s22112en/s22112en.pdf) 4. Guiding principles for small national drug regulatory authorities. In: WHO Expert Committee on Specifications for Pharmaceutical Preparations: thirty-first report. Geneva: World Health Organization; 1990: Annex 6 (WHO Technical Report Series, No. 790), (5), (http://apps.who.int/medicinedocs/documents/s21964en/s21964en.pdf) 5. National drug regulatory legislation: guiding principles for small drug regulatory authorities. In: WHO Expert Committee on Specifications for Pharmaceutical Preparations: thirty-fifth report. Geneva: World Health Organization; 1999: Annex 8 (WHO Technical Report Series, No. 885), (1), (http://apps.who.int/medicinedocs/documents/s21964en/s21964en.pdf)
Framework:	Output
Rating Scale:	➜ NOT IMPLEMENTED (NI): Inspection reports or summaries (or excerpts) are not publicly available. ➜ ONGOING IMPLEMENTATION (OI): The NRA established a procedure or mechanism by which relevant inspection reports or summaries (or excerpts) could be publicly available; however, this is not yet implemented. ➜ PARTIALLY IMPLEMENTED (PI): Inspection reports or summaries are publicly available, but only upon request (i.e. pull rather than push mechanism). ➜ IMPLEMENTED (I): Inspection reports or summaries (or excerpts) are regularly and consistently published and publicly available.
Limitations and remarks:	

07

Laboratory Testing (LT): Indicators and Fact Sheets

WHO Global Benchmarking Tool (GBT) for Evaluation of National Regulatory System of Medical Products

07. Laboratory Testing (LT): Indicators and Fact Sheets

Function:	07 – LABORATORY TESTING (LT)
Description:	The laboratory testing regulatory function is intended to ensure that the National Regulatory Authority (NRA) is able to assess the quality of medical products by performing quality tests on them in certain situations. For example, this testing can be a requirement to corroborate manufacturer's test results as a part of the evaluation for marketing authorization or for a variation to a marketing authorization. Testing can be a requirement for lot release for certain products depending upon national regulations. Testing also may be needed for products for which there has been a complaint or a report or for products that are under investigation due to an adverse event. As part of the market surveillance function, laboratory testing is utilized for checking and confirming the quality of medical products placed on the market and for detecting substandard and falsified medical products. In order to do this product testing, the NRA must have access to suitable laboratories where these tests can be performed. If a country is able to provide all the resources needed, a laboratory under the responsibility of the NRA or a governmental laboratory represents the best choice. Commonly, this governmental laboratory is a national control laboratory (NCL). As an alternative option, the regulatory system may have access to external laboratories, either inside or outside the country, to perform the required tests on behalf on the NRA. When external laboratories are used, regulatory decisions and actions remain at the discretion of the NRA and the NRA retains accountability. A well-functioning laboratory for medical products testing is an important resource for the national regulatory system. The staff generally has expertise in different life science disciplines and can help in other regulatory activities, for example, the assessment and review of marketing authorization applications and the review of clinical trial data. When the regulatory laboratory testing activities are decentralized to one or more internal or external laboratories, the NRA or NCL must ensure that a continuous information exchange mechanism is established so the central authority can issue guidance and the decentralized entity can report back with the information needed for making decisions.
Indicator:	**LT01 Legal provisions, regulations and guidelines required to define the regulatory framework of laboratory testing activities.**
Objective:	The objective of this indicator is to ensure that laboratory testing activities are supported by a comprehensive set of legal provisions, regulations and guidelines which provide the necessary mandate to implement all activities related to this regulatory function.
Category:	01. Legal provisions, regulations and guidelines
Sub Indicator:	**LT01.01: There are legal provisions to establish a national quality control laboratory (NCL) to perform quality control (QC) testing, and/or to authorize the National Regulatory Authority (NRA) to sub-contract the required testing services.**
Maturity Level:	1

Scope:	1. Medicines 2. Vaccines
Description:	The assessor should verify that legal provisions exist and are enacted for establishing a NCL that is responsible for controlling medical products and/or for authorizing the national authority to establish an operational agreement with an independent external laboratory. In the latter case, the independent laboratory may be inside or outside the-country. The assessor should verify that legal provisions exist and are enacted that authorize the NCL to perform QC testing and to issue official results of these tests.
Objective:	The objective of this sub-indicator is to ensure the existence of legal provisions, regulations or other official government publications that establish the laboratory testing function and that provide the mandate for the responsible entity to actually implement these activities.
Requirement:	Legal provisions for establishing the laboratory testing function through an established NCL and/or authorizing the NRA to have an operational agreement with an independent laboratory. Legal provisions authorizing the NCL to issue official results of these tests.
Evidence to review:	The assessor should ask for and review: 1. Legal provisions establishing the laboratory testing function; 2. Regulations or other official government publication establishing the laboratory testing function; 3. Legal provisions authorizing the NCL to perform testing and officially issue results of the same; 4. Regulations or other official government publication establishing NRA's responsibilities when sub-contracting the required testing services.
References:	1. Guidelines for national authorities on quality assurance for biological products. In: WHO Expert Committee on Biological Standardization: forty-second report World Health Organization; 1992: Annex 2 (WHO Technical Report Series, No. 822), (2), (http://www.who.int/biologicals/publications/trs/areas/biological_products/WHO_TRS_822_A2.pdf) 2. WHO good practices for pharmaceutical quality control laboratories, (35), (http://digicollection.org/whoqapharm/p/about and http://apps.who.int/medicinedocs/en)
Framework:	Structure/Foundation/Input
Rating Scale:	➜ NOT IMPLEMENTED (NI): There is no legal basis, regulation, or other official government publication establishing an NCL to perform QC testing, authorizing the NRA to sub-contract the required testing services, or authorizing the NCL to issue official results ➜ ONGOING IMPLEMENTATION (OI): Although there is no legal basis, demonstrable steps have been taken towards establishing one. ➜ PARTIALLY IMPLEMENTED (PI): The legal basis was recently established and implementation is underway. ➜ IMPLEMENTED (I): There is a legal basis authorizing the NRA to establish a national control laboratory that has the duties and responsibilities required to perform this function or to sub-contract the required testing services.
Limitations and remarks:	Scoring this sub-indicator as "not applicable NA" is excluded (i.e. this sub-indicator will always apply for all benchmarked NRAs).
Sub Indicator:	**LT01.02: Legal provisions and regulations allow the NRA to recognize and use laboratory testing-related decisions, reports or information from other NRAs or regional and international bodies.**
Maturity Level:	1

Scope:	1. Medicines 2. Vaccines
Description:	The assessor should verify that legal provisions and regulations allow the NRA and the NCL to recognize and /or rely on laboratory decisions, data and information from NCLs of other countries or regional and international institutions.
Objective:	The objective of this sub-indicator is to ensure that legal provisions and regulations provide the necessary mandate for the NCL to implement regulatory recognition and/or reliance.
Requirement:	Legal provisions and regulations allowing the reliance on and/or recognition of regulatory decisions in the area of laboratory testing
Evidence to review:	The assessor should ask for and review: 1. Legal provisions allow reliance on and/or recognition of other NCL regulatory decisions; 2. Agreements and memoranda of understanding with other NCLs to apply reliance on and/or recognition of regulatory decisions; 3. Documentation providing the rationale and justification for reliance on and/or recognition of other NCL regulatory decisions. 4. Examples of communication with other NCLs; 5. Examples of NRA consideration of decisions, information and data from other NCLs; 6. If legal provisions prevent the NCL from relying on and/or recognizing other NCLs regulatory decisions, examples of any impact this condition may have in the laboratory testing function.
References:	1. Guidelines for national authorities on quality assurance for biological products. In: WHO Expert Committee on Biological Standardization: forty-second report World Health Organization; 1992: Annex 2 (WHO Technical Report Series, No. 822), (2), (http://www.who.int/biologicals/publications/trs/areas/biological_products/WHO_TRS_822_A2.pdf)
Framework:	Structure/Foundation/Input
Rating Scale:	➔ NOT IMPLEMENTED (NI): There is no evidence of legal provisions or regulations allowing reliance on and/or recognition of other NCL regulatory decisions. ➔ ONGOING IMPLEMENTATION (OI): The NRA is preparing to draft such legal provisions and regulations, but there is no evidence of results from such activities. ➔ PARTIALLY IMPLEMENTED (PI): The legal basis was established recently and is at the implementation stage, so this practice is not consolidated yet. ➔ IMPLEMENTED (I): The NRA has such legal provisions and regulations and also consistently maintains documentation of the results of related activities over time. ➔ NA: When the legal provisions prevent reliance on and/or recognition of other NCL regulatory decisions.
Limitations and remarks:	In some countries legal provisions may prevent the NCL from relying on and/or recognizing other NCL regulatory decisions; in this case the sub-indicator may be considered as not applicable.
Indicator:	**LT02 Arrangement for effective organization and good governance.**
Objective:	The objective of this indicator is to ensure the implementation of effective organization and good governance practices at the entities responsible for laboratory testing activities which, in turn, contribute to effective and efficient functioning of this regulatory function.
Category:	02. Organization and governance
Sub Indicator:	**LT02.01: There is a defined organizational structure with clear responsibilities to conduct laboratory testing activities.**
Maturity Level:	2

Scope:	1. Medicines 2. Vaccines
Description:	The assessor should identify the organization designated to establish, implement or maintain the laboratory testing regulatory function, as well as the specific organizational structure taking on the different relevant activities. Responsibilities, duties and roles of these structures should be clearly defined and documented. If more than one structure is involved, the assessor should check the ways and approaches by which coordination among these structures is taking place. When some of the activities of the NCL can be performed by laboratories of other national or international institutions, these institutions must not have any conflict of interests.
Objective:	The objective of this sub-indicator is to ensure effective organization and good governance of laboratory testing of medical products and that these activities are taken over by defined structures with clear roles and responsibilities.
Requirement:	Defined structure and clear responsibilities
Evidence to review:	The assessor should ask for and review: 1. Organization chart of the organizations responsible for the implementation of laboratory testing activities along with identification of the particular structures implementing the function. 2. Documentation clarifying roles and responsibilities of the organizational structures implementing laboratory testing activities. This may include administrative decrees, terms of reference, and other relevant documents. 3. Documented contract with laboratories of other national or international institutions, when applicable, establishing responsibilities of each party and stating there is no conflict of interest.
References:	
Framework:	Structure/Foundation/Input
Rating Scale:	➔ NOT IMPLEMENTED (NI): There are no documents available establishing a defined structure with clear responsibilities to conduct laboratory testing activities. ➔ ONGOING IMPLEMENTATION (OI): Although there are no approved documents, there is evidence that they are being prepared. ➔ PARTIALLY IMPLEMENTED (PI): Such documents were approved recently (e.g. less than one year ago). ➔ IMPLEMENTED (I): Such documents were approved some time ago and there has already been a cycle of internal or external audits (with or without accreditation) or a system review.
Limitations and remarks:	▪ In some countries there may be a centralized NCL; in this case the assessor should look at roles and responsibilities within the structure implementing the laboratory testing function. ▪ Scoring this sub-indicator as "not applicable NA" is excluded (i.e. this sub-indicator will always apply for all benchmarked NRAs).
Sub Indicator:	**LT02.02: Documented procedures are implemented to ensure the involvement and contributions of the NCL to support regulatory oversight.**
Maturity Level:	3
Scope:	1. Medicines 2. Vaccines
Description:	The assessor should verify the existence of written documentation defining the responsibilities and roles of the NCL for its involvement and contribution to other regulatory functions. Examples of the responsibilities and roles include, but are not limited to, providing

	technical and scientific input before and after a product receive marketing authorizations (MAs), contributing to clinical trials authorizations, participating in regulatory inspections, performing quality testing on samples collected within the context of the market surveillance programme, detecting substandard and falsified medical products, contributing to analyses of vigilance data, and providing technical advice for national lot release.
Objective:	The objective of this sub-indicator is to ensure that standard procedures are implemented for effective involvement and contributions of the NCL in support of other regulatory functions.
Requirement:	Procedures relevant to involvement and contributions of the NCL to other regulatory functions.
Evidence to review:	The assessor should ask for and review: 1. Standard procedures and other documentations detailing roles and responsibilities of the NCL with respect to its contribution to other regulatory functions and to regulatory oversight as applicable. 2. Records demonstrating active involvement and contribution of the NCL to other regulatory functions.
References:	1. WHO good practices for pharmaceutical quality control laboratories, (35), (http://digicollection.org/whoqapharm/p/about and http://apps.who.int/medicinedocs/en)
Framework:	Structure/Foundation/Input
Rating Scale:	➜ NOT IMPLEMENTED (NI): There are no documented procedures or results that demonstrate the NCL involvement in and contributions to other regulatory functions or to regulatory oversight. ➜ ONGOING IMPLEMENTATION (OI): Although there are no approved documents, there is evidence that they are being prepared. ➜ PARTIALLY IMPLEMENTED (PI): Such documents were approved recently (e.g. less than one year ago). ➜ IMPLEMENTED (I): Such documents were approved some time ago (at least one year ago), and there has already been a cycle of internal or external audits (with or without accreditation) or system review.
Limitations and remarks:	Scoring this sub-indicator as "not applicable NA" is excluded (i.e. this sub-indicator will always apply for all benchmarked NRAs).
Indicator:	**LT03 Laboratory activities implemented as per well-established plans and policies according a Quality Management System (QMS).**
Objective:	The objective of this indicator is to ensure that the laboratory establishes, implements, and maintains a Quality Management System appropriate to the scope of its activities. It is essential to have clear policies and plans in place for effective and reliable laboratory operations. Laboratory policies should cover a range of activities, including calibration and qualification of equipment, validation of testing methods, establishment of reference standards, and performance of testing and retesting. In addition, policies should be in place that cover the establishment, qualification, distribution, and use of reference materials for laboratory testing, including their calibration against international reference materials or standards, when available. The policies should cover the various types of reference materials used in the laboratory, e.g., primary standards, working standards, and official national or international reference preparations.
Category:	03. Policy and strategic planning
Sub Indicator:	**LT03.01: Documented and implemented policy for testing exists that is based on the product's risk.**
Maturity Level:	3

Scope:	1. Medicines 2. Vaccines
Description:	The assessor should identify documented evidence that demonstrates there is a risk-based assessment to support products to be tested and the testing to be done. Market surveillance methodologies, such as field screening technologies, can serve as a basis for prioritizing products for testing in the laboratory.
Objective:	The objective of this sub- indicator is to ensure efficient use of resources to address products of concern for public health such as substandard and falsified medical products.
Requirement:	Prioritization of testing activities using a risk-based approach.
Evidence to review:	The assessor should ask for and review: 1. Documents outlining the information used to support decisions. 2. Documentation of the criteria used to arrive at decisions, and evidence confirming these are risk-based.
References:	1. WHO good practices for pharmaceutical quality control laboratories, (35), (http://digicollection.org/whoqapharm/p/about and http://apps.who.int/medicinedocs/en) 2. General requirements for the competence of testing and calibration laboratories, ISO ISO/IEC 17025:2015 International Organization for Standardization, 2015, (33), (https://www.iso.org/standard/66912.html) 3. WHO good practices for pharmaceutical microbiology laboratories, (34), (http://digicollection.org/whoqapharm/p/about and http://apps.who.int/medicinedocs/en) 4. WHO guidelines on quality risk management, (55), (http://digicollection.org/whoqapharm/p/about and http://apps.who.int/medicinedocs/en)
Framework:	Structure/Foundation/Input
Rating Scale:	➜ NOT IMPLEMENTED (NI): There is no documented evidence that a risk-based testing policy exists ➜ ONGOING IMPLEMENTATION (OI): Although there are no approved documents, there is evidence that they are being prepared. ➜ PARTIALLY IMPLEMENTED (PI): Such documents were approved recently (e.g. less than one year ago). ➜ IMPLEMENTED (I): Such documents were approved some time ago and there has already been a cycle of internal or external audits (with or without accreditation) or system review.
Limitations and remarks:	Testing should be based on the products' characteristics. The choice of tests and the extent of testing should be based on risk management principles. Scoring this sub-indicator as "not applicable NA" is excluded (i.e. this sub-indicator will always apply for all benchmarked NRAs).
Sub Indicator:	**LT03.02: Documented and implemented policy exists on the validation, verification and transfer of analytical procedures.**
Maturity Level:	3
Scope:	1. Medicines 2. Vaccines
Description:	The assessor should verify there is a policy on validation, verification and transfer of analytical procedures, which establishes that all procedures should be validated. This policy should include pharmacopoeial procedures, manufacturer's procedures, NCL procedures, and other procedures used to support the regulatory oversight function. The assessor should verify that the NCL is using validated analytical methodologies that ensure reliable results. If validated methods are transferred into the NCL from a manufacturer or any other laboratory, the assessor should verify that the transferred

	procedure was re-validated, and that supporting documentation is available. The process by which these methodologies were validated should be described, and documentation should identify the validation parameters that were evaluated. The validation parameters should be selected based on the category of analysis. Documentation should also identify the required validation parameters when pharmacopoeial methodologies are used or when methods are transferred. To evaluate this, the assessor should check and review protocols and reports of test method validations.
Objective:	The objective of this sub- indicator is to ensure that policies and procedures that cover test method validation, verification, and transfer are available and will ensure reliability of laboratory test results.
Requirement:	Test method validation and verification protocols and reports. Standard procedures for transfer of validated test methods from the manufacturer or other laboratories.
Evidence to review:	The assessor should ask for and review: 1. Policies and procedures for validation and verification of test methods and transfer of validated test methods; 2. List of transferred validated test methods; 3. Examples of documentation of validation or revalidation of transferred test methods; 4. List of validated test methods; 5. Examples of validation protocols for selected test methods; 6. Examples of validation reports of selected test methods.
References:	1. WHO good manufacturing practices for pharmaceutical products: main principles, (51), (http://digicollection.org/whoqapharm/p/about and http://apps.who.int/medicinedocs/en) 2. General requirements for the competence of testing and calibration laboratories, ISO ISO/IEC 17025:2015 International Organization for Standardization, 2015, (33), (https://www.iso.org/standard/66912.html) 3. WHO good practices for pharmaceutical quality control laboratories, (35), (http://digicollection.org/whoqapharm/p/about and http://apps.who.int/medicinedocs/en) 4. Quality Management (QM) documents, European Directorate for the Quality of Medicines and Healthcare (EDQM), Council of Europe (107) (https://www.edqm.eu/en/quality-management-guidelines-86.html) 5. WHO good practices for pharmaceutical microbiology laboratories, (34), (http://digicollection.org/whoqapharm/p/about and http://apps.who.int/medicinedocs/en) 6. Validation of analytical procedures, European Directorate for the Quality of Medicines and Healthcare (EDQM), OMCL Network of the Council of Europe, PA/PH/. MCL (13) 82 2R, (106), (https://www.edqm.eu/medias/fichiers/validation_of_analytical_procedures_paphomcl_13_82_2r.pdf) 7. WHO International Reference Preparations Catalogue, (103), (http://www.who.int/bloodproducts/catalogue/en/) 8. WHO manual for the establishment of national and other secondary standards for vaccines. WHO/IVB/11.03, (136), (http://apps.who.int/iris/bitstream/10665/70669/1/WHO_IVB_11.03_eng.pdf) 9. WHO manual for the preparation of secondary reference materials for in vitro diagnostic assays designed for infectious disease nucleic acid or antigen detection: calibration to WHO International Standards, (137), (http://www.who.int/entity/bloodproducts/norms/SecStandManWHO_TRS_1004_web_ Annex_6.pdf?ua=1)
Framework:	Structure/Foundation/Input
Rating Scale:	➜ NOT IMPLEMENTED (NI): There is no documented evidence that a policy on the validation, verification, and transfer of analytical procedures exist. ➜ ONGOING IMPLEMENTATION (OI): Although there are no approved documents, there is evidence that they are being prepared. ➜ PARTIALLY IMPLEMENTED (PI): Such documents were approved recently (e.g. less than one year ago).

	➔ IMPLEMENTED (I): Such documents were approved some time ago (at least one year ago), and there has already been a cycle of internal or external audits (with or without accreditation) or system review.
Limitations and remarks:	▪ In this context, "verification" refers to the verification of compendial procedures, namely, the demonstration of acceptable performance under the conditions in which the procedure is used. ▪ Scoring this sub-indicator as "not applicable NA" is excluded (i.e. this sub-indicator will always apply for all benchmarked NRAs).
Sub Indicator:	**LT03.03: A policy is in place to establish or qualify all reference standards used in laboratory testing activities.**
Maturity Level:	3
Scope:	1. Medicines 2. Vaccines
Description:	The assessor should verify the existence of a national policy for establishment of all reference standards used in laboratory activities. The NCL may set a policy not to develop and establish reference standard materials, and instead, rely on reference standards developed by other entities (e.g. World Health Organization (WHO) or other NCLs). However, in this case, the policy should explain how the reliability of those reference standards that are used is ensured by the laboratory staff. If there is a policy to establish national reference standards, the assessor should review the policy in detail including guidance that it provides related to methodologies and criteria for establishing such national reference standards and for ensuring traceability to international reference standards. In all cases, the policy for establishment or qualification of national reference standards (if any) should be based on relevant WHO guidelines (listed in the reference section) or other internationally accepted standards and practices. In addition, the assessor should verify that a suitable system is in place for using reference standards in the laboratory. In addition, the assessor should verify that the policy includes plans and procedures for replacement or replenishment of reference standards in case the standards have exhausted. Furthermore, if an NCL is supplying national standards to users nationwide (i.e., as a major responsibility), there should be plans and procedures for distribution and monitoring the use of the standards. The reference standards should be identified, recorded and properly stored. An individual or entity within the NCL should be assigned to monitor their use and to verify that they used appropriately.
Objective:	The objective of this sub- indicator is to ensure that specific policies are in place with respect to establishment and maintenance of reference standard materials. Reliable reference standard materials, in turn, contribute to effective laboratory testing activities.
Requirement:	Policy for establishment or qualification of all reference standards used in laboratory activities.
Evidence to review:	The assessor should ask for and review: 1. Policy for establishment or qualification of all reference standards used in laboratory; 2. Implemented procedures for validation or bridging studies and for implementation and use of control charts; 3. Examples of reference standards used in the laboratory, if any, along with the documentation supporting qualification (including qualification criteria) and providing evidence for traceability to international reference standards.
References:	1. WHO good practices for pharmaceutical quality control laboratories, (35), (http://digicollection.org/whoqapharm/p/about and http://apps.who.int/medicinedocs/en) 2. Recommendations for the preparation, characterization and establishment, (37), (https://www.who.int/biologicals/reference_preparations/en/) 3. WHO good manufacturing practices for pharmaceutical products: main principles, (51), (http://digicollection.org/whoqapharm/p/about and http://apps.who.int/medicinedocs/en)

	4. General requirements for the competence of testing and calibration laboratories, ISO ISO/IEC 17025:2015 International Organization for Standardization, 2015, (33), (https://www.iso.org/standard/66912.html) 5. WHO International Reference Preparations Catalogue, (103), (http://www.who.int/bloodproducts/catalogue/en/) 6. WHO manual for the establishment of national and other secondary standards for vaccines. WHO/IVB/11.03, (136), (http://apps.who.int/iris/bitstream/10665/70669/1/WHO_IVB_11.03_eng.pdf) 7. WHO manual for the preparation of secondary reference materials for in vitro diagnostic assays designed for infectious disease nucleic acid or antigen detection: calibration to WHO International Standards, (137), (http://www.who.int/entity/bloodproducts/norms/SecStandManWHO_TRS_1004_web_ Annex_6.pdf?ua=1)
Framework:	Structure/Foundation/Input
Rating Scale:	➜ NOT IMPLEMENTED (NI): There is no documented evidence of a policy in place to establish or qualify all reference standards used in the laboratory. ➜ ONGOING IMPLEMENTATION (OI): Although there are no approved documents, there is evidence that they are being prepared. ➜ PARTIALLY IMPLEMENTED (PI): Such documents were approved recently (e.g. less than one year ago). ➜ IMPLEMENTED (I): Such documents were approved some time ago (at least one year ago), and there has already been a cycle of internal or external audits (with or without accreditation) or system review.
Limitations and remarks:	
Sub Indicator:	**LT03.04: Documented and implemented procedures exist for handling atypical or out-of-specification (OOS) results, including a retest policy.**
Maturity Level:	2
Scope:	1. Medicines 2. Vaccines
Description:	The assessor should verify the existence and implementation of a re-testing policy in case of OOS test results. The policy should initially define OOS and set clear rules to handle these results. The assessor should check the policy and make sure it considers the properties procedures provide guidelines on handling appeals against the decisions of the NCL. of different test methods including their variabilities and sensitivities (e.g. qualitative or quantitative methods or in vitro or in vivo methods). The assessor should verify the establishment and implementation of standard procedures for handling events of non-compliance with pre-set specifications. Procedures should provide comprehensive guidance on how to report such non-compliant events and how to communicate and report these cases to supervisors or higher-level officials in the laboratory. In addition, the procedures should provide guidance for notifying the manufacturer and for meeting with its representatives, when necessary. Relevant procedures should cover notification of other departments or entities within the regulatory system. In all cases, assessor should check that a notice of non-compliance authorized by pre-assigned official is issued by the NCL. The assessor should verify that procedures for the evaluation of test results and decision-making are available and enacted. The assessor should also confirm that relevant
Objective:	The objective of this sub- indicator is to ensure that specific policies are in place that contribute to effective laboratory testing activities. In particular, a re-testing policy is required to ensure consistency in handling OOS test results.
Requirement:	Standard procedures for dealing with and handling events of non-compliance.Re- testing policy is established and implemented. Standard procedures for evaluation of test results and decision-making.

Evidence to review:	The assessor should ask for and review: 1. Policy for handling OOS test results. 2. List of OOS test results. 3. Examples of documentation detailing the handling of selected OOS test results. 4. Standard procedures for dealing with and handling events of confirmed non-compliance of test results with pre-set specifications. 5. List of non- compliant events within a particular time interval (e.g. last year). 6. Example records of non-compliant (i.e., OOS) events along with their investigations and final decisions. . 7. Standard procedures for evaluation of test results and for decision-making regarding compliance or non-compliance. 8. Example records for which test results were evaluated and for decisions made on compliance or non-compliance (i.e., for specific test methods that are being reviewed by the assessor). 9. Standard procedures for handling appeals against decisions made by the NCL. 10. List of appeals against NCL decisions within a particular time interval (e.g., last year). 11. Example records (i.e., for specific test methods that are being reviewed by the assessor) from selected cases in which the NCL decision was appealed.
References:	
Framework:	Structure/Foundation/Input Proces
Rating Scale:	➜ NOT IMPLEMENTED (NI): There is no documented evidence of a policy and procedures in place to handle atypical or OOS results and no evidence for a retesting policy. ➜ ONGOING IMPLEMENTATION (OI): Although there are no approved documents, there is evidence that they are being prepared. ➜ PARTIALLY IMPLEMENTED (PI): Such documents were approved recently (e.g. less than one year ago). ➜ IMPLEMENTED (I): Such documents were approved some time ago (at least one year ago), and there has already been a cycle of internal or external audits (with or without accreditation) or system review.
Limitations and remarks:	Scoring this sub-indicator as "not applicable NA" is excluded (i.e. this sub-indicator will always apply for all benchmarked NRAs).
Indicator:	**LT04 Human resources to perform laboratory testing activities.**
Objective:	The objective of this indicator is to ensure to that all entities within an NRA are adequately resourced with a trained, experienced and skilled workforce that is empowered to fully perform the function of laboratory testing of medical products. This will ensure that medical products testing activities are performed in accordance with international best practices. The objective of this indicator is to evaluate the human resource capacity of the entities with respect to the number of personnel, the skills and experience of the personnel, and the overall composition the workforce, with the goal of evaluating whether the workforce possesses the specific expertise required to perform the laboratory testing function.
Category:	Resources (HR, FR, infrastructure and equipment)
Sub Indicator:	**LT04.01: Sufficient competent staff (i.e., education, training, skills and experience) are assigned to perform laboratory testing activities.**
Maturity Level:	3
Scope:	1. Medicines 2. Vaccines

Description:	The assessor should verify that the human resources assigned to perform laboratory testing activities should be sufficient with respect to numbers and competent with respect to the requisite skills, education, experience and training. There should be technical documents and standard operating procedures (SOPs) that provide guidance on the required background for laboratory testing activities and that consider the requirements for educational background, competencies, skills, experience, and training. The assessor should verify that the NRA estimated the number of staff required to effectively and efficiently perform laboratory testing function and that the NRA actually recruited that number. In addition, the assessor should verify that these competency requirements are well-established and maintained by the NRA. Metrics and statistics on the different activities performed as well as performance indicators can be used for estimating the adequacy of the number of the assigned staff. The assessor should also verify that the competency of the assigned staff is built, maintained and improved through recruitment as well as continuous on-the-job training.
Objective:	The objective of this sub-indicator is to ensure the existing human resources for laboratory testing is sufficient, in terms of numbers, experience, and specific competencies, to perform all the activities along the entire laboratory testing chain.
Requirement:	Sufficient number of competent human resources in charge of laboratory testing activities.
Evidence to review:	The assessor should ask for and review: 1. Evidence that the number of staff members involved in each of the documented activities along the entire laboratory testing process flow is adequate. 2. Evidence that the systems and structures are in place to ensure appropriate placement of staff with respect to competence and skills. 3. Evidence that the system and structures have been implemented. The documentation should include the records to verify that the staff competence is appropriate for the job requirements. 4. Evidence that the professional profiles of the human resources engaged in laboratory testing activities are appropriate with respect to education, skills, and expertise, to perform a particular function along the laboratory testing chain. Documentation should include a list of the requisite skills and training for each position. 5. Recruitment plan.
References:	1. National drug regulatory legislation: guiding principles for small drug regulatory authorities. In: WHO Expert Committee on Specifications for Pharmaceutical Preparations: thirty-fifth report. Geneva: World Health Organization; 1999: Annex 8 (WHO Technical Report Series, No. 885), (1), (http://apps.who.int/medicinedocs/documents/s21964en/s21964en.pdf) 2. WHO good manufacturing practices for pharmaceutical products: main principles, (51), (http://digicollection.org/whoqapharm/p/about and http://apps.who.int/medicinedocs/en)
Framework:	Structure/Foundation/Input
Rating Scale:	➜ NOT IMPLEMENTED (NI): The NRA does not have enough competent staff (i.e., education, training, skills and experience) to perform laboratory testing activities ➜ ONGOING IMPLEMENTATION (OI): The NRA has recently developed a plan to recruit adequate competent staff; however, the plan has not been implemented. ➜ PARTIALLY IMPLEMENTED (PI): The NRA has initiated the implementation of the human resources development plan; however, there is need to complete the competency profile. ➜ IMPLEMENTED (I): The NRA has a sustained number of competent staff (i.e., education, training, skills and experience) assigned to perform laboratory testing activities.
Limitations and remarks:	▪ Assessment of the adequacy and appropriateness of the number of staff members is quite subjective and should be linked to some process or output indicators. When estimating staff adequacy, the assessor should consider the workload, backlog, and delays in delivery based on established timeframes.

- Scoring this sub-indicator as "not applicable NA" is excluded (i.e. this sub-indicator will always apply for all benchmarked NRAs).

Sub Indicator:	**LT04.02: Duties, functions, and responsibilities of the staff in charge of laboratory testing activities are established and updated in the respective job descriptions.**
Maturity Level:	3
Scope:	1. Medicines 2. Vaccines
Description:	The assessor should verify that procedures are in place to maintain a current and updated structure for managing job descriptions for personnel participating in laboratory testing activities. In addition, job descriptions should address current staff duties, responsibilities and the requisite competencies. A job description with this format and content should be established and implemented for all staff. The management of job descriptions should be supported by a guidance document that provides direction on when and how to update the information and where the information should be kept for easy access. The guidance document should present the appropriate duties and responsibilities that are assigned to each member of the organization involved in laboratory testing activities. Thus, the professional profiles of staff are reflected in their respective roles and responsibilities within the NRA. There should be procedures to guide responsible persons to document that duties, functions and responsibilities are revised and kept up to date. In addition, procedures should be available to guide the keeping and documenting of up to date work schedules and enforcing the implementation of the documented guidelines and procedures.
Objective:	The objective of this sub-indicator is to ensure that duties and responsibilities of the staff are clear and well defined, that job descriptions are kept up to date with current duties, functions and responsibilities, and that these activities are adequately documented.
Requirement:	Duties, roles and responsibilities of the staff relevant to laboratory testing activities.
Evidence to review:	The assessor should ask for and review: 1. Procedures and guidelines that guide placement of staff members within the NRA; 2. The professional profiles of staff (i.e., job descriptions) and documentation that they are related to their current roles and duties; 3. The professional profiles of the external experts and documentation which ensures that experts' profiles are complete and consistent with that prescribed in the legal provisions; 4. Procedures to guide the documentation of up to date duties and work schedules, and to enforce the implementation of the documented guidelines and procedures; 5. Job descriptions for designated staff.
References:	1. National drug regulatory legislation: guiding principles for small drug regulatory authorities. In: WHO Expert Committee on Specifications for Pharmaceutical Preparations: thirty-fifth report. Geneva: World Health Organization; 1999: Annex 8 (WHO Technical Report Series, No. 885), (1), (http://apps.who.int/medicinedocs/documents/s21964en/s21964en.pdf) 2. Quality management systems — Requirements. International Standard ISO 9001:2015 International Organization for Standardization, 2015, (4), (https://www.iso.org/iso-9001-quality-management.html) 3. Guiding principles for small national drug regulatory authorities. In: WHO Expert Committee on Specifications for Pharmaceutical Preparations: thirty-first report. Geneva: World Health Organization; 1990: Annex 6 (WHO Technical Report Series, No. 790), (5), (http://apps.who.int/medicinedocs/documents/s21964en/s21964en.pdf) 4. Effective drug regulation: A multicountry study. Geneva: World Health Organization; 2002, (7), (http://apps.who.int/medicinedocs/pdf/s2300e/s2300e.pdf)
Framework:	Structure/Foundation/Input

Rating Scale:	➔ NOT IMPLEMENTED (NI): There is no evidence of defined or established duties, functions, responsibilities, respective job descriptions and necessary required competencies. ➔ ONGOING IMPLEMENTATION (OI): The NRA has recently drafted or developed the role and responsibilities document but it has not yet been implemented. ➔ PARTIALLY IMPLEMENTED (PI): The NRA has initiated implementation of this requirement but it has not been defined or followed for all staff or the roles and responsibilities documents, including staff job descriptions, are not up to date. ➔ IMPLEMENTED (I): The NRA has defined and established all required duties, functions, and responsibilities, and respective job descriptions are up-to-date.
Limitations and remarks:	Scoring this sub-indicator as "not applicable NA" is excluded (i.e. this sub-indicator will always apply for all benchmarked NRAs).
Sub Indicator:	**LT04.03: Training plan developed, implemented and updated at least once a year for staff in charge of laboratory testing activities.**
Maturity Level:	3
Scope:	1. Medicines 2. Vaccines
Description:	The assessor should verify that training plans are developed, implemented and updated at least once every year to reflect the current situation by considering education and experience of the staff. The training plan should be complemented with guidelines or similar documents that guide the development and implementation of training plans. The assessor should ensure that induction training for new staff as well as continued on- the-job training for staff is planned and implemented. There should be procedures to approve the training plan and the budget allocated for implementing and updating the training plan. The plans should present clearly defined training goals and should include training in certain topics and skills to address identified deficiencies. Learning objectives, training methods and activities, evidence of learning, and evaluation and assessment of training should be documented. This documentation should confirm that the learning objectives were achieved and were designed to address weaknesses within the entities. Procedures should be in place to ensure that a training plan is developed, implemented and updated at least once every year. The assessor should verify that there is a system in place for monitoring the implementation and effectiveness of the training plan and for documenting the skills acquired in training activities for internal and external experts.
Objective:	The objective of this sub-indicator is to ensure that a training plan for staff exists, and that it is implemented and updated annually. Through the training plan, NRA can be sure that competency of staff in charge of laboratory testing activities is maintained and enhanced.
Requirement:	Implementation of training plan
Evidence to review:	The assessor should ask for and review: 1. Guidelines for development, implementation and annual update (i.e., at least once per year) of the training plan. Guidelines should also provide for a mechanism to measure effectiveness of training. 2. Documentation for the system or structures used to approve the training plan and to evaluate the adequacy of the budget allocated to the training activities. 3. The current or existing staff training plan (or matrix) for staff. The assessor should assess this in in relation to the respective individual job descriptions. 4. SOP for developing and maintaining the training plan. 5. Evidence that the NRA has investigated and identified training needs. 6. List of trainings performed. 7. Example records for training activities.
References:	1. Effective drug regulation: A multicountry study. Geneva: World Health Organization; 2002, (7), (http://apps.who.int/medicinedocs/pdf/s2300e/s2300e.pdf)

	2. Quality systems requirements for national good manufacturing practice inspectorates. In: WHO Expert Committee on Specifications for Pharmaceutical Preparations: thirty-sixth report. Geneva: World Health Organization; 2002: Annex 8 (WHO Technical Report Series, No. 902), (8), (http://apps.who.int/medicinedocs/documents/s22112en/s22112en.pdf)
Framework:	Process
Rating Scale:	➜ NOT IMPLEMENTED (NI): There is no systematic training program including training plan (or matrix). ➜ ONGOING IMPLEMENTATION (OI): The NRA has recently drafted or developed the training plan but there is no evidence of implementation. ➜ PARTIALLY IMPLEMENTED (PI): The NRA has developed and initiated the training plan implementation. However, the NRA has not fulfilled all required planned training or has been applying the plan for less than two years. ➜ IMPLEMENTED (I): The NRA has an updated training plan developed that is supported by adequate records to demonstrate effective plan implementation, including induction training for new staff and routine on-the-job training for recruited staff.
Limitations and remarks:	▪ Training plans must be updated regularly; ideally on an annual basis, but not less frequently that once every two years. ▪ Some regulatory functions may include many training activities that are not incorporated in the institutional training programme. Such training normally is offered by invitation. In this case, the assessor should recognize reports from non-routine laboratory testing relevant training not included in the NRA training plan. ▪ Scoring this sub-indicator as "not applicable NA" is excluded (i.e. this sub-indicator will always apply for all benchmarked NRAs).
Sub Indicator:	**LT04.04: The NRA generates and maintains records of staff training activities and training effectiveness verification.**
Maturity Level:	3
Scope:	1. Medicines 2. Vaccines
Description:	The assessor should verify that records of staff training that is performed or organized by the NRA are generated, maintained, regularly updated. This activity should be supported by guidelines that direct the NRA to generate and maintain records of staff training activities. Procedures should be in place to document and propose staff training needs and to allocate a budget for continuous staff capacity building and development. The assessor should check that there is an evaluation or assessment mechanism to verify the quality of learning and to confirm that learning objectives are achieved. Documentation should include an inventory (i.e., soft and/or hard) system that records all impactful and non-impactful trainings and identifies all staff members who participated. A system to measure or estimate impact of trainings should be established.
Objective:	The objective of this sub-indicator is to ensure that training organized by the NRA or responsible regulatory authority is adequately documented and that the training records are adequately maintained and kept. Staff training records are considered an integral part of staff file and are a tool for measuring and tracking staff competency, development and adequacy.
Requirement:	Training records
Evidence to review:	The assessor should ask for and review: 1. Guidelines or similar documents that guide the NRA to generate and maintain records of staff training activities; 2. Evaluations of training effectiveness; 3. The training inventory, and procedures for completing the inventory; 4. Examples of archived records of staff training, and procedures for the archiving system

References:	1. National drug regulatory legislation: guiding principles for small drug regulatory authorities. In: WHO Expert Committee on Specifications for Pharmaceutical Preparations: thirty-fifth report. Geneva: World Health Organization; 1999: Annex 8 (WHO Technical Report Series, No. 885), (1), (http://apps.who.int/medicinedocs/documents/s21964en/s21964en.pdf) 2. Quality management systems — Requirements. International Standard ISO 9001:2015 International Organization for Standardization, 2015, (4), (https://www.iso.org/iso-9001-quality-management.html) 3. Guiding principles for small national drug regulatory authorities. In: WHO Expert Committee on Specifications for Pharmaceutical Preparations: thirty-first report. Geneva: World Health Organization; 1990: Annex 6 (WHO Technical Report Series, No. 790), (5), (http://apps.who.int/medicinedocs/documents/s21964en/s21964en.pdf) 4. Effective drug regulation: A multicountry study. Geneva: World Health Organization; 2002, (7), (http://apps.who.int/medicinedocs/pdf/s2300e/s2300e.pdf)
Framework:	Output
Rating Scale:	➜ NOT IMPLEMENTED (NI): There is no evidence that the NRA generates and maintains records of staff training activities. ➜ ONGOING IMPLEMENTATION (OI): The NRA has recently initiated plans to generate, document and keep records of staff training activities, however they are not yet followed. ➜ PARTIALLY IMPLEMENTED (PI): The NRA has recently initiated plans to generate, document and keep records of staff training activities but they are not fully followed for all training activities or they have been established for less than two years. ➜ IMPLEMENTED (I): The NRA generates and maintains records of staff training activities.
Limitations and remarks:	▪ The assessor should note that some NRAs out-source training including staff capacity development activities. In this case the assessor should request the identity of the provider, as well as evaluations of the provider. The assessor may request the professional profiles of tutors or resource persons used to offer training. The assessor may also request records covering the archiving systems in place. ▪ Scoring this sub-indicator as "not applicable NA" is excluded (i.e. this sub-indicator will always apply for all benchmarked NRAs).
Indicator:	**LT05 Well maintained and equipped infrastructures for laboratory activities.**
Objective:	The objective of this indicator is to confirm that buildings and equipment fulfill quality and technical requirements in order to enable adequate performance of the quality testing in the laboratories. For some tests, specific requirements for rooms might be necessary to achieve reliable results.
Category:	06. Resources (HR, FR, infrastructure and equipment)
Sub Indicator:	**LT05.01: Laboratory facilities are adequate to perform quality testing activities.**
Maturity Level:	3
Scope:	1. Medicines 2. Vaccines
Description:	The assessor should review the appropriateness and the adequacy of facilities for performing the laboratory testing and other NCL-related activities. The assessor should specifically evaluate and check the adequacy of the laboratory premises, the work environment and the work space.
Objective:	The objective of this sub-indicator is to confirm the adequacy of laboratory facilities for contributing to effectiveness and reliability of quality testing at the NCL.

Requirement:	Adequate facilities
Evidence to review:	The assessor should ask for and review: 1. Evidence for the adequacy of the laboratory premises and facilities, including the work environment and work space; 2. Evidence for the adequacy of the layout of the laboratory premises; 3. Evidence that the assigned biosafety level for the laboratory work is in accordance with WHO recommendations (when applicable).
References:	1. General requirements for the competence of testing and calibration laboratories, ISO ISO/IEC 17025:2015 International Organization for Standardization, 2015, (33), (https://www.iso.org/standard/66912.html) 2. WHO good manufacturing practices for pharmaceutical products: main principles, (51), (http://digicollection.org/whoqapharm/p/about and http://apps.who.int/medicinedocs/en) 3. Quality management systems — Requirements. International Standard ISO 9001:2015 International Organization for Standardization, 2015, (4), (https://www.iso.org/iso-9001-quality-management.html) 4. WHO good practices for pharmaceutical quality control laboratories, (35), (http://digicollection.org/whoqapharm/p/about and http://apps.who.int/medicinedocs/en) 5. WHO good practices for pharmaceutical microbiology laboratories, (34), (http://digicollection.org/whoqapharm/p/about and http://apps.who.int/medicinedocs/en) 6. Laboratory Biosafety Manual, World Health Organization, (105), (https://www.who.int/csr/resources/publications/biosafety/WHO_CDS_CSR_LYO_2004_11/en/)
Framework:	Structure/Foundation/Input
Rating Scale:	➜ NOT IMPLEMENTED (NI): Laboratory facilities are not adequate for performing the targeted testing activities. ➜ ONGOING IMPLEMENTATION (OI): The NCL is planning to establish, qualify or upgrade the laboratory facilities in order to be adequate for performing the targeted testing activities, however no evidence of such plans exists. ➜ PARTIALLY IMPLEMENTED (PI): The NCL recently (less than a year ago) established or upgraded the laboratory facilities so it became adequate for performing the targeted testing activities. ➜ IMPLEMENTED (I): Laboratory facilities are adequate and are used for performing the targeted testing activities in a proficient manner.
Limitations and remarks:	Scoring this sub-indicator as "not applicable NA" is excluded (i.e. this sub-indicator will always apply for all benchmarked NRAs).
Sub Indicator:	**LT05.02: Equipment calibration, qualification and maintenance plans have been defined and implemented and records have been maintained.**
Maturity Level:	3
Scope:	1. Medicines 2. Vaccines
Description:	The assessor should identify the equipment and instruments used in the laboratory and confirm the existence of the relevant operation manuals and SOPs. The assessor should verify the calibration, qualification and maintenance status of laboratory equipment as well as plans and procedures for regular updates. In addition, the assessor should check the log books and records to verify that the equipment is being correctly calibrated, qualified and maintained.
Objective:	The objective of this sub- indicator is to ensure that calibrated, qualified and well-maintained laboratory equipment is available and contributes to the effectiveness and reliability of laboratory tests.
Requirement:	Calibration, qualification and maintenance of laboratory equipment.

Evidence to review:	The assessor should ask for and review: 1. List of laboratory equipment; 2. Operational manuals and SOPs for selected equipment; 3. Log books that record use of selected equipment; 4. Log books that record calibration and maintenance of selected equipment; 5. Plans and procedures for annual equipment calibration; 6. Plans and procedures for annual equipment maintenance; 7. Sample calibration certificates; 8. Sample maintenance records.
References:	1. WHO good practices for pharmaceutical quality control laboratories, (35), (http://digicollection.org/whoqapharm/p/about and http://apps.who.int/medicinedocs/en) 2. General requirements for the competence of testing and calibration laboratories, ISO ISO/IEC 17025:2015 International Organization for Standardization, 2015, (33), (https://www.iso.org/standard/66912.html) 3. WHO good manufacturing practices for pharmaceutical products: main principles, (51), (http://digicollection.org/whoqapharm/p/about and http://apps.who.int/medicinedocs/en)
Framework:	Structure/Foundation/Input
Rating Scale:	➜ NOT IMPLEMENTED (NI): There are no plans for equipment calibration, qualification and maintenance. ➜ ONGOING IMPLEMENTATION (OI): Although there are no approved documents, there is evidence that they are being prepared. ➜ PARTIALLY IMPLEMENTED (PI): Such documents were approved recently (e.g. less than one year ago). ➜ IMPLEMENTED (I): The NCL has up-to-date equipment calibration, qualification and maintenance plans and records, which were approved some time ago (at least one year ago), and there has already been a cycle of internal or external audits (with or without accreditation) or system review.
Limitations and remarks:	Scoring this sub-indicator as "not applicable NA" is excluded (i.e. this sub-indicator will always apply for all benchmarked NRAs).
Indicator:	**LT06 Procedures established and implemented to perform laboratory testing activities according to Quality Management System.**
Objective:	The objective of this indicator is to ensure that a management system is in place to ensure traceability of actions. Standard procedures are an essential element of overall good regulatory practices; importantly, they contribute to consistency, effectiveness and impartiality of the regulatory processes. Written documentation supporting the laboratory quality system should exist, and the regulatory testing laboratory should have procedures in place for the different laboratory testing activities performed. Procedures should be available for receipt, storage and handling of test samples (including retention samples); receipt, handling, and storage of test reagents and materials (including reference standards); performance of different quality tests; notification and issuance of test results; handling of out-of-specification results (including re-testing when necessary); and handling events of non-compliance with pre-set specifications. An auditing system (internal and external) should be established and implemented to assess the performance of the management system of the laboratory testing activities with the objective of promoting on-going improvement.
Category:	07. Regulatory process
Sub Indicator:	**LT06.01: There are procedures for receipt, handling, storage and retention of samples.**
Maturity Level:	3

Scope:	1. Medicines 2. Vaccines
Description:	The assessor should verify that written and enforced standard procedures exist for receipt, handling and storage of medical products samples received for testing. The assessor should evaluate whether special handling procedures (e.g., requirements for storage temperature (i.e., cool or frozen) and humidity or recommendations to protect from light) are considered when required. The assessor should, as well, verify that procedures are providing instructions for storage and handling of retention samples which may be required for re-testing or verification purposes. In addition, the assessor should verify the existence of an identification system to ensure traceability.
Objective:	The objective of this sub- indicator is to ensure that implemented procedures for ensuring traceability and consistency of laboratory testing activities are available.
Requirement:	Standard procedures for handling and retention of samples under testing.
Evidence to review:	The assessor should ask for and review: 1. Standard procedures for receipt, handling, storage and retention of samples received for quality testing. 2. Example records of the reviewed procedures. 3. In the case of biological testing samples, verify that procedures for sampling from the manufacturer are available. 4. Documentation for the identification system used in paper or electronic records to trace samples from receipt to its testing and storage.
References:	1. General requirements for the competence of testing and calibration laboratories, ISO ISO/IEC 17025:2015 International Organization for Standardization, 2015, (33), (https://www.iso.org/standard/66912.html) 2. WHO good practices for pharmaceutical quality control laboratories, (35), (http://digicollection.org/whoqapharm/p/about and http://apps.who.int/medicinedocs/en) 3. WHO good manufacturing practices for pharmaceutical products: main principles, (51), (http://digicollection.org/whoqapharm/p/about and http://apps.who.int/medicinedocs/en)
Framework:	Process
Rating Scale:	➜ NOT IMPLEMENTED (NI): There are no documents for receipt, handling, storage or retention of samples. ➜ ONGOING IMPLEMENTATION (OI): Although there are no approved documents, there is evidence that they are being prepared. ➜ PARTIALLY IMPLEMENTED (PI): Such documents were approved recently (e.g. less than one year ago). ➜ IMPLEMENTED (I): The NCL has all the essential documents, which were approved some time ago (at least one year ago), and there has already been a cycle of internal or external audits (with or without accreditation) or system review.
Limitations and remarks:	▪ Samples may come from market surveillance or directly from manufacturers. ▪ Scoring this sub-indicator as "not applicable NA" is excluded (i.e. this sub-indicator will always apply for all benchmarked NRAs).
Sub Indicator:	**LT06.02: There are documented procedures for performing tests in accordance with MA documentation.**
Maturity Level:	3
Scope:	1. Medicines 2. Vaccines
Description:	The assessor should verify that documented procedures for testing are in accordance with the MA. The assessor should review the procedures by which the NCL staff has access to

	the MA. Ideally, the NCL staff should be involved in the MA evaluation process (at least with respect to information on pharmaceutical quality).
Objective:	The objective of this sub- indicator is to ensure that standard procedures for performing tests are in accordance with the MA in order to ensure consistency of laboratory testing activities.
Requirement:	Standard procedures for testing of medical products as per their MA documentation.
Evidence to review:	The assessor should ask for and review: 1. List of SOPs for testing of different medical products; 2. Examples of SOPs for quality testing of selected medical products; 3. Examples of records for testing done according to the SOPs reviewed in item #2 above; 4. Documented evidence that the NCL has access to the QC part of the MA (i.e., when the NCL is part of the NRA); 5. When testing activities are sub-contracted, the contract should reflect that the NCL should have access to the QC part of the MA (including updates), or a verified copy of the QC part of the MA.
References:	1. WHO good practices for pharmaceutical quality control laboratories, (35), (http://digicollection.org/whoqapharm/p/about and http://apps.who.int/medicinedocs/en)
Framework:	Process
Rating Scale:	➔ NOT IMPLEMENTED (NI): There is no documented evidence that tests are performed in accordance with MA documentation. ➔ ONGOING IMPLEMENTATION (OI): Although there are no approved documents, there is evidence that they are being prepared. ➔ PARTIALLY IMPLEMENTED (PI): Such documents were approved recently (e.g. less than one year ago). ➔ IMPLEMENTED (I): Procedures and records for performing tests in accordance with MA documentation were implemented some time ago (at least one year ago), and there has already been a cycle of internal or external audits (with or without accreditation) or system review.
Limitations and remarks:	▪ The methods approved in the MA application should ideally be used by the NCL. If not, the assessor should review the NCL justification for deviation from the MA approved testing methods along with the NCL procedure to handle this situation. If the method approved in the MA application is not routinely followed by the NCL because of some limitations in terms of technology or resources or for some other reason, the method included in the MA application should be determinative in the event of OOS test results. This is not only for technical and scientific reasons but also for legislative reasons. ▪ Scoring this sub-indicator as "not applicable NA" is excluded (i.e. this sub-indicator will always apply for all benchmarked NRAs).
Sub Indicator:	**LT06.03: A documented procedure is implemented for notification of test results and for ensuring that test results are issued following a standardized format.**
Maturity Level:	3
Scope:	1. Medicines 2. Vaccines
Description:	The assessor should verify that the NCL has established and implemented standard procedures for notifying interested parties (e.g., the manufacturer, the MA holder, and, when necessary, the inspectorate) of the test results. When the NCL is not part of the NRA, the test results should be forwarded to the NRA. Such procedures should provide guidance on issuing the test results in a standardized format containing the information needed to identify the sample, the testing laboratory, the applicant or other source of the sample, the type of tests conducted, the procedures applied, and the relevant specifications.

Objective:	The objective of this sub- indicator is to ensure the implementation of standard procedures for notification of test results and for issuing test results following a standardized format. These procedures will ensure consistency of laboratory testing activities.
Requirement:	Standard procedures for following a standardized format for laboratory test results.
Evidence to review:	The assessor should ask for and review: 1. Standard procedures for notification and issuance of test results; 2. List of issued test results within a specified time (e.g., last year); 3. Documentation of examples of decision-making process; 4. Examples of issued test results; 5. Examples of records showing implementation of the reviewed procedures; 6. Examples of test results forwarded to the NRA when the NCL is not part of the NRA.
References:	1. Model certificate of analysis, World Health Organization (WHO), (102), (http://digicollection.org/whoqapharm/p/about and http://apps.who.int/medicinedocs/en) 2. WHO good practices for pharmaceutical quality control laboratories, (35), (http://digicollection.org/whoqapharm/p/about and http://apps.who.int/medicinedocs/en)
Framework:	Process
Rating Scale:	➜ NOT IMPLEMENTED (NI): There is no documented evidence for a procedure for notification of test results or for ensuring that test results are issued following standardized format. ➜ ONGOING IMPLEMENTATION (OI): Although there are no approved documents, there is evidence that they are being prepared. ➜ PARTIALLY IMPLEMENTED (PI): Such documents were approved recently (e.g. less than one year ago). ➜ IMPLEMENTED (I): Procedures and records are in place for notification of test results and for ensuring that results are issued following standardized format.
Limitations and remarks:	Scoring this sub-indicator as "not applicable NA" is excluded (i.e. this sub-indicator will always apply for all benchmarked NRAs).
Sub Indicator:	**LT06.04: There are appropriate procedures for obtaining and handling of all materials required for testing.**
Maturity Level:	3
Scope:	1. Medicines 2. Vaccines
Description:	The assessor should verify the existence and implementation of standard procedures for procuring, receiving, storing and handling of all materials, including reference materials, required for quality testing. The procedures should ensure a regular and adequate supply of the required materials and standards. The assessor should verify that all reagents used in the NCL are of assured quality and labelled accordingly (e.g., preparation date, expiry date, specifications, storage conditions, and identity of tests in which they are used).
Objective:	The objective of this sub- indicator is to ensure the implementation of standard procedures for procuring and handling of all materials required for testing. These procedures will ensure consistency of laboratory testing activities.
Requirement:	Standard procedures for procuring and handling of materials required for laboratory testing.
Evidence to review:	The assessor should ask for and review: 1. Standard procedures for purchase, receipt, storage, handling, and use of all materials required for testing;

	2. Examples of records for the reviewed procedures; 3. List of materials required for different quality tests; 4. List of suppliers of materials required for testing.
References:	1. WHO good practices for pharmaceutical quality control laboratories, (35), (http://digicollection.org/whoqapharm/p/about and http://apps.who.int/medicinedocs/en) 2. General requirements for the competence of testing and calibration laboratories, ISO ISO/IEC 17025:2015 International Organization for Standardization, 2015, (33), (https://www.iso.org/standard/66912.html)
Framework:	Process
Rating Scale:	➜ NOT IMPLEMENTED (NI): There is no documented evidence of procedures for procuring and handling of all materials required for testing. ➜ ONGOING IMPLEMENTATION (OI): Although there are no approved documents, there is evidence that they are being prepared. ➜ PARTIALLY IMPLEMENTED (PI): Such documents were approved recently (e.g. less than one year ago). ➜ IMPLEMENTED (I): Documented procedures for procuring and handling of all materials required for testing are implemented some time ago.
Limitations and remarks:	Scoring this sub-indicator as "not applicable NA" is excluded (i.e. this sub-indicator will always apply for all benchmarked NRAs)
Sub Indicator:	**LT06.05: Staff has access to reference documents, including pharmacopoeias, textbooks and operational manuals.**
Maturity Level:	3
Scope:	1. Medicines 2. Vaccines
Description:	The assessor should verify that the laboratory staff has access to all documentation required for quality testing including, but not limited to, pharmacopoeias, textbooks, operational manuals, scientific publications, and publications of the WHO Technical Report Series. The assessor should also verify that the most updated version of each document is available.
Objective:	The objective of this sub- indicator is to ensure that staff has access to the documentation required for testing. Access to these documents will contribute to effective operations of the different laboratory activities.
Requirement:	Staff access to the necessary documentation for performing different laboratory activities.
Evidence to review:	The assessor should ask for and review: 1. Documentation of the information resources available to laboratory staff; 2. Evidence that current and updated versions are available to laboratory staff; 3. List of the scientific publications for which the NCL has subscriptions.; 4. Procedures describing access to documents and location.
References:	1. WHO good practices for pharmaceutical quality control laboratories, (35), (http://digicollection.org/whoqapharm/p/about and http://apps.who.int/medicinedocs/en) 2. Guidelines for EU Official Control Authority Batch Release, European Directorate for the Quality of Medicines and Healthcare (EDQM), Council of Europe, (104), (https://www.edqm.eu/en/human-ocabr-guidelines) 3. WHO Expert Committee on Biological Standardization (ECBS), Vaccine-specific standardization, (135), (https://www.who.int/biologicals/vaccines/en/)
Framework:	Process

Rating Scale:	➜ NOT IMPLEMENTED (NI): There are no documents establishing access to reference documents, including pharmacopoeias, textbooks and operational manuals. ➜ ONGOING IMPLEMENTATION (OI): Although there are no approved documents, there is evidence that they are being prepared. ➜ PARTIALLY IMPLEMENTED (PI): Such a document was approved recently (e.g. less than one year ago). ➜ IMPLEMENTED (I): The NCL has demonstrated access to the essential documents, and has had access for some time (at least one year), and there has already been a cycle of internal or external audits (with or without accreditation) or system review.
Limitations and remarks:	Scoring this sub-indicator as "not applicable NA" is excluded (i.e. this sub-indicator will always apply for all benchmarked NRAs).
Indicator:	**LT07 Mechanism exists to promote transparency, accountability and communication.**
Objective:	The objective of this indicator is to ensure that mechanisms are in place that promote effective communication of laboratory testing activities and related information within the NRA and NCL, that promote transparency and outreach to the public, and that establish milestones that encourage accountability of the NRA and NCL to its mandate. Additionally, these activities contribute to mutual understanding and involvement of all stakeholders relevant to laboratory testing activities. Consequently, confidence in the regulatory system is raised.
Category:	08. Transparency, accountability and communication
Sub Indicator:	**LT07.01: Laboratory testing activities are appropriately communicated to the public community.**
Maturity Level:	4
Scope:	1. Medicines 2. Vaccines
Description:	The assessor should verify that different laboratory testing activities and findings are appropriately communicated to the public community. This may be done through an annual report of the NCL or through other regular publications. In addition, the assessor should confirm that, when needed in the event of public health issues and concerns, immediate and rapid communications to the public community are done to inform them about the status of the issues of concern. Such communications will help avoid any misunderstandings.
Objective:	The objective of this sub- indicator is to ensure transparency to the pubic community. This transparency will contribute to accountability of the NRA and NCL, promote consistency in activities undertaken, and increase the public trust and confidence in the regulatory system.
Requirement:	Outreach and communication of laboratory testing activities to the public community.
Evidence to review:	The assessor should ask for and review: 1. Documentation of communication and any outreach to the public community regarding laboratory testing activities and findings. 2. Evidence for public communications from website
References:	1. Good regulatory practices: guidelines for national regulatory authorities for medical products, (112), (http://digicollection.org/whoqapharm/p/about and http://apps.who.int/medicinedocs/en)
Framework:	Output

Rating Scale:	➜ NOT IMPLEMENTED (NI): Laboratory testing activity reports are not publicly available. ➜ ONGOING IMPLEMENTATION (OI): The NRA established a procedure or mechanism by which laboratory testing activities could be publicly available, however, this is not yet implemented. ➜ PARTIALLY IMPLEMENTED (PI): There is evidence that the NRA has the elements (i.e., procedures, documentation, management systems, and other relevant information) and the capacity to perform the processes mentioned in the indicator; however, it has only limited experience or a limited number of documented events. ➜ IMPLEMENTED (I): Laboratory testing activity reports are regularly and consistently published and publicly available.
Limitations and remarks:	In some countries, these public communications may be done through the NRA. Scoring this sub-indicator as "not applicable NA" is excluded (i.e. this sub-indicator will always apply for all benchmarked NRAs).
Indicator:	**LT08 Mechanism in place to monitor regulatory performance and output.**
Objective:	The objective of this indicator is to ensure that mechanisms are in place to track regulatory effectiveness of laboratory testing activities, to measure relevant advancements in the programme, and to establish, implement and regularly verify performance indicators. The NRA or NCL should monitor and analyze laboratory results. These analyses are essential to monitor the quality of medical products for each specific product and manufacturer, to detect trends in non-compliance, and to detect shifts in results towards the specified upper or lower confidence limits.
Category:	09. Monitoring progress and assessing outcomes & impact
Sub Indicator:	**LT08.01: There is an updated database of all medical products batches that have undergone quality testing.**
Maturity Level:	4
Scope:	1. Medicines 2. Vaccines
Description:	The assessor should verify that a database (electronic or paper based) of all medical products batches tested is established and maintained. The database should include comprehensive information about these medical products batches including name, batch number, manufacturer, tests conducted, test results, and any other relevant information.
Objective:	The objective of this sub- indicator is to ensure the establishment of a database (electronic or paper based) of all medical products batches that have undergone quality testing by the NCL. This database is essential for storing, consolidating and analyzing information for these batches, including test results and test details (e.g., methods, analysts, reagents, and equipment). Thus, tracing of relevant regulatory testing activities and decisions for the sake of institutional memory is ensured. Furthermore, analyses of the data would contribute to optimization of regulatory performance.
Requirement:	An updated database of medical products batches tested for quality by the NCL.
Evidence to review:	The assessor should ask for and review: 1. Database (electronic and/or paper based) of medical products batches tested for quality by the NCL.
References:	1. WHO good practices for pharmaceutical quality control laboratories, (35), (http://digicollection.org/whoqapharm/p/about and http://apps.who.int/medicinedocs/en) 2. General requirements for the competence of testing and calibration laboratories, ISO ISO/IEC 17025:2015 International Organization for Standardization, 2015, (33), (https://www.iso.org/standard/66912.html)

	3. WHO good manufacturing practices for pharmaceutical products: main principles, (51), (http://digicollection.org/whoqapharm/p/about and http://apps.who.int/medicinedocs/en)
Framework:	Output
Rating Scale:	➜ NOT IMPLEMENTED (NI): There are no updated databases of all medical products batches that have undergone quality testing. ➜ ONGOING IMPLEMENTATION (OI): Although there are no databases, there is evidence that they are being prepared. ➜ PARTIALLY IMPLEMENTED (PI): Such databases were established recently (e.g. less than one year ago). ➜ IMPLEMENTED (I): The NCL has updated databases, which were established some time ago (at least one year ago), and there has already been a cycle of internal or external audits (with or without accreditation) or system review.
Limitations and remarks:	Scoring this sub-indicator as "not applicable NA" is excluded (i.e. this sub-indicator will always apply for all benchmarked NRAs).
Sub Indicator:	**LT08.02: Monitoring and trend analyses are carried out for laboratory testing results data of reference materials and medical products.**
Maturity Level:	3
Scope:	1. Medicines 2. Vaccines
Description:	The assessor should verify that quality of all reference materials and working standards that are used in routine testing are under control through use of control charts, and also that they are regularly monitored through periodic testing against established references (e.g. international, regional or national standards). Test results of the laboratory should be monitored using trend analyses to identify any trends (positive or negative) or deviations from their mean values. When required, confidence intervals could be reconsidered. When necessary, new replacement reference materials may be required when trend analyses reveal a problem with a current reference. The assessor should check the knowledge and understanding of the laboratory staff of basic statistical concepts and inference including, for example, the theory of probability and methods for detection of data trends.
Objective:	The objective of this sub- indicator is to ensure reliability and consistency of laboratory testing activities. Performance of reference materials should be monitored, and their test results should be evaluated using trend analyses. Laboratory test results of medical products should also be monitored using trend analyses.
Requirement:	Monitoring and trend analyses of laboratory result data of reference materials and medical products.
Evidence to review:	The assessor should ask for and review: 1. List of reference materials; 2. Documentation of periodic quality testing of selected reference materials; 3. Documentation of trend analyses of selected reference materials; 4. Documentation of trend analyses of medical products laboratory results.
References:	General requirements for the competence of testing and calibration laboratories, ISO ISO/IEC 17025:2015 International Organization for Standardization, 2015, (33), (https://www.iso.org/standard/66912.html)1
Framework:	Process
Rating Scale:	➜ NOT IMPLEMENTED (NI): There are no monitoring and trend analyses of laboratory testing data of reference materials and medical products.

	➜ ONGOING IMPLEMENTATION (OI): Although there are no monitoring and trend analyses of laboratory testing data of reference materials and medical products, the NCL is taking some actions to develop and formalize these procedures. ➜ PARTIALLY IMPLEMENTED (PI): There are monitoring and trend analyses of laboratory testing data of reference materials and medical products however these are recently implemented (e.g., less than two years ago). ➜ IMPLEMENTED (I): There are monitoring and trend analyses of laboratory testing data of reference materials and medical products, and these have been consistently implemented over a relatively long period of time (e.g. more than two years).
Limitations and remarks:	
Sub Indicator:	**LT08.03: Regular participation in proficiency schemes, collaborative studies and inter-laboratory comparisons.**
Maturity Level:	4
Scope:	1. Medicines 2. Vaccines
Description:	The assessor should verify that the technical competency of the NCL is periodically monitored to confirm consistency and reliability of test results. The monitoring may be conducted in various ways, including: performance evaluation systems, collaborative studies, and inter-laboratory comparisons. The assessor should verify that the NCL participates in proficiency schemes or collaborative studies organized by WHO, the European Directorate for the Quality of Medicines and HealthCare, the National Institute for Biological Standards and Control, or other institutions. Participation allows the NCL to compare its own performance to an international benchmark. The assessor should check dates of participation, scope of study, the product tested, and coordinating institution. In addition, the assessor should ascertain the number of collaborative studies in which laboratory participated, the specific tests evaluated, and whether or not the NCL had appropriate performance.
Objective:	The objective of this sub- indicator is to ensure that NCL participation in proficiency schemes, collaborative studies and inter-laboratory comparisons contributes to regulatory harmonization and networking. These, in turn, lead to improvements in the effectiveness and efficiency of the regulatory function.
Requirement:	Participation in proficiency schemes, collaborative studies and inter-laboratory comparisons.
Evidence to review:	The assessor should ask for and review: 1. Records of participation in proficiency schemes, collaborative studies and inter-laboratory comparisons. 2. Records of performance during participation in proficiency schemes, collaborative studies and inter- laboratory comparisons.
References:	1. WHO good practices for pharmaceutical quality control laboratories, (35), (http://digicollection.org/whoqapharm/p/about and http://apps.who.int/medicinedocs/en) 2. General requirements for the competence of testing and calibration laboratories, ISO ISO/IEC 17025:2015 International Organization for Standardization, 2015, (33), (https://www.iso.org/standard/66912.html) 3. WHO good manufacturing practices for pharmaceutical products: main principles, (51), (http://digicollection.org/whoqapharm/p/about and http://apps.who.int/medicinedocs/en)
Framework:	Output
Rating Scale:	➜ NOT IMPLEMENTED (NI): There are no documents establishing regular participation in international proficiency schemes, collaborative studies and inter-laboratory comparisons.

	➔ ONGOING IMPLEMENTATION (OI): At least some monitoring has been done with results that warrant actions for improvement. ➔ PARTIALLY IMPLEMENTED (PI): At least some monitoring has been done with acceptable results. Or, if there are decentralized activities, most of the laboratories involved have demonstrated acceptable results in at least one evaluation. ➔ IMPLEMENTED (I): Laboratory has participated in several studies to monitor performance. For these studies, acceptable results were obtained, demonstrating the technical competency of the NCL (including all laboratories when the activities are decentralized).
Limitations and remarks:	▪ When results from participation in proficiency studies are not satisfactory the NCL should show evidence of corrective actions and preventive actions. ▪ Scoring this sub-indicator as "not applicable NA" is excluded (i.e. this sub-indicator will always apply for all benchmarked NRAs).
Sub Indicator:	**LT08.04: Performance indicators for laboratory testing activities are established and implemented.**
Maturity Level:	4
Scope:	1. Medicines 2. Vaccines
Description:	The assessor should verify the existence and implementation of performance indicators for different activities included under the laboratory testing functions. Specifically, the system should define key performance indicators (KPIs) along the entire laboratory testing activity chain and all indicators should be adequately justified. For the purpose of clarity and consistency, established KPIs should be supported with guidelines for monitoring and maintenance of the KPIs. The guidelines in turn should be supported by SOPs and tools that define the procedures to be used for monitoring and evaluating the performance indicators and that define procedures and timelines for reviewing and revising the indicators. Examples of performance indicators for activities included under the laboratory access and testing function include, but are not limited to: number of product batches tested, number of tests performed, number of non-compliant events, mean time for performing different quality tests, and other relevant parameters. Established KPIs might be qualitative, quantitative or combination of both. In general, quantitative indicators are preferred to avoid bias or misinterpretation. However, qualitative indicators are also accepted. Qualitative indicators may or may not include scoring or scaling to render them semi-quantitative and thus more informative. The assessor should ensure that indicators are measured on a regular basis to monitor progress and advancement. ¨ In addition, the assessor should verify measured indicators are analyzed to identify trends or abnormalities. Justifications for any identified abnormalities should be provided; when necessary, process optimizations should be introduced to avoid recurrence.
Objective:	The objective of this sub-indicator is to ensure that a system, mechanism, or procedure exists to require the NRA to establish performance indicators along the entire laboratory testing chain. Additionally, the objective is to ensure that KPIs are actually contributing to monitoring of regulatory performance, to measuring effectiveness of laboratory testing regulatory activities, and to making any necessary adjustments or optimizations.
Requirement:	KPIs for laboratory testing activities
Evidence to review:	The assessor should ask for and review: 1. Documents supporting the system, mechanism, or procedure compelling the NRA to establish and implement performance indicators along the entire laboratory testing activity chain. 2. Evidence that the performance indicators have been established and implemented,

	and that the members of staff involved in the laboratory testing function are aware of the indicators and the guidelines and SOPs used for monitoring and evaluating their performance. 3. The current performance indicators for laboratory testing activities 4. Analyses of the measured indicators along with the investigations done to identify trends or abnormalities. 5. Documentation for follow-up of any observed abnormalities, including justifications for any identified abnormalities as well as any process optimizations introduced to avoid recurrence.
References:	1. Quality management -- Quality of an organization -- Guidance to achieve sustained success, ISO 9004:2018, International Organization for Standardization (ISO), (115), (https://www.iso.org/standard/70397.html)
Framework:	Output
Rating Scale:	➔ NOT IMPLEMENTED (NI): There are no KPIs for laboratory testing activities. ➔ ONGOING IMPLEMENTATION (OI): The NRA has recently drafted KPIs for laboratory testing activities but they have not yet been reported. ➔ PARTIALLY IMPLEMENTED (PI): The NRA has developed KPIs for laboratory testing activities and has been applying them for less than two year or they have not covered all critical steps. ➔ IMPLEMENTED (I): The NRA has established and implemented KPIs for laboratory testing activities. The indicators are reviewed regularly, and appropriate actions are taken, and decisions made.
Limitations and remarks:	▪ When they refer to outcomes, indicators may be ambiguous and difficult to interpret, as outcomes are the result of many factors that are difficult to disentangle. When they refer to processes, indicators are often too specific, as they may focus on a particular intervention or condition or they may quickly become outdated as business models develop. Different methodologies are used to measure the NRAs performance on laboratory testing activities. In this case, the assessor should verify that adequate supporting documents are available. The assessor should consider that developed performance indicators should be Specific, Measurable, Achievable, Realistic, and Time- bound (i.e., "SMART"). ▪ Scoring this sub-indicator as "not applicable NA" is excluded (i.e. this sub-indicator will always apply for all benchmarked NRAs).
Indicator:	**LT09 Measures for occupational health and safety.**
Objective:	The objective of this indicator is to ensure that safety issues to protect staff and the environment are considered of critical importance. Laboratory work is linked to specific risks because of the use of chemical, radiological and biological materials.
Category:	03. Policy and strategic planning
Sub Indicator:	**LT09.01: A laboratory hazardous substances list exists and documented procedures for storage, handling and disposal of these substances are implemented.**
Maturity Level:	3
Scope:	1. Medicines 2. Vaccines
Description:	The assessor should verify that lists of hazardous substances used in the laboratories are available. In addition, the assessor should determine if standard procedures for storing, labelling, handling and disposal of hazardous substances are available and implemented.

Objective:	The objective of this sub- indicator is to ensure that hazardous laboratory substances are carefully handled and adversely affect neither the health of the laboratory staff nor the environment.
Requirement:	List of hazardous substances and standard procedures for handling them.
Evidence to review:	The assessor should ask for and review: 1. List of hazardous substances used in the laboratory; 2. Standard procedures for the storage, handling and disposal for hazardous substances used in the laboratory; 3. Standard procedures for waste management and final disposal according national regulations; 4. Examples of records for each of the reviewed procedures.
References:	1. WHO good practices for pharmaceutical quality control laboratories, (35), (http://digicollection.org/whoqapharm/p/about and http://apps.who.int/medicinedocs/en) 2. WHO good manufacturing practices for pharmaceutical products: main principles, (51), (http://digicollection.org/whoqapharm/p/about and http://apps.who.int/medicinedocs/en) 3. Environmental management systems -- Requirements with guidance for use, ISO 14001:2015, International Organization for Standardization (ISO), (108), (https://www.iso.org/standard/60857.html)
Framework:	Process
Rating Scale:	➜ NOT IMPLEMENTED (NI): There is no list of hazardous substances used in the laboratory and no documented procedure for storage, handling and disposal of these substances. ➜ ONGOING IMPLEMENTATION (OI): Although there are no approved documents, there is evidence that they are being prepared. ➜ PARTIALLY IMPLEMENTED (PI): Such documents were approved recently (e.g. less than one year ago). ➜ IMPLEMENTED (I): The NCL has a list of laboratory hazardous substances used in the laboratory and documented procedures for storage, handling and disposal of these substances. These have been in place for at least one year, and there has already been a cycle of internal or external audits (with or without accreditation) or system review.
Limitations and remarks:	Scoring this sub-indicator as "not applicable NA" is excluded (i.e. this sub-indicator will always apply for all benchmarked NRAs).
Sub Indicator:	**LT09.02: A laboratory safety programme exists and a designated person is responsible for its management.**
Maturity Level:	4
Scope:	1. Medicines 2. Vaccines
Description:	The assessor should confirm that a laboratory safety programme is established and that a staff member (or a group of staff members) is responsible for managing all aspects within that safety programme. The programme should provide comprehensive guidance with general and specific instructions on occupational safety in the laboratory. Specific attention should be given to protection from microbiological materials such as live bacteria and viruses. In addition, the assessor should confirm that the laboratory safety programme is well communicated to all laboratory staff.
Objective:	The objective of this sub- indicator is to ensure that a laboratory safety programme exists. Hazardous laboratory activities should adversely affect neither the environment nor the health of the laboratory staff.

Requirement:	Establishment of a laboratory safety programme and designation of qualified staff for its management
Evidence to review:	The assessor should ask for and review: 1. Policies and procedures for the laboratory safety programme; 2. Evidence that staff has been designated to manage the laboratory safety programme; 3. Examples of documented communications of the laboratory safety programme to all laboratory staff; 4. Examples of laboratory staff training records covering the handling of hazardous substances and spills, and the protection of staff from exposure to chemical substances.
References:	
Framework:	Structure/Foundation/Input
Rating Scale:	➜ NOT IMPLEMENTED (NI): There is no laboratory safety programme. ➜ ONGOING IMPLEMENTATION (OI): Although there are no approved documents, there is evidence that they are being prepared. ➜ PARTIALLY IMPLEMENTED (PI): Such documents were approved recently (e.g. less than one year ago). ➜ IMPLEMENTED (I): The NCL has a laboratory safety programme, which was approved and implemented some time ago (at least one year ago), and there has already been a cycle of internal or external audits (with or without accreditation) or system review.
Limitations and remarks:	Scoring this sub-indicator as "not applicable NA" is excluded (i.e. this sub-indicator will always apply for all benchmarked NRAs).
Sub Indicator:	**LT09.03: Staff immunization requirements are defined, implemented and monitored.**
Maturity Level:	4
Scope:	1. Medicines 2. Vaccines
Description:	The assessor should verify that immunization programs for laboratory staff are defined, implemented and monitored. Staff compliance with the predefined immunization requirements should be verified prior to permitting access to designated work areas or use of designated equipment.
Objective:	The objective of this sub- indicator is to ensure that requirements for staff immunization are defined, implemented and monitored.
Requirement:	Laboratory staff immunization programme is established, implemented and monitored.
Evidence to review:	The assessor should ask for and review: 1. Immunization requirements, if any, for staff from different laboratory work areas 2. Examples of health records for selected staff; 3. Documentation of regular monitoring of staff immunization programme; 4. Examples of antibody titer measurement records for selected staff.
References:	1. WHO good practices for pharmaceutical quality control laboratories, (35), (http://digicollection.org/whoqapharm/p/about and http://apps.who.int/medicinedocs/en) 2. General requirements for the competence of testing and calibration laboratories, ISO ISO/IEC 17025:2015 International Organization for Standardization, 2015, (33), (https://www.iso.org/standard/66912.html)
Framework:	Structure/Foundation/Input

Rating Scale:	➜ NOT IMPLEMENTED (NI): There are no defined staff immunization requirements. ➜ ONGOING IMPLEMENTATION (OI): Although there are no defined requirements, there is evidence that they are being prepared. ➜ PARTIALLY IMPLEMENTED (PI): Such requirements were approved recently (e.g. less than one year ago). ➜ IMPLEMENTED (I): The NCL has defined staff immunization requirements, and there is documented evidence for implementation and monitoring. The program has been in place for some time ago (at least one year), and there has already been a cycle of internal or external audits (with or without accreditation) or system review.
Limitations and remarks:	
Indicator:	**LT10 Measures for good management of outsourced laboratory activities.**
Objective:	The objective of this indicator is to ensure that an NRA or NCL that is outsourcing laboratory testing activities has the following processes in place: an established, formal evaluation process for identifying qualified laboratories; a decision-making process for issuing, renewing or rescinding contracts for laboratory services; established and implemented procedures for managing outsourced activities; and procedures for handling communication exchanges.
Category:	07. Regulatory process
Sub Indicator:	**LT10.01: Documented procedures are implemented for managing outsourced QC activities.**
Maturity Level:	3
Scope:	1. Medicines 2. Vaccines
Description:	The assessor should verify the existence and implementation of standard procedures for managing all outsourced testing activities. The assessor should check these procedures and confirm that they are providing comprehensive guidance on implementation and management of quality agreements between the NCL (i.e., contract giver) and the independent laboratory or organization (i.e., contract acceptor). In addition, the procedures should provide guidance on the selection of contract acceptor, on the pathways of communication with clear roles and responsibilities (e.g., sourcing of materials required for testing including reference materials) and on a programme for regular audits (internal or external) of the contract acceptor by the NCL. The assessor should verify that the information exchange is handled in a confidential manner and that a system is in place to ensure there are no conflicts of interest.
Objective:	The objective of this sub- indicator is to ensure that outsourcing and sub-contracting is well controlled by the responsible NRA in order to ensure reliability of the outsourced test results.
Requirement:	Standard procedures for managing outsourced testing activities.
Evidence to review:	The assessor should ask for and review: 1. Standard procedures for managing outsourced testing activities; 2. Documentation of quality audits (internal or external) and other evidence that demonstrates that defined criteria have been met before accepting the sub-contracting laboratory; 3. Quality agreements between the NCL and the independent laboratory or organization; 4. Evidence from quality audits (internal or external) that confirm the sub-contracting laboratory has a QMS in place; 5. Documents that demonstrate that confidentiality agreements and declarations of Interests have been signed;

	6. Examples of records of communication (including notifications) between both parties.
References:	1. WHO good practices for pharmaceutical quality control laboratories, (35), (http://digicollection.org/whoqapharm/p/about and http://apps.who.int/medicinedocs/en) 2. General requirements for the competence of testing and calibration laboratories, ISO ISO/IEC 17025:2015 International Organization for Standardization, 2015, (33), (https://www.iso.org/standard/66912.html)
Framework:	Process
Rating Scale:	➜ NOT IMPLEMENTED (NI): There are no documented procedures implemented for managing outsourced QC activities. ➜ ONGOING IMPLEMENTATION (OI): Although there are no approved documents, there is evidence that they are being prepared. ➜ PARTIALLY IMPLEMENTED (PI): Such documents were approved recently (e.g. less than one year ago). ➜ IMPLEMENTED (I): The NCL has implemented documented procedures for managing outsourced QC activities. These procedures were approved some time ago (at least one year ago), and there has already been a cycle of internal or external audits (with or without accreditation) or system review.
Limitations and remarks:	

08

Clinical Trials Oversight (CT): Indicators and Fact Sheets

WHO Global Benchmarking Tool (GBT) for Evaluation of National Regulatory System of Medical Products

08. Clinical Trials Oversight (CT): Indicators and Fact Sheets

Function:	08 — CLINICAL TRIALS OVERSIGHT (CT)
Description:	National Regulatory Authorities (NRAs) should have the legal mandate to authorize regulate and, if necessary, terminate clinical trials (CTs). The necessary requirements, guidelines, procedures and forms should be developed to be in line with country and region-specific guidelines as well as major international CT guidance including guidelines from the Declaration of Helsinki, the Nuremberg code, International Council on Harmonization, and World Health Organization Good Clinical Practices. CT oversight is aimed at protecting the safety and rights of humans participating in CTs, ensuring that trials are adequately designed to meet scientifically sound objectives, and preventing any potential fraud and falsification of data. NRAs are responsible at two stages for the critical evaluation of the documentation supporting clinical studies: when CTs are being proposed for authorization and when the results are submitted in an application for marketing authorization. CT protocols should be reviewed and approved by Independent Ethics Committees before the trial commences. A CT review committee should review the protocols and should have the authority, when necessary, to require protocol revisions. The CT review committee should be composed of members who have the appropriate medical and scientific knowledge, experience and skills and who are free of conflicts of interest. In order to ensure the quality and safety of investigational products, the investigational products should be manufactured in compliance with Good Manufacturing Practices for investigational medical products, and the supporting preclinical studies should be in compliance with Good Laboratory Practices. Additionally, the importation, storage, use, and/or destruction of investigational products should follow national requirements. Qualified and experienced inspectors should carry out on-site inspections of the CT sites to verify compliance with Good Clinical Practices, ethical principles and regulatory requirements, and to provide assurance of the quality and reliability of the data obtained. The oversight activities should be conducted with due concern for confidentiality. The legal provisions should allow the NRA to recognize and/or rely on relevant CT decisions, reports and information from other NRAs or from designated regional and international bodies. In special circumstances (e.g., for public health interest), the legal provisions should allow the NRA to elect not to follow the routine CT procedures. Transparency in the entire oversight process is fundamental to ensuring the safety of patients and to ensuring that no product with unacceptable benefit to risk balance will be made available to the public.
Indicator:	**CT01 Legal provisions, regulations and guidelines required to define regulatory framework of clinical trials oversight.**
Objective:	The objective of this indicator is to ensure that the NRA has the legal mandate to both authorize and suspend the implementation of CTs. Among other benefits, the mandate will ensure that regulations and guidelines are in place to protect the safety and rights of the subjects participating in a trial and to ensure that trials are adequately designed to meet scientifically sound objectives.
Category:	Legal provisions, regulations and guidelines

Sub Indicator:	**CT01.01: Legal provisions and regulations for clinical trials (CTs) oversight exist.**
Maturity Level:	1
Scope:	1. Medicines 2. Vaccines
Description:	The assessor should verify that the legal provisions and regulations for CTs oversight exist and are enacted and implemented. The legal provisions should clearly specify the entities with the mandate for CT oversight and the extent of the mandate for each entity. When more than one entity is involved, the provisions should specify the responsibilities shared among the entities. The assessor should verify that legal provisions and regulations that require National Regulatory Authority (NRA) authorization prior to initiation of clinical studies exist and are enacted and implemented. The assessor should check a representative sample of provided documentation to verify that acceptable procedures were followed. Examples include: 1. Review the mandate for on-site inspections that ensure the location is acceptable and that product quality is maintained during storage; 2. Review informed consent forms and investigator brochure to verify that information and documentation provided are following Good Clinical Practices (GCPs). The assessor should be guided by the existing law and regulation before applying the scoring.
Objective:	The objective of this sub-indicator is to ensure the existence of legal provisions and regulations that require that CTs be authorized by the NRA prior to initiation. The NRA should review the protocol and other relevant documentation to be sure safety of participants is considered and that all required aspects are conducted according to GCPs.
Requirement:	Legislation on CT oversight
Evidence to review:	The assessor should ask for and review: 1. Legal provisions and regulations that grant the NRA the legal mandate for CT oversight. 2. The sections in the law that define the extent and scope of the CT oversight mandate allocated to the NRA and other entities involved in CT-related activities. 3. Relevant sections of the law on CTs that stipulate that NRA authorization is required prior to initiating and conducting a clinical study. 4. The guidelines that define the format and content of protocol, the procedure for submission, and the timeframe for review of application.
References:	1. Regulation and licensing of biological products in countries with newly developing regulatory authorities. In: WHO Expert Committee on Biological Standardization: forty-fifth report. World Health Organization; 1995: Annex 1 (WHO Technical Report Series, No. 858), (3), (http://www.who.int/bloodproducts/publications/WHO_TRS_858_A1.pdf) 2. Guidelines for good clinical practice (GCP) for trials on pharmaceutical products, (40), (http://apps.who.int/medicinedocs/en)
Framework:	Structure/Foundation/Input
Rating Scale:	➜ NOT IMPLEMENTED (NI): There are no legal provisions or regulations for CTs oversight. ➜ ONGOING IMPLEMENTATION (OI): The NRA has recently drafted and adopted legal provisions for CTs oversight but they have not yet been followed. ➜ PARTIALLY IMPLEMENTED (PI): The NRA has legal provisions for conducting CTs oversight and has been applying it for less than two years. ➜ IMPLEMENTED (I): The NRA has legal provisions for conducting CTs oversight and has adequate documented evidence to support this.
Limitations and remarks:	Scoring this sub-indicator as "not applicable NA" is excluded (i.e. this sub-indicator will always apply for all benchmarked NRAs).

Sub Indicator:	**CT01.02: Legal provisions and regulations that stipulates that notification to the NRAand authorization from the NRA is required for any changes or variations (i.e., amendments) in the original protocol or in any relevant documents of the CT.**
Maturity Level:	2
Scope:	1. Medicines 2. Vaccines
Description:	The assessor should verify the existence, enactment, and implementation of legal provisions and regulations related to changes or variations to the original (approved) CT protocols. These provisions should state clearly that the NRA should be notified of any changes or variations to the original protocol, and that authorization from the NRA is required before the changes or variations (i.e., amendments) are implemented. The assessor should note that some protocol amendments may not require authorization from the NRA prior to implementation. Some changes may require a notification prior to or even after implementation, while others require NRA approval before implementation. The assessor should be guided by the existing laws and regulations before applying the scoring.
Objective:	The objective of this sub-indicator is to ensure that legal provisions and regulations require that the NRA should be notified of changes or variations (i.e., amendments) to the original protocol, and should authorize changes and variations to the original protocol before they are implemented.
Requirement:	Changes and variations to already approved (original) CT protocols
Evidence to review:	The assessor should ask for and review: 1. Relevant sections of the legal provisions (laws, decrees, regulations or any legal binding documents) on CTs with emphasis on the requirement for notification and authorization prior to implementation of changes or variations to original protocol and related documents. 2. The guidelines that specify the format and content of submissions related to changes or variations to original protocol, the procedure for submission, and the timeframe for review.
References:	1. WHO guidelines on nonclinical evaluation of vaccines, (39), (https://www.who.int/biologicals/WHO_ECBS/en/ and https://www.who.int/biologicals/vaccines/en/) 2. Guidelines for good clinical practice (GCP) for trials on pharmaceutical products, (40), (http://apps.who.int/medicinedocs/en) 3. Guidelines on clinical evaluation of vaccines: regulatory expectations, (38), (https://www.who.int/biologicals/WHO_ECBS/en/ and https://www.who.int/biologicals/vaccines/en/) 4. WHO guidelines on the nonclinical evaluation of vaccines adjuvants and adjuvanted vaccines, (119), (https://www.who.int/biologicals/WHO_ECBS/en/ and https://www.who.int/biologicals/vaccines/en/)
Framework:	Structure/Foundation/Input
Rating Scale:	➜ NOT IMPLEMENTED (NI): There are no legal provisions or regulations requiring notification to and authorization from the NRA when there are changes or variations (i.e., amendments) in the original protocol of the CT. ➜ ONGOING IMPLEMENTATION (OI): The NRA has recently drafted or adopted this legal provision but they have not yet been followed. ➜ PARTIALLY IMPLEMENTED (PI): The NRA has legal provision and has been applying it for less than two years. ➜ IMPLEMENTED (I): The NRA has legal provisions and regulations requiring notification to the NRA and authorization from NRA on changes or variations (i.e., amendments) in the original protocol of the CT; these amendments should be supported with documented evidence.
Limitations and remarks:	Scoring this sub-indicator as "not applicable NA" is excluded (i.e. this sub-indicator will always apply for all benchmarked NRAs).

Sub Indicator:	**CT01.03: Legal provisions and regulations requiring research centers, researchers, sponsors, clinical research organizations (CROs) and all relevant institutions in the CT to comply with GCP**
Maturity Level:	2
Scope:	1. Medicines 2. Vaccines
Description:	The assessor should verify the existence, enactment, and implementation of legal provisions and regulations that require stakeholders, including research centers, researchers, sponsors, CROs and everyone involved in CTs to comply with the principles of GCP. GCP is an international ethical and scientific quality standard for designing, conducting, recording and reporting trials that involve the participation of human participants. Compliance with this standard provides assurance that the rights, safety and well-being of trial subjects are protected consistent with the principles established in the Declaration of Helsinki, and that CT data are credible. The legal provisions should be supported by detailed and published regulatory requirements for GCP. The published GCP principles should be current and up to date with information on inspections and on suspension or stoppage of trials. When GCP is referenced or adopted, documentation should be available to demonstrate compliance. The assessor should verify that Ethics Committees (ECs) and the NRA consider GCP principles when conducting evaluations.
Objective:	The objective of this sub-indicator is to ensure the existence of legal provisions and regulations that mandates stakeholders, including research centers, researchers, sponsors, CROs and everyone involved in CTs to comply with GCP. These provisions will ensure all stakeholders, including research centers, researchers, sponsors, CROs and everyone involved CTs operate within a set of globally-accepted standards for the conduct of biomedical research on human participants.
Requirement:	Stakeholder acting in compliance with GCP
Evidence to review:	The assessor should ask for and review: 1. The legal provisions (laws, decrees, regulations or any legal binding document) that require stakeholders involved in CT to comply with GCP principles. 2. The current GCP requirements for all CTs. The GCP standards should be published and easily accessible. 3. Guidelines or similar documents (e.g., checklists and standard operating procedures (SOPs)) used to provide guidance in the application of the legal provisions and regulations.
References:	1. Guidelines for good clinical practice (GCP) for trials on pharmaceutical products, (40), (http://apps.who.int/medicinedocs/en) 2. Regulation and licensing of biological products in countries with newly developing regulatory authorities. In: WHO Expert Committee on Biological Standardization: forty-fifth report. World Health Organization; 1995: Annex 1 (WHO Technical Report Series, No. 858), (3), (http://www.who.int/bloodproducts/publications/WHO_TRS_858_A1.pdf) 3. Guidelines on clinical evaluation of vaccines: regulatory expectations, (38), (https://www.who.int/biologicals/WHO_ECBS/en/ and https://www.who.int/biologicals/vaccines/en/) 4. WHO guidelines on the nonclinical evaluation of vaccines adjuvants and adjuvanted vaccines, (119), (https://www.who.int/biologicals/WHO_ECBS/en/ and https://www.who.int/biologicals/vaccines/en/)
Framework:	Structure/Foundation/Input
Rating Scale:	➜ NOT IMPLEMENTED (NI): There are no legal provisions or regulations requiring research centers, researchers, sponsors, CROs and everyone involved in the CTs to comply with GCP ➜ ONGOING IMPLEMENTATION (OI): The NRA has recently drafted or adopted these legal

provisions and regulations but they have not yet been followed.
- ➔ PARTIALLY IMPLEMENTED (PI): The NRA has developed this legal provision and has been applying it for less than two years, or not all involved organizations have fully followed this regulation.
- ➔ IMPLEMENTED (I): The NRA has legal provisions and regulations requiring research centers, researchers, sponsors, CROs and everyone involved in CTs to comply with GCP; compliance is supported with documented evidence.

Limitations and remarks:	The assessor should consider that existing written documents are legally binding. Scoring this sub-indicator as "not applicable NA" is excluded (i.e. this sub-indicator will always apply for all benchmarked NRAs).
Sub Indicator:	**CT01.04: Legal provisions, regulations and guidelines requiring that investigational medical products (IMPs) comply with good manufacturing practices (GMP) for IMPs.**
Maturity Level:	3
Scope:	1. Medicines 2. Vaccines
Description:	The assessor should verify the existence, enactment, and implementation of legal provisions, regulations and guidelines that require that IMPs comply with the GMPs for IMPs. The legal provisions should clearly state that only IMPs produced in compliance with current GMP standards for IMPs will be used in CTs, and that the applicant or sponsor of the CT is responsible for supplying IMPs produced in accordance with GMP principles. The legal provisions should be supported by regulations or guidelines that clearly present the applicable GMP requirements and the type of supporting evidence to present (e.g., certificates and summary product release documents). The assessor should note that some NRAs may not require a GMP certificate if the IMP is already licensed or registered in the country of origin. However, according to good regulatory practices, a current GMP certificate from the NRA of the country of origin should be required when the IMP has a marketing authorization in the country of origin or has a marketing authorization, but the original indication is modified for the purpose of the trial.
Objective:	The objective of this sub-indicator is ensure the existence of legal provisions, regulations and guidelines that mandate that IMPs used in CTs comply with GMP requirements.
Requirement:	IMPs GMP requirements
Evidence to review:	The assessor should ask for and review: 1. The legal provisions (laws, decrees, regulations or any legal binding document) and guidelines requiring that IMPs used in CTs are produced in compliance with the principles of GMPs for IMPs. 2. The legal provisions, regulations and guidelines that state that it is the responsibility of the sponsors or applicants to supply IMPs produced in compliance with the principles of GMP for IMPs. 3. Documentation specifying the format for the IMP's GMP certificate that is required prior to CT authorization. The GMP certificate should be issued by the national competent authority of the country of origin of the IMP.
References:	1. WHO good manufacturing practices for pharmaceutical products: main principles, (51), (http://digicollection.org/whoqapharm/p/about and http://apps.who.int/medicinedocs/en) 2. Guidelines for good clinical practice (GCP) for trials on pharmaceutical products, (40), (http://apps.who.int/medicinedocs/en) 3. Good manufacturing practice: supplementary guidelines for the manufacture of investigational pharmaceutical products for clinical trials in humans, (120), (http://apps.who.int/medicinedocs/en)
Framework:	Structure/Foundation/Input

Rating Scale:	➜ NOT IMPLEMENTED (NI): There is no evidence of existence of legal provisions, regulations or guidelines requiring that IMPs comply with GMPs for IMPs. ➜ ONGOING IMPLEMENTATION (OI): The NRA has recently drafted or adopted these legal provisions, regulations and guidelines but they have not yet been implemented. ➜ PARTIALLY IMPLEMENTED (PI): The NRA has legal provisions, regulations and guidelines and has been applying them for less than two years. ➜ IMPLEMENTED (I): The NRA has legal provisions, regulations and guidelines requiring that IMPs comply with GMPs for IMPs.
Limitations and remarks:	Scoring this sub-indicator as "not applicable NA" is excluded (i.e. this sub-indicator will always apply for all benchmarked NRAs).
Sub Indicator:	**CT01.05: There are legal provisions or regulations covering circumstances in which the routine CT evaluation procedures may not be followed (e.g. for public-health interests).**
Maturity Level:	2
Scope:	1. Medicines 2. Vaccines
Description:	The assessor should verify the existence, enactment, and implementation of legal provisions or regulations that allow the NRA to apply non-routine CT procedures such as fast-track or expedited decision-making (e.g., receipt, screening, evaluation, review, and authorization) of a CT application under certain circumstances (e.g., public health emergencies). The legal provisions and regulations should provide clear directives on the circumstances under which the non-routine CT authorization should apply. The provisions should provide guidance on the relationship between the non-routine CT authorization and the mandate of the Independent Ethics Committee (IEC). The legal provisions should be supported with guidelines that describe the content (e.g., the critical requirements) and format of CT applications submitted for approval by the non- routine authorization procedure. This guidance should also describe the scope of the review and evaluation process (i.e., screening, verification, and other relevant activities). The supporting guidelines may provide clarity on whether a CT application rejected through the non-routine procedure could be re-submitted through the routine procedure. In addition, there should be a guidance document to provide direction to the NRA on how to justify application of the non-routine procedure to the CT. The assessor should verify that the proposed procedures meet targeted timeframes for public health emergencies or any other unmet medical needs.
Objective:	The objective of this sub-indicator is to ensure legal provisions and regulations are established to allow the NRA or responsible regulatory authority to apply non-routine CT procedures such as fast-track or expedited receipt, evaluation, and authorization of a CT application under certain circumstances (e.g. public health emergencies). This sub- indicator will establish whether there is an abridged route other than the normal CT application route for CT authorization.
Requirement:	Exemptions from routine CT application evaluation procedures
Evidence to review:	The assessor should ask for and review: 1. Guidelines or similar document that provides the list of situations in which the routine CT procedures may not be required. 2. Legal provisions (laws, decrees, regulations or any legal binding document) that cover circumstances or instances under which the non-routine CT procedures such fast-track CT authorization may be applied. Assessor should review evidence that the legal provisions are published and implemented. 3. The supporting guidelines and regulations. 4. Guidelines describing the content and format of CT applications requesting application of non-routine CT procedures such as fast-track. 5. Guidelines specifying the scope of the evaluation process (i.e., screening, verification, or other relevant activities).

References:	1. Guidelines for good clinical practice (GCP) for trials on pharmaceutical products, (40), (http://apps.who.int/medicinedocs/en) 2. Emergency Use Assessment and Listing Procedure (EUAL) for Candidate Medicines for use in the Context of a Public Health Emergency, (121), (http://apps.who.int/medicinedocs/en/) 3. Emergency Use Assessment and Listing Procedure (EUAL) for Candidate Vaccines for use in the Context of a Public Health Emergency, (122), (http://apps.who.int/medicinedocs/en/)
Framework:	Structure/Foundation/Input
Rating Scale:	➔ NOT IMPLEMENTED (NI): There are no legal provisions or regulations to cover circumstances under which the NRA may elect to follow the non-routine CT application process ➔ ONGOING IMPLEMENTATION (OI): The NRA has drafted or adopted these legal provisions or regulations, but they have not yet been followed. ➔ PARTIALLY IMPLEMENTED (PI): The NRA has legal provision or regulation and has been applying it for less than two years. ➔ IMPLEMENTED (I): The NRA has legal provisions or regulations to cover circumstances in which the NRA may elect to follow the non-routine CT application process (e.g., for public health interest).
Limitations and remarks:	The assessor should consider any kind of legal document that address this requirement.
Sub Indicator:	**CT01.06: Legal provisions, regulations or guidelines exist for NRA to inspect, suspend or stop CTs.**
Maturity Level:	3
Scope:	1. Medicines 2. Vaccines
Description:	The assessor should verify the existence, enactment, and implementation of legal provisions or regulations that give the NRA enforcement powers to inspect, suspend or stop CTs. The legal provisions should be supported with clear regulations or guidance on when (i.e., routine, random or for specific reasons) and how to inspect, suspend or stop a CT. Clear guidance on what to inspect (e.g., evidence supporting quality and reliability of data and reported results or records for subjects, equipment, protocols, and environment) should also be considered.
Objective:	The objective of this sub-indicator is to ensure legal provisions or regulations are established to give the NRA enforcement powers to inspect, suspend or stop CTs.
Requirement:	Legal provisions, regulations or guidelines to inspect, suspend or stop CTs
Evidence to review:	The assessor should ask for and review: 1. The legal provisions (laws, decrees, regulations or any legal binding document) that give the NRA the enforcement power to inspect, suspend or stop CTs. 2. Documents providing guidance on procedures to follow for inspecting, suspending or stopping CTs. 3. List of CTs inspected, suspended or stopped.
References:	1. Guidelines on clinical evaluation of vaccines: regulatory expectations, (38), (https://www.who.int/biologicals/WHO_ECBS/en/ and https://www.who.int/biologicals/vaccines/en/) 2. WHO guidelines on nonclinical evaluation of vaccines, (39), (https://www.who.int/biologicals/WHO_ECBS/en/ and https://www.who.int/biologicals/vaccines/en/) 3. Guidelines for good clinical practice (GCP) for trials on pharmaceutical products, (40), (http://apps.who.int/medicinedocs/en) 4. WHO guidelines on the nonclinical evaluation of vaccines adjuvants and adjuvanted vaccines, (119), (https://www.who.int/biologicals/WHO_ECBS/en/ and https://www.who.int/biologicals/vaccines/en/)

Framework:	Structure/Foundation/Input
Rating Scale:	➔ NOT IMPLEMENTED (NI): There are no legal provisions, regulations or guidelines for NRA to inspect, suspend or stop CT ➔ ONGOING IMPLEMENTATION (OI): The NRA has recently drafted or developed the regulations or guidelines, but these have not yet been followed. ➔ PARTIALLY IMPLEMENTED (PI): The NRA has legal provisions, regulations or guidelines and has been applying them for less than two years or the guidelines or regulations are not fully implemented for all CT applications. ➔ IMPLEMENTED (I): The NRA has legal provisions, regulations or guidelines to inspect, suspend or stop CTs and these are implemented and followed for all approved CT applications.
Limitations and remarks:	▪ If there is no CT ongoing, the assessor may score this sub-indicator as implemented by reviewing guidelines or other required documentation. ▪ Scoring this sub-indicator as "not applicable NA" is excluded (i.e. this sub-indicator will always apply for all benchmarked NRAs).
Sub Indicator:	**CT01.07: There are legal provisions or regulations that require the establishment of an IEC.**
Maturity Level:	2
Scope:	1. Medicines 2. Vaccines
Description:	The assessor should verify the existence, issuance, and implementation of regulations that require the establishment of an IEC. The regulations should be clear on the specific authority that should host the IEC and that should assist it to successfully discharge its duties and mandates. The legal provisions should provide guidance on what it means to be "independent", and also provide supporting regulations and guidelines that ensure that the independence of the IEC is sustained. The objectives, functions and composition of the IEC should be clearly defined and documented, and a general policy on potential conflicts of interest for IEC members should be provided. The assessor should note that there may be more than one legally established IEC in a country. The assessor should therefore verify the legal mandate of the IEC in question and the scope of its activities.
Objective:	The objective of this sub-indicator is to ensure regulations are in place requiring the establishment of an IEC to review the CTs. For each CT, the IEC should verify that safety, integrity, and human rights of participating subjects are protected. The IEC should consider the general ethics of the trials, and thereby promote public reassurance.
Requirement:	Establishment of IEC
Evidence to review:	The assessor should ask for and review: 1. Legal provisions (laws, decrees, regulations or any legal binding document) mandating the establishment of an IEC. 2. Documentation defining the identity of the designated authority that has the mandate to host the IEC and to assist the IEC in discharging its duties. 3. Documentation defining the selection criteria for the members of the IEC, the number of members on the IEC, and the term of office for each member. 4. Documentation defining the mechanisms and structures to ensure the independence of the IEC, and documentation providing the code of conduct for ICE members. 5. The policy on potential conflicts of interest for members of the IEC.
References:	1. Handbook for good clinical research practice (GCP): Guidance for Implementation, (41), (http://apps.who.int/medicinedocs/en) 2. Guidelines for good clinical practice (GCP) for trials on pharmaceutical products, (40), (http://apps.who.int/medicinedocs/en)

Framework:	Structure/Foundation/Input
Rating Scale:	➜ NOT IMPLEMENTED (NI): There are no legal provisions or regulations requiring the establishment of an IEC. ➜ ONGOING IMPLEMENTATION (OI): The legal provisions or regulations that require the establishment of an IEC have recently defined or drafted, but these have not yet been implemented. ➜ PARTIALLY IMPLEMENTED (PI): The legal provisions or regulations requiring the establishment of an IEC have been developed and the IEC has been established for less than two years. ➜ IMPLEMENTED (I): The NRA has legal provisions or regulations requiring the establishment of an IEC and the IEC is established.
Limitations and remarks:	Scoring this sub-indicator as "not applicable NA" is excluded (i.e. this sub-indicator will always apply for all benchmarked NRAs).
Sub Indicator:	**CT01.08: Legal provisions, regulations and guidelines that require authorization for the import or destruction of IMPs.**
Maturity Level:	2
Scope:	1. Medicines 2. Vaccines
Description:	The assessor should verify the existence, enactment, and implementation of legal provisions, regulations and guidelines requiring that the NRA authorize the import and destruction of IMPs. The legal provisions should be supported with regulations and guidelines that provide guidance on the permitted quantities to import. The assessor should note that the quantities to import or destroy should be justified in relation to the timelines for the CT and the use of the IMPs as specified in the CT protocol. The provisions should provide guidance on the import or destruction process, and define the roles and responsibilities of the various stakeholders, including the sponsor, principal investigator, and other participants. The guidelines should include: 1. Guidelines on the acceptable or allowable quantities of IMPs to import; 2. Guidelines on the appropriate destruction methods (i.e., by the NRA or supervised by the NRA); 3. Procedures for a feedback mechanism to inform the NRA on quantities left over after the CT. The guideline and application forms should be developed and easily available to the sponsor and other stakeholders. The processes and procedures to seek authorization for import or destruction should be published and easily available.
Objective:	The objective of this sub-indicator is to ensure the existence of legal provisions, regulations and guidelines that require the NRAs (or responsible regulatory authority) to authorize import and destruction of IMPs.
Requirement:	Legal provisions, regulations and guidelines to import and destroy IMPs
Evidence to review:	The assessor should ask for and review: 1. Legal provisions (laws, decrees, regulations or any legal binding document) and guidelines on the import and destruction of IMPs. The assessor should verify that IMPs imported for the purposes of CT application submissions require authorization. 2. The guidance documents and application forms for requesting assistance from the NRA to import or destroy IMPs, as well as guidance on the processes to be executed upon receipt of an application. 3. Records of IMPs imported or destroyed since the last NRA inspection. 4. Guidelines or similar documents providing guidance on the justifiable quantities of IMPs that should be imported relative to the timelines in the CT protocol. 5. Guidance defining the stage in the CT application process at which IMPs may be imported.

References:	1. Guidelines for good clinical practice (GCP) for trials on pharmaceutical products, (40), (http://apps.who.int/medicinedocs/en) 2. Guidelines on clinical evaluation of vaccines: regulatory expectations, (38), (https://www.who.int/biologicals/WHO_ECBS/en/ and https://www.who.int/biologicals/vaccines/en/) 3. WHO guidelines on nonclinical evaluation of vaccines, (39), (https://www.who.int/biologicals/WHO_ECBS/en/ and https://www.who.int/biologicals/vaccines/en/) 4. WHO guidelines on the nonclinical evaluation of vaccines adjuvants and adjuvanted vaccines, (119), (https://www.who.int/biologicals/WHO_ECBS/en/ and https://www.who.int/biologicals/vaccines/en/)
Framework:	Structure/Foundation/Input
Rating Scale:	➜ NOT IMPLEMENTED (NI): There are no legal provisions, regulations or guidelines that require authorization for the import and destruction of IMPs. ➜ ONGOING IMPLEMENTATION (OI): The legal provisions, regulations or guidelines that require authorization for the import, and destruction of IMPs exist, but these have not yet been implemented. ➜ PARTIALLY IMPLEMENTED (PI): The legal provisions, regulations or guidelines that require authorization for the import and destruction of IMPs have been established for less than two years. ➜ IMPLEMENTED (I): The NRA has legal provisions, regulations or guidelines that require authorization for the import and destruction of IMPs, and there is documented evidence that it is applied to all IMPs
Limitations and remarks:	Scoring this sub-indicator as "not applicable NA" is excluded (i.e. this sub-indicator will always apply for all benchmarked NRAs).
Sub Indicator:	**CT01.09: There are requirements for monitoring and reporting of adverse events and reactions during conduct of CT.**
Maturity Level:	2
Scope:	1. Medicines 2. Vaccines
Description:	The assessor should verify the existence and implementation of requirements for monitoring and reporting of adverse events and reactions. Such requirements should clearly provide guidance on monitoring of adverse reactions and on following up when they are observed. The guidance should provide clarity on the roles, responsibilities, and duties of all stakeholders, including the NRA. The guidance should also specify the exact requirements for monitoring during the period of the CT, including, for example, collection and evaluation of data and reporting of adverse reactions and events. The guidance should define the type, nature, and form of adverse reactions or events to report. In the event that reporting to more than one NRA, authority, or stakeholder (e.g., sponsor) is required, the sequence for reporting should be indicated. The guideline should be supported by a form for monitoring and reporting adverse reactions and events.
Objective:	The objective of this sub-indicator is to ensure the existence of requirements that mandate that investigators and sponsors monitor all subjects involved in CTs. The requirements should include an obligation to report, to the NRA or responsible regulatory authority, all adverse or serious adverse reactions and events within the approved time frame for reporting.
Requirement:	Monitoring and reporting adverse reactions and events
Evidence to review:	The assessor should ask for and review: 1. The guidelines and regulations on monitoring and reporting of adverse events and reactions, as well as the guidance on required follow up. The assessor should verify that the guidelines have been implemented.

	2. Documentation that specifies the exact roles, responsibilities, and duties of each stakeholder. These should be compared to World Health Organization (WHO) recommendations or other international standards. 3. The NRA recommendations to the sponsors and investigators on the procedures for monitoring and reporting of adverse events and reactions. The assessor should verify that the recommendations are in line with WHO or other international standards. 4. Documentation establishing the committee responsible for reviewing reports of adverse reactions and events, and documentation defining the composition of the committee and specialties of committee members. 5. Guidelines defining the timelines allocated for reporting adverse reactions and events on the part of the investigator or sponsor and timelines for generating and submitting a report on the adverse reaction or event to the NRA. 6. Examples of records of completed forms sent to the NRA. The assessor should verify that the format and content is in compliance with applicable guidelines.
References:	1. Handbook for good clinical research practice (GCP): Guidance for Implementation, (41), (http://apps.who.int/medicinedocs/en) 2. Guidelines for good clinical practice (GCP) for trials on pharmaceutical products, (40), (http://apps.who.int/medicinedocs/en)
Framework:	Structure/Foundation/Input
Rating Scale:	➔ NOT IMPLEMENTED (NI): There are no requirements or guidelines on monitoring and reporting of adverse events and reactions. ➔ ONGOING IMPLEMENTATION (OI): The requirements on monitoring and reporting of adverse events and reactions are drafted or defined, but these have not yet been followed. ➔ PARTIALLY IMPLEMENTED (PI): The requirements and guidance on monitoring and reporting of adverse events and reactions have been developed for less than two years or there are no reports from any CTs. ➔ IMPLEMENTED (I): The requirements and guidance on monitoring and reporting adverse events and reactions exist and all sponsors are following them.
Limitations and remarks:	▪ The assessor may score this sub-indicator as implemented if there are no records because there are no ongoing CT studies. ▪ The review of the reported adverse events and reactions can be conducted by internal staff if the NRA has access to adequate number of competent reviewers and experts. ▪ Scoring this sub-indicator as "not applicable NA" is excluded (i.e. this sub-indicator will always apply for all benchmarked NRAs).
Sub Indicator:	**CT01.10: There are guidelines on the format and content of CT applications.**
Maturity Level:	2
Scope:	1. Medicines 2. Vaccines
Description:	The assessor should verify that guidelines on the format and content of CT applications exist and are issued and implemented. The guidelines should provide clear guidance on the format and content (i.e., a list of required information and documents) of the CT application dossier to be submitted to the NRA. The content may include but is not limited to; 1. CT registration with a registry that is approved and recognized by the NRA; 2. covering letter addressed to head of the NRA; 3. completed CT application forms that should be signed and dated by authorized persons; 4. CT Protocol; 5. investigator's brochure; 6. investigational product dossier; 7. GMP certificate;

	8. evidence of approvals from EC and institutional review board; 9. evidence of insurance coverage (from a recognized insurance company); 10. statement or evidence of financial support and declaration of support; 11. data safety monitoring board membership and signed charter; 12. evidence of contractual agreement between sponsor and principal investigator; 13. sample of informed consent form; 14. assent forms (if applicable); 15. statistical analysis plan, if applicable; 16. professional profile (i.e., qualifications, experience, expertise, evidence of excellent knowledge of local CT regulatory requirements, and list of previous CTs managed) for potential principal investigator, study pharmacist, local monitor, and other relevant participants. The guidelines should also provide guidance on the sequence of events to be followed before the actual submission (e.g., meetings, workshops, seminars, IEC meetings, and other relevant activities). The guidelines may provide guidance on choosing a CT site and selection of subjects.
Objective:	The objective of this sub-indicator is to ensure the existence of a clear guidance document that guides the applicant and sponsor on the information (i.e., content and format) to be included in the application package. The guidance should include the procedure for submitting the application to the NRA for evaluation. The content of the guidance document should be sufficient to facilitate CT activities.
Requirement:	Format and content of CT applications
Evidence to review:	The assessor should ask for and review: 1. Evidence that the guidelines on the format and content of the CT application are available, implemented and published on the NRA's website. 2. Evidence that accessory documents such as CT application forms and other CT related forms exist and are issued and used. 3. Documentation specifying the format and nature of CT application submission package (i.e. electronic or face-to-face communications, hard or soft copies, and number of copies to be submitted). 4. List of critical documents that should be included in the application package.
References:	1. Guidelines on clinical evaluation of vaccines: regulatory expectations, (38), (https://www.who.int/biologicals/WHO_ECBS/en/ and https://www.who.int/biologicals/vaccines/en/) 2. Guidelines for good clinical practice (GCP) for trials on pharmaceutical products, (40), (http://apps.who.int/medicinedocs/en) 3. Handbook for good clinical research practice (GCP): Guidance for Implementation, (41), (http://apps.who.int/medicinedocs/en) 4. WHO guidelines on nonclinical evaluation of vaccines, (39), (https://www.who.int/biologicals/WHO_ECBS/en/ and https://www.who.int/biologicals/vaccines/en/) 5. WHO guidelines on the nonclinical evaluation of vaccines adjuvants and adjuvanted vaccines, (119), (https://www.who.int/biologicals/WHO_ECBS/en/ and https://www.who.int/biologicals/vaccines/en/)
Framework:	Structure/Foundation/Input
Rating Scale:	➜ NOT IMPLEMENTED (NI): There are no guidelines on the format and content of CT applications. ➜ ONGOING IMPLEMENTATION (OI): The guidelines on the format and content of CT applications have been drafted or adopted, but they have not yet been implemented. ➜ PARTIALLY IMPLEMENTED (PI): The format and content of CT applications has been established and they have been applied for less than two years. ➜ IMPLEMENTED (I): The NRA has guidelines on the format and content of CT applications and they are being followed for all received CT applications.
Limitations and remarks:	Scoring this sub-indicator as "not applicable NA" is excluded (i.e. this sub-indicator will always apply for all benchmarked NRAs).

Sub Indicator:	**CT01.11: Legal provisions or regulations allow the NRA to recognize and use relevant CT decisions, reports or information from other NRAs or from regional and international bodies.**
Maturity Level:	1
Scope:	1. Medicines 2. Vaccines
Description:	The assessor should verify the existence, enactment, and implementation of legal provisions or regulations that allow the NRAs to recognize and use relevant CT decisions, reports or information from other NRAs or from regional and international bodies. The legal provision and regulations should provide guidance on the modalities, processes and procedures to employ when recognizing and using relevant CT decisions, reports or information from other NRAs or from regional and international bodies. The legal provisions should also provide guidance on the conditions (i.e., when and how) to recognize and use relevant CT decisions, reports or information from other NRAs or from regional and international bodies. The legal provisions and regulations should also provide clear directives on the scope or extent of recognition and use of the CT decisions, reports or information from other NRAs or from regional and international bodies.
Objective:	The objective of this sub-indicator is to ensure the existence of legal provisions or regulations that allow the NRA to recognize and use relevant CT decisions, reports or information from other NRAs or from regional and international bodies.
Requirement:	Recognition of and reliance on CT application decisions and information
Evidence to review:	The assessor should ask for and review: 1. The legal provisions (laws, decrees, regulations or any legal binding document) that permits the NRA to recognize and use relevant CT decisions, reports or information from other NRAs or from regional and international bodies. 2. Guidelines that define the scope and extent of recognition and use of relevant CT decisions, reports or information from other NRAs or from regional and international bodies. 3. Examples of instances or situations in which the NRA permitted recognition and use relevant CT decisions, reports or information from other NRAs or from regional and international bodies. 4. List of NRAs or regional and international bodies whose relevant decisions, reports or information may be used to influence a CT application decision. Documentation that indicate whether those NRAs or regional and international bodies are aware that their relevant CT decisions, reports or information on certain CTs may be used (i.e., aware of the legal provision).
References:	1. Good regulatory practices: guidelines for national regulatory authorities for medical products, (112), (http://digicollection.org/whoqapharm/p/about and http://apps.who.int/medicinedocs/en)
Framework:	Structure/Foundation/Input
Rating Scale:	➔ NOT IMPLEMENTED (NI): There are no legal provisions or regulations that allow the NRA to recognize and use relevant CT decisions, reports or information from other NRAs or from regional and international bodies. ➔ ONGOING IMPLEMENTATION (OI): The legal provisions or regulations that allow the NRA to recognize and use relevant CT decisions, reports or information from other NRAs or from regional and international bodies are drafted or pending for adoption. ➔ PARTIALLY IMPLEMENTED (PI): Legal provisions or regulations allowing the NRA to recognize and use relevant CT decisions, reports or information from other NRAs or from regional and international bodies have been established and the NRA has been applying them for less than two years.

	➔ IMPLEMENTED (I): There are legal provisions or regulations allowing the NRA to recognize and use relevant CT decisions, reports or information from other NRAs or from regional and international bodies; this is supported with adequate documentation (e.g., criteria for selection or list of NRAs recognized or used)
Limitations and remarks:	Reliance or recognition should be considered optional if the NRA has the expertise, capacity, and resources to conduct reviews of all CT applications received.
Indicator:	**CT02 Arrangement for effective organization and good governance.**
Objective:	The objective of this indicator is to ensure that there is a legal basis for the organizational structure and governance that allows for the smooth exchange of information within and outside the entity responsible for CTs (e.g., NRA, ethical committee, or clinical research organization). The arrangement should define the roles and responsibilities of those persons within the entities which are in charge of the various component activities within the CT. The arrangement should also clarify how the roles of these individuals relate to the governance structure of the organization responsible for CTs, as well as how they relate to outside organizations such as the other CT-related NRAs or other competent regulatory authorities. Effective implementation of these arrangements will ensure that the NRA responsible for CTs has complete control of all the information related to CTs, including information about ongoing CTs, new directives, authorizations, suspensions and rejections, and other relevant activities. The objective of this indicator is to establish that structures are in place at the organizational and governance levels to promote effective intra- and inter-NRA relationships so that information traffic is efficiently managed.
Category:	Organization and governance
Sub Indicator:	**CT02.01: There is a defined structure with clear responsibilities to conduct CT oversight activities.**
Maturity Level:	2
Scope:	1. Medicines 2. Vaccines
Description:	The assessor should verify that the existence and implementation of a defined structure with clear responsibilities to conduct CT oversight activities. The organizational structure should be supported by legal provisions, regulations and guidelines. These legal provisions should clearly delineate the roles, responsibilities and duties of all stakeholders inside and outside the NRA. The guidelines should define the scope and extent of the roles and responsibilities of those within the NRA with respect to CT oversight activities. Additionally, lines of reporting should be clearly established. The structure of the entity or authority, with respect to relationships and ranks, should be established and implemented. Similarly, the mechanisms for information exchange within and outside (e.g., the IEC) the entity or authority should be established and implemented. Assessor should verify the existence and implementation of guidelines for the establishment of advisory committees (e.g., technical expert committees or external expert committees) with clearly-defined objectives, functions, composition, and terms of reference (ToRs).
Objective:	The objective of this sub-indicator is to ensure there are structures in place, with clearly defined roles and responsibilities for each structural and governance level, for CT oversight activities.
Requirement:	Structure and Responsibilities
Evidence to review:	The assessor should ask for and review: 1. Guidelines that define the roles, responsibilities, and duties of the entity responsible for CT oversight within the NRA, and guidelines that define their placement on the organizational chart in relation to other entities involved in CTs.

	2. The regulations or guidelines that provide the mandate to this entity or authority to conduct CT oversight activities within the NRA. 3. Documentation of a clearly defined policy on conflicts of interest. 4. The operational manual (or similar document) of the entity responsible for this activity. The manual should contain all the authorized and approved guidelines (published or not), application forms (published or not), and SOPs (or similar documents). 5. Published CT application processing flow diagrams and corresponding timelines. 6. Published schedule of any applicable fees and charges.
References:	
Framework:	Structure/Foundation/Input
Rating Scale:	➔ NOT IMPLEMENTED (NI): There is no defined structure with clear responsibilities to conduct CT oversight activities. ➔ ONGOING IMPLEMENTATION (OI): The NRA has recently drafted a defined structure with clear responsibilities to conduct CT oversight activities. ➔ PARTIALLY IMPLEMENTED (PI): The NRA has established a defined structure with clear responsibilities to conduct CT oversight activities; however there is the need to improve this function by providing required support for effective implementation and coordination. ➔ IMPLEMENTED (I): The NRA has established a defined structure with clear responsibilities to conduct CT oversight activities that is fully supported with required resources.
Limitations and remarks:	Scoring this sub-indicator as "not applicable NA" is excluded (i.e. this sub-indicator will always apply for all benchmarked NRAs).
Sub Indicator:	**CT02.02: Documented procedures are implemented to ensure the involvement and communication among all stakeholders relevant to CTs.**
Maturity Level:	3
Scope:	1. Medicines 2. Vaccines
Description:	The assessor should verify the existence and implementation of documented procedures that promote involvement and communication among all stakeholders. The procedures should provide clear directives on the regulatory divisions and guidance on how to implement the operational procedures to ensure the involvement and communication among all stakeholders within and outside the NRA (e.g., the entity responsible for CT oversight, IEC, GCP inspectorate, sponsors, principal investigator, and other relevant entities). Procedures should be clear on the scope and extent of the roles and responsibilities of each stakeholder. In addition, the procedure should be supported by an information and documentation transfer policy to ensure that directives, information, and documentation reach the intended recipients and that feedback is received. SOPs or similar documents and guidelines should be approved, authorized and implemented.
Objective:	The objective of this sub-indicator is to ensure there are documented procedures, structures, and mechanisms in place to ensure proper relationships within and among the entities involved in CTs in order to ensure effective and efficient exchange of information among stakeholders.
Requirement:	CT stakeholders interactions
Evidence to review:	The assessor should ask for and review: 1. Evidence that procedures are documented and implemented, and that the impact of the implementation is periodically assessed. 2. SOPs or similar documents that guide and inform effective communication and collaboration among stakeholders.

	3. The CT application guidelines that capture the duties, roles and responsibilities of the various stakeholders involved in CT activities. The assessor should request evidence that the document is known to the relevant organizations, institutions, and departments. 4. Documentation for the CT application processing flow that captures the roles, duties and responsibilities of the various stakeholders and that defines the timelines allocated to the various stages 5. Documentation for the feedback mechanisms in the information and documentation transfer policy among the various stakeholders.
References:	
Framework:	Process
Rating Scale:	➔ NOT IMPLEMENTED (NI): There are no procedures to ensure involvement and communication with all stakeholders relevant to CTs. ➔ ONGOING IMPLEMENTATION (OI): The NRA has recently drafted procedures to ensure involvement and communication among all stakeholders relevant to CTs. ➔ PARTIALLY IMPLEMENTED (PI): The NRA established the procedures to ensure involvement and communication among all stakeholders relevant to CTs but these have not been fully incorporated and are not consistent with relevant guidance. ➔ IMPLEMENTED (I): The NRA has implemented procedures to ensure involvement and communication with all relevant stakeholders including required documentation and records of communications and of feedback for these communications.
Limitations and remarks:	Scoring this sub-indicator as "not applicable NA" is excluded (i.e. this sub-indicator will always apply for all benchmarked NRAs).
Indicator:	**CT03 Human resources to perform clinical trials oversight activities.**
Objective:	The objective of this indicator is to ensure to that all entities within an NRA are adequately resourced with a trained, experienced and skilled workforce that is empowered to fully perform CT oversight activities. This will ensure that CT oversight activities are performed in accordance with international best practices. The objective of this indicator is to evaluate the human resource capacity of the entities with respect to the number of personnel, the skills and experience of the personnel, and the overall composition of the workforce, with the goal of evaluating whether the workforce possesses the specific expertise required to perform CT oversight activities. The assessor should consider that some NRAs may outsource CT activities.
Category:	Resources (HR, FR, infrastructure and equipment)
Sub Indicator:	**CT03.01: Sufficient competent staff (i.e., education, training, skills and experience) are assigned to perform CT oversight activities.**
Maturity Level:	3
Scope:	1. Medicines 2. Vaccines
Description:	The assessor should verify that the human resources assigned to perform CT oversight activities should be sufficient with respect to numbers and competent with respect to the requisite skills, education, experience and training. There should be technical documents and SOPs that provide guidance on the required background for CT oversight activities and that consider the requirements for educational background, competencies, skills, experience, and training. The assessor should verify that the NRA estimated the number of staff required to effectively and efficiently perform CT oversight function and that the NRA actually recruited that number. In addition, the assessor should verify that these competency requirements are well-established and maintained by the NRA. Metrics and statistics on the different

	activities performed as well as performance indicators can be used for estimating the adequacy of the number of the assigned staff. The assessor should also verify that the competency of the assigned staff is built, maintained and improved through recruitment as well as continuous on- the-job training.
Objective:	The objective of this sub-indicator is to ensure the existing human resources for CT oversight is sufficient, in terms of numbers, experience, and specific competencies, to perform all the activities along the entire CT oversight chain.
Requirement:	Sufficient number of competent human resources in charge of CT oversight activities
Evidence to review:	The assessor should ask for and review: 1. Evidence that the number of staff members involved in each of the documented activities along the entire CT oversight process flow is adequate. 2. Evidence that the systems and structures are in place to ensure appropriate placement of staff with respect to competence and skills. 3. Evidence that the system and structures have been implemented. The documentation should include the records to verify that the staff competence is appropriate for the job requirements. 4. Evidence that the professional profiles of the human resources engaged in CT oversight activities are appropriate with respect to education, skills, and expertise, to perform a particular function along the CT oversight chain. Documentation should include a list of the requisite skills and training for each position. 5. Recruitment plan.
References:	1. National drug regulatory legislation: guiding principles for small drug regulatory authorities. In: WHO Expert Committee on Specifications for Pharmaceutical Preparations: thirty-fifth report. World Health Organization; 1999: Annex 8 (WHO Technical Report Series, No. 885), (1), (http://apps.who.int/medicinedocs/documents/s21964en/s21964en.pdf)
Framework:	Structure/Foundation/Input
Rating Scale:	➜ NOT IMPLEMENTED (NI): The NRA does not have enough competent staff (i.e., education, training, skills and experience) to perform CT oversight activities ➜ ONGOING IMPLEMENTATION (OI): The NRA has recently developed a plan to recruit adequate competent staff; however, the plan has not been implemented. ➜ PARTIALLY IMPLEMENTED (PI): The NRA has initiated the implementation of the human resources development plan; however, there is need to complete the competency profile. ➜ IMPLEMENTED (I): The NRA has a sustained number of competent staff (i.e., education, training, skills and experience) assigned to perform CT oversight activities.
Limitations and remarks:	▪ Assessment of the adequacy and appropriateness of the number of staff members is quite subjective and should be linked to some process or output indicators. When estimating staff adequacy, the assessor should consider the workload, backlog, and delays in delivery based on established timeframes. ▪ Assessor should recognize the existence of personnel from other departments who are often engaged in CT oversight functions such as assessments of protocols and GCP inspections. All of these, together with in-house staff, should be included when number and competency of CT oversight staff are evaluated. Other government officials from outside the NRA should also be included in this assessment. ▪ Scoring this sub-indicator as "not applicable NA" is excluded (i.e. this sub-indicator will always apply for all benchmarked NRAs).
Sub Indicator:	**CT03.02: Duties, functions, and responsibilities of the staff in charge of CT oversight activities are established and updated in the respective job descriptions.**
Maturity Level:	3

Scope:	1. Medicines 2. Vaccines
Description:	The assessor should verify that procedures are in place to maintain a current and updated structure for managing job descriptions for personnel participating in CT oversight activities. In addition, job descriptions should address current staff duties, responsibilities and the requisite competencies. A job description with this format and content should be established and implemented for all staff. The management of job descriptions should be supported by a guidance document that provides direction on when and how to update the information, and where the information should be kept for easy access. The guidance document should present the appropriate duties and responsibilities that are assigned to each member of the organization involved in CT oversight activities. Thus, the professional profiles of staff are reflected in their respective roles and responsibilities within the NRA. There should be procedures to guide responsible persons to document that duties, functions and responsibilities are revised and kept up to date. In addition, procedures should be available to guide the keeping and documenting of up to date work schedules and enforcing the implementation of the documented guidelines and procedures.
Objective:	The objective of this sub-indicator is to ensure that duties and responsibilities of the staff are clear and well defined, that job descriptions are kept up to date with current duties, functions and responsibilities, and that these activities are adequately documented
Requirement:	Duties, roles and responsibilities of the staff relevant to CT oversight activities.
Evidence to review:	The assessor should ask for and review: 1. Procedure and guidelines that guide placement of staff members within the NRA; 2. The professional profiles of staff (i.e., job descriptions) and documentation that they are related to their current roles and duties; 3. The professional profiles of the external experts and documentation that the profiles provide a composition that is complete and consistent with that prescribed in the legal provisions; 4. Procedures to guide the documentation of up to date duties and work schedules and to enforce the implementation of the documented guidelines and procedures; 5. Job descriptions for designated staff.
References:	1. National drug regulatory legislation: guiding principles for small drug regulatory authorities. In: WHO Expert Committee on Specifications for Pharmaceutical Preparations: thirty-fifth report. World Health Organization; 1999: Annex 8 (WHO Technical Report Series, No. 885), (1), (http://apps.who.int/medicinedocs/documents/s21964en/s21964en.pdf) 2. Quality management systems — Requirements. International Standard ISO 9001:2015. Geneva. International Organization for Standardization, 2015, (4), (https://www.iso.org/iso-9001-quality-management.html) 3. Guiding principles for small national drug regulatory authorities. In: WHO Expert Committee on Specifications for Pharmaceutical Preparations: thirty-first report. World Health Organization; 1990: Annex 6 (WHO Technical Report Series, No. 790), (5), (http://apps.who.int/medicinedocs/documents/s21964en/s21964en.pdf) 4. Effective drug regulation: A multicountry study. World Health Organization; 2002, (7), (http://apps.who.int/medicinedocs/pdf/s2300e/s2300e.pdf)
Framework:	Structure/Foundation/Input
Rating Scale:	➔ NOT IMPLEMENTED (NI): There is no evidence of defined or established duties, functions, responsibilities, respective job descriptions and necessary required competencies. ➔ ONGOING IMPLEMENTATION (OI): The NRA has recently drafted or developed the role and responsibilities document but it has not yet been implemented. ➔ PARTIALLY IMPLEMENTED (PI): The NRA has initiated implementation of this requirement but it has not been defined or followed for all staff or the roles and responsibilities documents, including staff job descriptions, are not up to date.

	➔ IMPLEMENTED (I): The NRA has defined and established all required duties, functions, and responsibilities, and respective job descriptions are up-to-date.
Limitations and remarks:	Scoring this sub-indicator as "not applicable NA" is excluded (i.e. this sub-indicator will always apply for all benchmarked NRAs).
Sub Indicator:	**CT03.03: Training plan developed, implemented and updated at least once a year for staff in charge of CT oversight activities.**
Maturity Level:	3
Scope:	1. Medicines 2. Vaccines
Description:	The assessor should verify that training plans are developed, implemented and updated at least once every year to reflect the current situation by considering education and experience of the staff. The training plan should be complemented with guidelines or similar documents that guide the development and implementation of training plans. The assessor should ensure that induction training for new staff as well as continued on- the-job for staff is planned and implemented. There should be procedures to approve the training plan and the budget allocated for implementing and updating the training plan. The plans should present clearly defined training goals and should include training in certain topics and skills to address identified deficiencies. Learning objectives, training methods and activities, evidence of learning, and evaluation and assessment of training should be documented. This documentation should confirm that the learning objectives were achieved and were designed to address weaknesses within the entities. Procedures should be in place to ensure that a training plan is developed, implemented and updated at least once every year. The assessor should verify that there is a system in place for monitoring the implementation and effectiveness of the training plan and for documenting the skills acquired in training activities for internal and external experts.
Objective:	The objective of this sub-indicator is to ensure that a training plan for staff exists, and that it is implemented and updated annually. Through the training plan, NRA can be sure that competency of staff in charge of CT oversight activities is maintained and enhanced.
Requirement:	Implementation of training plan
Evidence to review:	The assessor should ask for and review: 1. Guidelines for development, implementation and annual update (i.e., at least once per year) of the training plan. Guidelines should also provide for a mechanism to measure effectiveness of training. 2. Documentation for the system or structures used to approve the training plan and to evaluate the adequacy of the budget allocated to the training activities. 3. The current or existing staff training plan (or matrix) for staff. The assessor should assess this in in relation to the respective individual job descriptions. 4. SOP for developing and maintaining the training plan. 5. Evidence that the NRA has investigated and identified training needs. 6. List of trainings performed. 7. Example records for training activities.
References:	1. National drug regulatory legislation: guiding principles for small drug regulatory authorities. In: WHO Expert Committee on Specifications for Pharmaceutical Preparations: thirty-fifth report. World Health Organization; 1999: Annex 8 (WHO Technical Report Series, No. 885), (1), (http://apps.who.int/medicinedocs/documents/s21964en/s21964en.pdf) 2. Quality management systems — Requirements. International Standard ISO 9001:2015. Geneva. International Organization for Standardization, 2015, (4), (https://www.iso.org/iso-9001-quality-management.html) 3. Guiding principles for small national drug regulatory authorities. In: WHO Expert Committee on Specifications for Pharmaceutical Preparations: thirty-first report. World Health Organization; 1990: Annex 6 (WHO Technical Report Series, No. 790), (5), (http://

	apps.who.int/medicinedocs/documents/s21964en/s21964en.pdf) 4. Effective drug regulation: A multicountry study. World Health Organization; 2002, (7), (http://apps.who.int/medicinedocs/pdf/s2300e/s2300e.pdf) 5. Quality systems requirements for national good manufacturing practice inspectorates. In: WHO Expert Committee on Specifications for Pharmaceutical Preparations: thirty-sixth report. World Health Organization; 2002: Annex 8 (WHO Technical Report Series, No. 902), (8), (http://apps.who.int/medicinedocs/documents/s22112en/s22112en.pdf)
Framework:	Process
Rating Scale:	➜ NOT IMPLEMENTED (NI): There is no systematic training program including training plan (or matrix). ➜ ONGOING IMPLEMENTATION (OI): The NRA has recently drafted or developed the training plan but there is no evidence of implementation. ➜ PARTIALLY IMPLEMENTED (PI): The NRA has developed and initiated the training plan implementation. However, the NRA has not fulfilled all required planned training or has been applying the plan for less than two years. ➜ IMPLEMENTED (I): The NRA has an updated training plan developed that is supported by adequate records to demonstrate effective plan implementation, including induction training for new staff and routine on-the-job training for recruited staff.
Limitations and remarks:	▪ Training plans must be updated regularly; ideally on an annual basis, but not less frequently that once every two years. ▪ Some regulatory functions may include many training activities that are not incorporated in the institutional training programme. Such training normally is offered by invitation. In this case, the assessor should recognize reports from non-routine CT oversight-relevant training not included in the NRA training plan. ▪ Scoring this sub-indicator as "not applicable NA" is excluded (i.e. this sub-indicator will always apply for all benchmarked NRAs).
Sub Indicator:	**CT03.04: The NRA generates and maintains records of staff training activities and training effectiveness verification.**
Maturity Level:	3
Scope:	1. Medicines 2. Vaccines
Description:	The assessor should verify that records of staff training that is performed or organized by the NRA are generated, maintained, regularly updated. This activity should be supported by guidelines that direct the NRA to generate and maintain records of staff training activities. Procedures should be in place to document and propose staff training needs and to allocate a budget for continuous staff capacity building and development. The assessor should check that there is an evaluation or assessment mechanism to verify the quality of learning, and to confirm that learning objectives are achieved. Documentation should include an inventory (i.e., soft and/or hard) system that records all impactful and non-impactful trainings and identifies all staff members who participated. A system to measure or estimate impact of trainings should be established.
Objective:	The objective of this sub-indicator is to ensure that training organized by the NRA or responsible regulatory authority is adequately documented and that the training records are adequately maintained and kept. Staff training records are considered an integral part of staff file and are a tool for measuring and tracking staff competency, development and adequacy.
Requirement:	Training records
Evidence to review:	The assessor should ask for and review: 1. Guidelines or similar documents that guide the NRA to generate and maintain records of

	staff training activities; 2. Evaluations of training effectiveness; 3. The training inventory, and procedures for completing the inventory; 4. Examples of archived records of staff training, and procedures for the archiving system
References:	1. National drug regulatory legislation: guiding principles for small drug regulatory authorities. In: WHO Expert Committee on Specifications for Pharmaceutical Preparations: thirty-fifth report. World Health Organization; 1999: Annex 8 (WHO Technical Report Series, No. 885), (1), (http://apps.who.int/medicinedocs/documents/s21964en/s21964en.pdf) 2. Quality management systems — Requirements. International Standard ISO 9001:2015. Geneva. International Organization for Standardization, 2015, (4), (https://www.iso.org/iso-9001-quality-management.html) 3. Guiding principles for small national drug regulatory authorities. In: WHO Expert Committee on Specifications for Pharmaceutical Preparations: thirty-first report. World Health Organization; 1990: Annex 6 (WHO Technical Report Series, No. 790), (5), (http://apps.who.int/medicinedocs/documents/s21964en/s21964en.pdf) 4. Effective drug regulation: A multicountry study. World Health Organization; 2002, (7), (http://apps.who.int/medicinedocs/pdf/s2300e/s2300e.pdf)
Framework:	Output
Rating Scale:	➔ NOT IMPLEMENTED (NI): There is no evidence that the NRA generates and maintains records of staff training activities. ➔ ONGOING IMPLEMENTATION (OI): The NRA has recently initiated plans to generate, document and keep records of staff training activities, however they are not yet followed. ➔ PARTIALLY IMPLEMENTED (PI): The NRA has recently initiated plans to generate, document and keep records of staff training activities but they are not fully followed for all training activities or they have been established for less than two years. ➔ IMPLEMENTED (I): The NRA generates and maintains records of staff training activities
Limitations and remarks:	▪ The assessor should note that some NRAs out-source training including staff capacity development activities. In this case the assessor should request the identity of the provider, as well as evaluations of the provider. The assessor may request the professional profiles of tutors or resource persons used to offer training. The assessor may also request records covering the archiving systems in place. ▪ Scoring this sub-indicator as "not applicable NA" is excluded (i.e. this sub-indicator will always apply for all benchmarked NRAs).
Indicator:	**CT04 Procedures established and implemented to perform clinical trials oversight.**
Objective:	The objective of this indicator is to ensure that the NRA (or responsible regulatory authority) has documented procedures establishing how CTs should be implemented. The documented procedures should be efficiently designed to assist in the preparation of the CT application and in the receipt and evaluation of the enclosed information. The procedures should present an overview of the activities to be carried out, the steps to be followed, the resources required, the processes to be followed in evaluation of the submitted documents, and the interrelationships among the various documents. The responsible authority should verify that all procedures follow and address all legal principles. The established procedures will give guidance on how CT applications are handled to ensure efficient CTs. The objective of this indicator is to establish whether procedures have been established and implemented to effectively perform CT oversight activities.
Category:	Regulatory process

Sub Indicator:	**CT04.01: NRA has access to an advisory committee for review of CT applications and post-approval safety and compliance issues.**
Maturity Level:	4
Scope:	1. Medicines 2. Vaccines
Description:	The assessor should verify that the involvement of an advisory committee, which is external to the NRA and which participates in the review of CT applications, is documented and supported by legal provisions and regulations. The assessor should also verify that the legal provisions and regulations that guide the establishment and use of an advisory committee in the review of CT applications are established and implemented. There should be clear guidance on when and how to use the committee, as well as guidance on the scope and extent of the use of committee expertise in the review of CT applications and in the evaluation of post approval safety and compliance issues. The ToRs of the members of the committee should be available and documented. There should be documented objectives and functions for the committee and for each member of the committee. Professional profile of the committee members should be available, and the composition of the committee should be guided by a legal provisions or regulations. In addition, supporting guidelines should clearly define, for each member of the committee, their roles and responsibilities in the review of CT applications. The code of conduct for the committee members, as well as a general policy on conflicts of interest, should also be documented and available. The assessor should note that some NRAs (or responsible regulatory authorities) may not involve the advisory committee in the review of the submitted CT applications. In such cases, the NRAs may consult the advisory committee for direction in response to adverse events or reactions including serious ones.
Objective:	The objective of this sub-indicator is to ensure that the NRA has the option, when needed, of using an advisory committee in the review of CT applications and in the evaluation of post approval safety and compliance issues. This option is particularly important in the event of new or emerging technology.
Requirement:	Advisory committee for CT
Evidence to review:	The assessor should ask for and review: 1. Legal provisions (laws, decrees, regulations or any legal binding document) for the establishment and use of an advisory committee in the review of CT applications 2. The ToRs of the committee and members of the committee, including their signed updated conflicts of interest forms. 3. Documentation of the composition of the advisory committee, and evidence that it is in line with the directives prescribed in the legal provision and regulations 4. Guidelines that define the scope and extent of the advisory committee contributions in the review of CT applications. 5. SOPs for the advisory committee activities. 6. Records of advisory committee reports
References:	
Framework:	Process
Rating Scale:	➔ NOT IMPLEMENTED (NI): The NRA does not have access to an advisory committee involved in the review of CT applications or post-approval safety and compliance issues. ➔ ONGOING IMPLEMENTATION (OI): The NRA has drafted a proposal to establish the advisory committee that is involved in the review of CT activities. ➔ PARTIALLY IMPLEMENTED (PI): The advisory committee has been established for less than two years or is not involved in all required CT activities. ➔ IMPLEMENTED (I): The expert advisory committee is established, officially endorsed and involved in all required CT activities, as needed, to ensure quality of CT reviews.

Limitations and remarks:	▪ In the case the NRA has all required internal resources for CT oversight activities, this sub-indicator can be scored as not applicable. ▪ The assessor should consider this sub- indicator as implemented, if the NRA can provide adequate evidence of access to advisory committees when needed.
Sub Indicator:	**CT04.02: The existence of the ECs with clearly defined composition.**
Maturity Level:	3
Scope:	1. Medicines 2. Vaccines
Description:	The assessor should verify the existence, enactment, and implementation of legal provisions and regulations that define the composition of the ECs. The legal provisions and regulations should stipulate that the composition of the ECs should be multidisciplinary and multi-sectorial and should have a balanced age and gender distribution. Additionally, the EC should include members with relevant scientific expertise and laypersons who represent the interests and the concerns of the community. The legal provisions should be supported with guidelines or SOPs that provide guidance on selection of members, on selection of the committee chair, and on the ToRs for members. The legal provisions and regulations should also provide direction on how the activities of the ECs should be regulated.
Objective:	The objective of this sub-indicator is to ensure there is a defined and documented composition of the ECs for CT activities.
Requirement:	Existence, performance and composition of ECs
Evidence to review:	The assessor should ask for and review: 1. Legal provisions (laws, decrees, regulations or any legal binding document) that provide guidance on the composition of the ECs 2. The ToRs for each member along with guidelines on the selection process. The assessor should review the ToRs and SOPs that provide guidance. 3. Professional profiles for members of the ECs. Assessor should assess these for balance in terms of relevant expertise, gender, age and representation. 4. Current list of the EC members.
References:	1. Guidelines on clinical evaluation of vaccines: regulatory expectations, (38), (https://www.who.int/biologicals/WHO_ECBS/en/ and https://www.who.int/biologicals/vaccines/en/) 2. WHO guidelines on nonclinical evaluation of vaccines, (39), (https://www.who.int/biologicals/WHO_ECBS/en/ and https://www.who.int/biologicals/vaccines/en/) 3. WHO guidelines on the nonclinical evaluation of vaccines adjuvants and adjuvanted vaccines, (119), (https://www.who.int/biologicals/WHO_ECBS/en/ and https://www.who.int/biologicals/vaccines/en/)
Framework:	Structure/Foundation/Input
Rating Scale:	➔ NOT IMPLEMENTED (NI): ECs are not established for CT activities. ➔ ONGOING IMPLEMENTATION (OI): The composition of the ECs has been recently drafted but the committees have not been implemented. ➔ PARTIALLY IMPLEMENTED (PI): The ECs are established but are not officially approved or are not routinely involved in CT activities. ➔ IMPLEMENTED (I): The ECs are established, officially endorsed and routinely involved in CT activities.
Limitations and remarks:	▪ The assessor should note that in most cases, the NRA will not be the agency that hosts the EC, and as a result may not be able to provide sufficient information to address this sub-indicator. The assessor may have to consult the Ministry of Health or the relevant Ministry or institution for more information. Failure to secure information should justify the scoring of this sub-indicator as “not or partially implemented”.

	▪ Scoring this sub-indicator as "not applicable NA" is excluded (i.e. this sub-indicator will always apply for all benchmarked NRAs).
Sub Indicator:	**CT04.03: Nonclinical data is considered within CT application review.**
Maturity Level:	3
Scope:	1. Medicines 2. Vaccines
Description:	The assessor should verify the existence and implementation of the regulations and guidelines on the preclinical data requirements for CT applications. The guidelines should clearly state that the CT application requirements include submission of preclinical data which is generated in accordance with the principles of Good Laboratory Practices. The guidelines should provide guidance on the type and scope of data to submit to support the CT application.
Objective:	The objective of this sub-indicator is to ensure the availability of data from preclinical studies that will provide sufficient insight into potential safety issues which may influence eventual clinical application of the IMP. The objective of the sub-indicator is to ensure that preclinical data are part of the application package, and that the data submitted are reviewed according to a documented procedure.
Requirement:	Preclinical data as part of CT application
Evidence to review:	The assessor should ask for and review: 1. The regulations and guidelines that states that nonclinical data may be required in a CT application. 2. SOPs that provide guidance during the review of the nonclinical data submitted as part of the CT application. 3. Sample records of CT application forms.
References:	1. Guidelines for good clinical practice (GCP) for trials on pharmaceutical products, (40), (http://apps.who.int/medicinedocs/en) 2. WHO guidelines on nonclinical evaluation of vaccines, (39), (https://www.who.int/biologicals/WHO_ECBS/en/ and https://www.who.int/biologicals/vaccines/en/)
Framework:	Process
Rating Scale:	➜ NOT IMPLEMENTED (NI): The NRA does not require submission and review of nonclinical data within CT application. ➜ ONGOING IMPLEMENTATION (OI): The NRA has recently drafted guideline or similar documents to consider nonclinical data as part of CT application. ➜ PARTIALLY IMPLEMENTED (PI): The NRA considers nonclinical data as part of CT application however there is no systematic review, records or capacity to review these data. ➜ IMPLEMENTED (I): The NRA requires submission of nonclinical data within CT applications, and these data are reviewed.
Limitations and remarks:	Scoring this sub-indicator as "not applicable NA" is excluded (i.e. this sub-indicator will always apply for all benchmarked NRAs).
Sub Indicator:	**CT04.04: There are defined roles for ECs at all levels (e.g., national, sub-national, or institutional).**
Maturity Level:	3
Scope:	1. Medicines 2. Vaccines

Description:	The assessor should verify that the legal provisions, regulations and guidelines which establish the EC, also provide guidance on the composition of the EC, and on the roles and responsibilities at each level. These legal provisions should be up to date. The regulations and guidelines should define the objectives, functions, mandates, missions, roles and responsibilities of the ECs as a whole, as well as for each member of the EC. In addition, the scope and extent of their mandate should be well-described. The interactions among the different levels of ECs should be defined and documented.
Objective:	The objective of this sub-indicator is to ensure that there are defined roles for the ECs at all levels
Requirement:	Defined roles for ECs
Evidence to review:	The assessor should ask for and review: 1. The legal provisions (laws, decrees, regulations or any legal binding document) and guidelines that provide defined roles for the EC at each level of CT activity including guidance on information sharing and interactions with relevant stakeholders. 2. Guidelines detailing the objectives, functions, roles and responsibilities of the EC at each level of CT activity. 3. Evidence that the legally mandated scope of work is acceptable according to WHO guidelines 4. Records of interaction among different EC levels.
References:	1. WHO guidelines on nonclinical evaluation of vaccines, (39), (https://www.who.int/biologicals/WHO_ECBS/en/ and https://www.who.int/biologicals/vaccines/en/) 2. Guidelines on clinical evaluation of vaccines: regulatory expectations, (38), (https://www.who.int/biologicals/WHO_ECBS/en/ and https://www.who.int/biologicals/vaccines/en/) 3. WHO guidelines on the nonclinical evaluation of vaccines adjuvants and adjuvanted vaccines, (119), (https://www.who.int/biologicals/WHO_ECBS/en/ and https://www.who.int/biologicals/vaccines/en/)
Framework:	Process
Rating Scale:	➜ NOT IMPLEMENTED (NI): The role and responsibilities of all levels of ECs have not been defined. ➜ ONGOING IMPLEMENTATION (OI): The role and responsibilities of ECs have been drafted at all levels however they are not yet followed. ➜ PARTIALLY IMPLEMENTED (PI): The role and responsibilities of ECs have been assigned at all levels however they have been used for less than two years or they are not fully documented. ➜ IMPLEMENTED (I): The role and responsibilities of ECs have been established and documented for CTs, and there is evidence of consistent implementation.
Limitations and remarks:	Scoring this sub-indicator as "not applicable NA" is excluded (i.e. this sub-indicator will always apply for all benchmarked NRAs).
Sub Indicator:	**CT04.05: Documented and implemented procedures exist to review CT applications.**
Maturity Level:	3
Scope:	1. Medicines 2. Vaccines
Description:	The assessor should verify the existence and implementation of guidelines or SOPs that provide the guidance needed for review of CT applications. The guidelines or SOPs should provide guidance on how to review the various components of the CT application. The guidance should be supported by a checklist or CT application review form that should be completed during the review process. Such a form or checklist

	should be used to generate a review report that captures the recommendations and comments that are used to justify authorization, rejection or deferral of the CT application.
Objective:	The objective of this sub-indicator is to ensure a uniform evaluation of CT applications that is devoid of bias. There should be regulations and guidelines instituting a defined set of criteria for the NRA (or responsible regulatory authority) to follow and use in the discharge of their duties. Employment of this approach will avoid bias.
Requirement:	Document procedures to review CT applications
Evidence to review:	The assessor should ask for and review: 1. The guidelines and SOPs that establish the criteria for reviewing CT applications. 2. Evidence that the guidelines and SOPs are implemented during the review process. 3. Examples of completed review reports. The assessor should review completed review reports and compare for compliance with the applicable guidance.
References:	
Framework:	Process
Rating Scale:	➜ NOT IMPLEMENTED (NI): There are no documented procedures for review of CT applications. ➜ ONGOING IMPLEMENTATION (OI): The NRA has drafted or adopted the documented procedures for review of CT applications. ➜ PARTIALLY IMPLEMENTED (PI): The NRA developed and officially approved the documented procedures for review of CT applications less than two years ago or there is no evidence to demonstrate the implementation of this procedure for all applications. ➜ IMPLEMENTED (I): The NRA has developed and implemented the documented procedures for review of CT applications and has adequate evidence to demonstrate that they have been followed for all CT applications.
Limitations and remarks:	Scoring this sub-indicator as "not applicable NA" is excluded (i.e. this sub-indicator will always apply for all benchmarked NRAs).
Sub Indicator:	**CT04.06: There are procedures for EC responsibility for clearance and follow up until completion of the CT.**
Maturity Level:	3
Scope:	1. Medicines 2. Vaccines
Description:	The assessor should verify the existence, documentation, implementation of procedures that provide guidance on the ECs responsibility for clearance and follow-up until completion of the CT. The documentation of procedures should be in the form of guidelines or SOPs, and should provide detailed guidance on the roles and responsibilities of the EC in the clearance and follow-up processes through the completion of the CT. The guidelines should specify the scope and extent of the EC's activity in the CT activities, the corresponding timelines for each activity, the expected outcomes of their activities, and the impact of each activity on the entire CT. Importantly, EC retains these responsibilities until CT is completed.
Objective:	The objective of this sub-indicator is to ensure the NRA (or responsible regulatory authority) has established procedures on the responsibilities of the EC from CT clearance until the completion of the CT.
Requirement:	Documented procedures for the EC along the entire CT authorization chain

Evidence to review:	The assessor should ask for and review: 1. The regulations, guidelines and SOPs detailing the roles and responsibilities of the EC in the clearance and follow-up process of CTs until completion of the trial. The assessor should verify that the procedures have been appropriately documented and implemented. 2. Documentation that defines the scope and extent of EC responsibility at each stage of the CT. 3. The processes and procedures guiding the EC operations and activities at each stage of the CT.
References:	
Rating Scale:	➔ NOT IMPLEMENTED (NI): There are no procedures that define EC responsibility for clearance and follow up until completion of the CT. ➔ ONGOING IMPLEMENTATION (OI): There are drafted or adopted procedures to define EC responsibility for clearance and follow up until completion of the CT. ➔ PARTIALLY IMPLEMENTED (PI): There are procedures to define EC responsibility for clearance and follow up until completion of the CT, however they have not been implemented. ➔ IMPLEMENTED (I): The defined procedures regarding EC responsibility for clearance and follow up until completion of the CT are implemented and supported with documented evidence.
Limitations and remarks:	▪ The assessor should note that some ECs may have a limited mandate along the entire CT chain in accordance to the existing regulations. In such cases, the assessor should be guided by the existing laws or regulations. The scoring may be partial or not applicable depending on the country regulation. ▪ Scoring this sub-indicator as "not applicable NA" is excluded (i.e. this sub-indicator will always apply for all benchmarked NRAs).
Sub Indicator:	**CT04.07: The same policies are used for the evaluation of CT applications regardless of the applicant (e.g., domestic, foreign, public sector, or private sector).**
Maturity Level:	3
Scope:	1. Medicines 2. Vaccines
Description:	The assessor should verify the existence, enactment, and implementation of regulations and guidelines that dictate that the criteria applied to evaluate CT applications should be the same regardless of the applicant. A single set of criteria for the evaluation process should be employed during evaluation of all CT applications. The criteria should be supported with a checklist or evaluation form that should be completed during the evaluation process. The assessor should note that in some instance, such as emergencies, this defined set of criteria for evaluating CT applications may not apply. The assessor should request for and review the documented and implemented procedures and processes that are used to provide guidance for the review of CT applications in the event of emergencies.
Objective:	The objective of this sub-indicator is to ensure that the same criteria are applied to evaluate CT applications from various sources. Use of consistent procedures will avoid bias.
Requirement:	Uniform criteria and policy for evaluating CT application regardless of applicant
Evidence to review:	The assessor should ask for and review: 1. The regulations and guidelines that require that all CT applications are evaluated with the same single set of criteria regardless of the applicant. 2. The guidelines and SOPs that specify the detailed criteria to be used for evaluating CT applications.

	3. Evidence that the reviewers of CT applications are aware of the criteria and understand how to apply the criteria in their assessment activities. Assessor should review evidence that the criteria are documented, published and implemented.
References:	
Framework:	Process
Rating Scale:	➔ NOT IMPLEMENTED (NI): There are no defined policies and criteria, or different policies are used for the evaluation of CT applications from different sources (e.g. domestic, foreign, public sector, or private sector). ➔ ONGOING IMPLEMENTATION (OI): There is a drafted policy or documentation that requires that the same criteria should be followed for the evaluation of CT applications regardless of the applicant (e.g. domestic, foreign, public sector, or private sector). ➔ PARTIALLY IMPLEMENTED (PI): There are regulations or guidelines that require that the same criteria are used for the evaluation of CT applications regardless of the applicant (e.g. domestic, foreign, public sector, or private sector); however, these have been available for less than two years or there is no evidence to demonstrate full implementation for all received CT applications. ➔ IMPLEMENTED (I): The same criteria and policy are used for the evaluation of CT applications regardless of the applicant (e.g. domestic, foreign, public sector, or private sector) for all received and approved CT applications.
Limitations and remarks:	▪ The assessor should note that in some countries only one source may exist. The assessor can score this sub-indicator as implemented if all regulation and requirements are the same. The assessor should consider there are different requirements based on the nature of each product. ▪ Scoring this sub-indicator as "not applicable NA" is excluded (i.e. this sub-indicator will always apply for all benchmarked NRAs).
Indicator:	**CT05 Mechanism exists to promote transparency, accountability and communication.**
Objective:	The objective of this indicator is to ensure mechanisms are in place to ensure that information on CT applications, including authorized, suspended, rejected and completed CTs, are published to promote transparency and information sharing among stakeholders and potential stakeholders such as trial subjects.
Category:	Transparency, accountability and communication
Sub Indicator:	**CT05.01: There is clarity about the funding of the EC and its members**
Maturity Level:	3
Scope:	1. Medicines 2. Vaccines
Description:	The assessor should verify that the source of funding for the EC activities is known, documented, perceived as appropriate, and devoid of any conflicts of interest. The source of funding for EC activities should be documented and supported by regulations that provide clarity on the funding mechanisms and on the management and disbursement of funds. All fees and charges should be legally approved and implemented. The regulation should provide clarity on the source of funding and provide assurance about the absence of any conflicts of interest.
Objective:	The objective of this sub-indicator is to ensure that there is a dedicated source of funding for the operations of the EC and that the source of funding is known, transparent and devoid of any conflicts of interest.

Requirement:	Clarity on the source of funding
Evidence to review:	The assessor should ask for and review: 1. The regulation detailing the source of funding that is made available to the EC to fund its activities. 2. Evidence that the identity of the source is in compliance with the general policy on conflicts of interest. 3. Evidence that the level of transparency regarding the source of funding and the management of the funds is sufficient to eliminate doubts on conflicts of interest. 4. Evidence that the fees and charges are legally approved. 5. Records and reports of EC funding.
References:	1. Guidelines on clinical evaluation of vaccines: regulatory expectations, (38), (https://www.who.int/biologicals/WHO_ECBS/en/ and https://www.who.int/biologicals/vaccines/en/) 2. WHO guidelines on nonclinical evaluation of vaccines, (39), (https://www.who.int/biologicals/WHO_ECBS/en/ and https://www.who.int/biologicals/vaccines/en/) 3. WHO guidelines on the nonclinical evaluation of vaccines adjuvants and adjuvanted vaccines, (119), (https://www.who.int/biologicals/WHO_ECBS/en/ and https://www.who.int/biologicals/vaccines/en/)
Framework:	Structure/Foundation/Input
Rating Scale:	➜ NOT IMPLEMENTED (NI): NRA does not have information or clarity about the funding of the EC and its members. ➜ ONGOING IMPLEMENTATION (OI): There are drafted procedures and policies to provide information about the funding process of the EC and its members. ➜ PARTIALLY IMPLEMENTED (PI): There are procedures to provide information about the funding process of the EC and its members, however there is no evidence to demonstrate availability of this information regarding all ECs. ➜ IMPLEMENTED (I): The NRA has clear information about the funding of the EC and its members. Information is supported with documented evidence.
Limitations and remarks:	Scoring this sub-indicator as "not applicable NA" is excluded (i.e. this sub-indicator will always apply for all benchmarked NRAs).
Sub Indicator:	**CT05.02: The list of the CTs (approved and rejected applications), including summarized evaluation reports by the NRA, are publicly available or recorded in a domestic or international database.**
Maturity Level:	4
Scope:	1. Medicines 2. Vaccines
Description:	The assessor should verify the existence of regulations, guidelines or similar documents that dictate that all CT applications, either approved or rejected, should be listed in a domestic or international database. This database should also include summaries of the evaluation for each CT application. The regulations should be supported with guidelines that provide guidance on the information to be listed, as well as the content, format and information that should be included in the summary evaluation reports that are made available to the public. The guidelines should provide guidance on the database to the used (i.e., local, international, hosting organization, and other relevant details) and on the mechanism to be used for updating the database.
Objective:	The objective of this sub-indicator is to ensure that approved and rejected CT applications, as well as summarized CT evaluation reports, are listed and published in a local or international database.
Requirement:	Publication of approved and rejected CT applications as well as CT evaluation reports

Evidence to review:	The assessor should ask for and review: 1. Regulations and guidelines that require that all approved and rejected CT applications, as well as summary evaluation reports, should be listed and available in an easily-accessible local or international database. 2. Regulations and guidelines that require that the list of all approved and rejected CT applications, as well as summary evaluation reports, should be updated periodically. 3. Documentation for the rate (i.e., when and how) at which the list is updated. 4. The list of approved and rejected CT applications, as well as summary evaluation reports, on the local or international database. 5. Guidelines and SOPs that provide guidance on the content, format and information that should be uploaded to the database. 6. Evidence that stakeholders are aware of the availability of the list, and that they have a clear understanding of how and where to access the list and its contents.
References:	1. Guidelines on clinical evaluation of vaccines: regulatory expectations, (38), (https://www.who.int/biologicals/WHO_ECBS/en/ and https://www.who.int/biologicals/vaccines/en/) 2. WHO guidelines on nonclinical evaluation of vaccines, (39), (https://www.who.int/biologicals/WHO_ECBS/en/ and https://www.who.int/biologicals/vaccines/en/) 3. WHO guidelines on the nonclinical evaluation of vaccines adjuvants and adjuvanted vaccines, (119), (https://www.who.int/biologicals/WHO_ECBS/en/ and https://www.who.int/biologicals/vaccines/en/)
Framework:	Output
Rating Scale:	➜ NOT IMPLEMENTED (NI): There is no list of CTs (approved and rejected applications), including summarized NRA evaluation reports, that is publicly available or recorded in a domestic or international database. ➜ ONGOING IMPLEMENTATION (OI): There is a draft procedure to publish the list of CTs (approved and rejected applications), including summarized NRA evaluation reports, however it is not yet published. ➜ PARTIALLY IMPLEMENTED (PI): There is a list of CTs (approved and rejected applications), including summarized NRA evaluation reports, and list is publicly available or recorded in a domestic or international database; however, it is not updated or it was published less than two years ago. ➜ IMPLEMENTED (I): There is an updated list of CTs (approved and rejected applications), including summarized NRA evaluation reports, that is publicly available or recorded in a domestic or international database.
Limitations and remarks:	Scoring this sub-indicator as "not applicable NA" is excluded (i.e. this sub-indicator will always apply for all benchmarked NRAs).
Indicator:	**CT06 Mechanism in place to monitor regulatory performance and output.**
Objective:	The objective of this indicator is to ensure that CT oversight mechanisms are in place to verify that all CT activities are subjected to quality controls and other checks to reduce errors, increase objectivity and ensure that the processes are consistent. These activities will generate an assured output and enhance the reliability of results at the various stages of the CT application processing flow. Oversight activities should cover the various stages of the CT application processing flow, including receipt of CT applications, acknowledgement of applications, processing, evaluation, and assessment of the various parts of the applications, generation of recommendations (i.e., approval, deferral, or rejection) following the evaluation and assessment process, issuance of certificates, implementation of regulatory actions when necessary (e.g. stoppage or termination of CTs) and publication of the decision made for each application (i.e., approval or rejection) along with summary evaluation reports. This would lead to consistency in the regulatory performance of the CT oversight function as well as reliable outputs.
Category:	Monitoring progress and assessing outcomes and impact

Sub Indicator:	**CT06.01: There is an internal list or database of all approved and rejected CTs, and the NRA maintains a record of each approved and rejected CT.**
Maturity Level:	3
Scope:	1. Medicines 2. Vaccines
Description:	The assessor should verify the establishment of a register, list, or database into which all approved or rejected CT applications are entered. The register, list or database should be continually updated and maintained to reflect the current situation. The establishment and maintenance of the register, list, or database should be supported by guidelines and SOPs. These procedures should also provide guidance on the content, format and type of information to enter and maintain in the database and guidance on procedures (i.e., when and how) to update the register, list or database. In addition, guidance on who should be given access to the stored information should be clearly documented.
Objective:	The objective of this sub-indicator is to ensure that an internal list or database is kept for all approved and rejected CT applications and that the NRA (or responsible regulatory authority) maintains a record of all approved and rejected CTs.
Requirement:	Internal list or database for all CT applications
Evidence to review:	The assessor should ask for and review: 1. The guidelines requiring the establishment and maintenance of a register, list or database of approved or rejected CT applications. 2. The register, list or database of all CT applications that have been approved or rejected, including details of the type of information that was entered and kept. 3. List of persons with the authority to access stored information, as well as information on the documentation that must be completed before access is granted.
References:	1. Guidelines on clinical evaluation of vaccines: regulatory expectations, (38), (https://www.who.int/biologicals/WHO_ECBS/en/ and https://www.who.int/biologicals/vaccines/en/) 2. WHO guidelines on nonclinical evaluation of vaccines, (39), (https://www.who.int/biologicals/WHO_ECBS/en/ and https://www.who.int/biologicals/vaccines/en/) 3. WHO guidelines on the nonclinical evaluation of vaccines adjuvants and adjuvanted vaccines, (119), (https://www.who.int/biologicals/WHO_ECBS/en/ and https://www.who.int/biologicals/vaccines/en/)
Framework:	Output
Rating Scale:	➜ NOT IMPLEMENTED (NI): There is not an internal list or database of all approved and rejected CTs. ➜ ONGOING IMPLEMENTATION (OI): There is a drafted procedure to create an internal list or database; however the list or database does not yet exist. ➜ PARTIALLY IMPLEMENTED (PI): There is an internal list or database of all approved and rejected CTs, and the NRA maintains a record of each approved and rejected CT; however, the list or database is not up to date or all applications are not included. ➜ IMPLEMENTED (I): There is an updated internal list or database of all approved and rejected CTs, and the NRA has maintained records of each approved and rejected CT for more than two years.
Limitations and remarks:	Scoring this sub-indicator as "not applicable NA" is excluded (i.e. this sub-indicator will always apply for all benchmarked NRAs).
Sub Indicator:	**CT06.02: Performance indicators for CT oversight activities are established and implemented.**
Maturity Level:	4

Scope:	1. Medicines 2. Vaccines
Description:	The assessor should verify the existence and implementation of performance indicators for different activities included under the CT oversight functions. Specifically, the system should define key performance indicators (KPIs) along the entire CT oversight activity chain and all indicators should be adequately justified. For the purpose of clarity and consistency, established KPIs should be supported with guidelines for monitoring and maintenance of the KPIs. The guidelines in turn should be supported by SOPs and tools that define the procedures to be used for monitoring and evaluating the performance indicators and that define procedures and timelines for reviewing and revising the indicators. Examples of performance indicators for CT oversight function include: CT applications received, granted or rejected, timelines for CT application processing, and regulatory actions taken with respect to CTs. Established KPIs might be qualitative, quantitative or combination of both. In general, quantitative indicators are preferred to avoid bias or misinterpretation. However, qualitative indicators are also accepted. Qualitative indicators may or may not include scoring or scaling to render them semi- quantitative and thus more informative. The assessor should ensure that indicators are measured on a regular basis to monitor progress and advancement. In addition, the assessor should verify measured indicators are analyzed to identify trends or abnormalities. Justifications for any identified abnormalities should be provided; when necessary, process optimizations should be introduced to avoid recurrence.
Objective:	The objective of this sub-indicator is to ensure that a system, mechanism, or procedure exists to require the NRA to establish performance indicators along the entire CT oversight chain. Additionally, the objective is to ensure that KPIs are actually contributing to monitoring of regulatory performance, to measuring effectiveness of CT oversight regulatory activities, and to making any necessary adjustments or optimizations.
Requirement:	KPIs for CT oversight activities
Evidence to review:	The assessor should ask for and review: 1. Documents supporting the system, mechanism, or procedure compelling the NRA to establish and implement performance indicators along the entire CT oversight activity chain. 2. Evidence that the performance indicators have been established and implemented, and that the members of staff involved in the CT oversight function are aware of the indicators and the guidelines and SOPs used for monitoring and evaluating their performance. 3. The current performance indicators for CT oversight activities 4. Analyses of the measured indicators along with the investigations done to identify trends or abnormalities. 5. Documentation for follow-up of any observed abnormalities, including justifications for any identified abnormalities as well as any process optimizations introduced to avoid recurrence.
References:	1. Guidelines on clinical evaluation of vaccines: regulatory expectations, (38), (https://www.who.int/biologicals/WHO_ECBS/en/ and https://www.who.int/biologicals/vaccines/en/) 2. WHO guidelines on nonclinical evaluation of vaccines, (39), (https://www.who.int/biologicals/WHO_ECBS/en/ and https://www.who.int/biologicals/vaccines/en/) 3. WHO guidelines on the nonclinical evaluation of vaccines adjuvants and adjuvanted vaccines, (119), (https://www.who.int/biologicals/WHO_ECBS/en/ and https://www.who.int/biologicals/vaccines/en/)
Framework:	Structure/Foundation/Input
Rating Scale:	➔ NOT IMPLEMENTED (NI): There are no KPIs for CT oversight activities. ➔ ONGOING IMPLEMENTATION (OI): The NRA has recently drafted KPIs for CT oversight activities but they have not yet been reported.

	➔ PARTIALLY IMPLEMENTED (PI): The NRA has developed KPIs for CT oversight activities and has been applying them for less than two year or they have not covered all critical steps. ➔ IMPLEMENTED (I): The NRA has established and implemented KPIs for CT oversight activities. The indicators are reviewed regularly, and appropriate actions are taken and decisions made.
Limitations and remarks:	When they refer to outcomes, indicators may be ambiguous and difficult to interpret, as outcomes are the result of many factors that are difficult to disentangle. When they refer to processes, indicators are often too specific, as they may focus on a particular intervention or condition or they may quickly become outdated as business models develop. Different methodologies are used to measure the NRAs performance on CT oversight activities. In this case, the assessor should verify that adequate supporting documents are available. The assessor should consider that developed performance indicators should be Specific, Measurable, Achievable, Realistic, and Time-bound (i.e., "SMART"). Scoring this sub-indicator as "not applicable NA" is excluded (i.e. this sub-indicator will always apply for all benchmarked NRAs).
Sub Indicator:	**CT06.03: Progress reports from sponsors or CROs during and after CTs sent to and shared among NRAs and ECs.**
Maturity Level:	3
Scope:	1. Medicines 2. Vaccines
Description:	The assessor should verify the establishment and implementation of mechanisms to receive, store and disseminate information received from stakeholders during and after CTs. The mechanism should be supported with guidelines that state that feedback reports along the entire CT chain should be sent periodically by the sponsor (or CRO) to the NRAs and ECs. Receipt of the reports should be documented by the NRAs and ECs. The guidelines should provide guidance on the content and format for preparing the reports, as well as guidance on the procedures for submitting the reports. In addition, SOPs should provide guidance on how to review, summarize and store the reports received. The database where reports are kept should be documented.
Objective:	The objective of this sub-indicator is to ensure a progress reporting and documentation system is in place to receive, store and disseminate reports from sponsors or CROs.
Requirement:	Accessibility and availability of feedback from stakeholders
Evidence to review:	The assessor should ask for and review: 1. The guidelines that stipulate that feedback reports along the entire CT chain should be sent periodically by the sponsor (or CRO) to the NRAs and ECs and that the NRAs and ECs should document receipt of the reports. The content of these reports may differ between NRA and ECs. 2. Guidelines on the content and format for preparing the reports, as well as on the procedure for submitting the reports. 3. Documented list of reports received from sponsors or CROs. Content and format should be reviewed for compliance with guidelines 4. Examples of reports from sponsors and CROs. 5. Documentation for the database or data storage facility where the reports are stored.
References:	1. Guidelines on clinical evaluation of vaccines: regulatory expectations, (38), (https://www.who.int/biologicals/WHO_ECBS/en/ and https://www.who.int/biologicals/vaccines/en/) 2. WHO guidelines on nonclinical evaluation of vaccines, (39), (https://www.who.int/biologicals/WHO_ECBS/en/ and https://www.who.int/biologicals/vaccines/en/) 3. WHO guidelines on the nonclinical evaluation of vaccines adjuvants and adjuvanted vaccines, (119), (https://www.who.int/biologicals/WHO_ECBS/en/ and https://www.who.int/biologicals/vaccines/en/)

Framework:	Process
Rating Scale:	➔ NOT IMPLEMENTED (NI): There is no mechanism for feedback and progress reporting between sponsors or CROs and NRAs and ECs during and after CTs. ➔ ONGOING IMPLEMENTATION (OI): There are draft guidelines to define feedback mechanisms and to send progress reports from sponsors or CROs to NRAs and ECs during and after CTs; however, it is not followed. ➔ PARTIALLY IMPLEMENTED (PI): There are mechanisms for feedback and progress reporting from sponsors or CROs to NRAs and ECs during and after CTs, however all reports are not available. ➔ IMPLEMENTED (I): There are mechanisms for feedback and progress reporting from sponsors or CROs to NRAs and ECs during and after CTs. The mechanisms have been established for more than two years and are supported with adequate documentation, guidelines and records.
Limitations and remarks:	Scoring this sub-indicator as "not applicable NA" is excluded (i.e. this sub-indicator will always apply for all benchmarked NRAs).
Sub Indicator:	**CT06.04: There are timelines for the assessment of CT applications and an internal tracking system to follow the targeted time frames.**
Maturity Level:	3
Scope:	1. Medicines 2. Vaccines
Description:	The assessor should verify the establishment and implementation of documented timelines and internal timeline tracking systems that guide the CT application processing. These timelines should be supported by guidelines requiring that CT applications should be processed and assessed according to published timelines. The timelines should be monitored internally for compliance. The guidelines should be supported with SOPs that provide guidance on how to establish the timelines and how to monitor the established timelines. The guidance should be designed to be adaptable for routine and non-routine CT applications (e.g., public health emergencies). In addition, the guidance should be designed to address each stage of the CT application process flow. The timelines should be known by all stakeholders for the purposes of transparency and trust.
Objective:	The objective of this sub-indicator is to ensure that timelines exist for processing CT applications and that internal systems or mechanisms are in place to monitor the CT application processing for compliance with the timelines.
Requirement:	Availability of timelines and a system to monitor processing of CT applications
Evidence to review:	The assessor should ask for and review: 1. The guidelines that stipulate that CT applications should be processed and assessed according to prescribed timelines. 2. Regulations establishing that timelines for CT application assessment should be internally monitored for compliance with published timelines. 3. Documentation for the prescribed timelines for CT application assessment, and guidelines for the internal tracking system used to monitor the timelines for effectiveness; 4. Sample report from the internal tracking system for CT application assessment. Assessor should review for content as well as for compliance with CT application assessment guidelines. 5. The work schedules and work plans for staff responsible for monitoring timelines.
References:	1. Guidelines on clinical evaluation of vaccines: regulatory expectations, (38), (https://www.who.int/biologicals/WHO_ECBS/en/ and https://www.who.int/biologicals/vaccines/en/) 2. WHO guidelines on nonclinical evaluation of vaccines, (39), (https://www.who.int/biologicals/WHO_ECBS/en/ and https://www.who.int/biologicals/vaccines/en/) 3. WHO guidelines on the nonclinical evaluation of vaccines adjuvants and adjuvanted

	vaccines, (119), (https://www.who.int/biologicals/WHO_ECBS/en/ and https://www.who.int/biologicals/vaccines/en/)
Framework:	Process
Rating Scale:	➜ NOT IMPLEMENTED (NI): There are no defined timelines for the assessment of CT applications and no internal tracking system to follow the targeted time frames. ➜ ONGOING IMPLEMENTATION (OI): There are drafted timelines and an internal tracking system to follow the targeted time frames for the assessment of CT; however, they are not followed. ➜ PARTIALLY IMPLEMENTED (PI): The timelines for the assessment of CT applications are defined; however, the internal tracking system to follow the targeted time frames has not been fully documented. ➜ IMPLEMENTED (I): The timelines for the assessment of CT applications and an internal tracking system to follow the targeted time frames have been implemented for more than two years.
Limitations and remarks:	Scoring this sub-indicator as "not applicable NA" is excluded (i.e. this sub-indicator will always apply for all benchmarked NRAs).

09

NRA Lot Release (LR): Indicators and Fact Sheets

WHO Global Benchmarking Tool (GBT) for Evaluation of National Regulatory System of Medical Products

09. NRA Lot Release (LR): Indicators and Fact Sheets

Function:	09 – NRA LOT RELEASE (LR)
Description:	National Regulatory Authority (NRA) lot release (also called official authority batch release) is a non-common regulatory function that does not apply to all medical products. Lot release is a system specifically established for the regulatory release of specified biological products. The goal of the regulatory function is to ensure the quality, safety and efficacy of biological products through a regulatory release system. Lot release is done on a lot-by-lot basis and takes into account the nature and inherent variability of these products. NRAs should have the legal mandate to perform independent lot release. They should develop and implement the necessary policies, guidelines, procedures and forms in line with World Health Organization and major international guidelines. In the case of vaccines, different approaches are currently used for conducting lot release. The options include: review of the summary protocols only, review of the summary protocols combined with independent testing (i.e., either full or selected testing), and recognition and acceptance of lot release certificates from the responsible NRA or National Control Laboratory (NCL). The NRA or NCL has the responsibility to decide on an appropriate strategy for each vaccine. The decision should take into consideration the nature of the vaccine, the post-marketing experience for each vaccine (including production history and safety profile), and the availability of other independent evidence of product quality.
Indicator:	**LR01 Legal provisions, regulations and guidelines required to define regulatory framework of independent lot release by the NRA.**
Objective:	The objective of this indicator is to ensure that NRA activities are backed by legislation and provisions for independent lot release. The lot release of vaccines by regulatory authorities is part of the regulation of vaccines and involves the independent assessment of each lot of a licensed vaccine before it is released onto the market. The impact of using substandard lots may not be known for a very long time (i.e., years). Similarly, safety issues with a particular lot may not be known immediately (i.e., within a few hours) after administration. Due to these delays, there could be a drastic impact if a large number of healthy persons receive a vaccine before a problem is recognized. For these reasons, a careful, independent review of manufacturing and quality control data on every lot is necessary before a lot is marketed.
Category:	01. Legal provisions, regulations and guidelines
Sub Indicator:	**LR01.01: Legal provisions and regulations exist to conduct and enforce lot release for all vaccines.**
Maturity Level:	1
Scope:	Vaccines
Description:	The assessor should verify the existence of legal provisions, regulations or other administrative provisions that give the National Regulatory (NRA) authority to implement and enforce lot release for vaccines. The legal provisions should define the responsible officer authorized to sign the regulatory lot release certificate. The assessor should verify that the legal basis to perform lot release applies for all vaccines marketed in the country and includes Expanded Programme on Immunization and non- Expanded Programme on Immunization vaccines as well as imported and domestically- produced vaccines. Current approaches for conducting lot release of

	vaccines include: review of the summary protocol only; review of the summary protocol with independent testing (i.e., either full or selected testing); and recognition and acceptance of lot release certificates from the responsible NRA or National Control Laboratory (NCL). These approaches are not mutually exclusive and different approaches may be used for different products in the same country. It is the responsibility of the NRA or NCL to decide on the appropriate strategy for each vaccine, taking into consideration the nature of the vaccine, the post-marketing experience (including production history and safety profile) for the vaccine, and the availability of other independent evidence of product quality. The assessor should verify that the criteria have been defined when the NRA may elect to follow non-routine procedures for lot release. Reasons for exemption from lot release could include, for example, a shortage of a product on the market or the need to import a non-authorized product for a defined time. The assessor should verify that legal provisions and regulations permit the use of a fast -track mechanism with specific lot release requirements.
Objective:	The objective of this sub-indicator is to ensure that lot release of vaccines is part of the regulatory framework and involves the independent assessment of each lot of a licensed vaccine before it is released on to the market. Each country should establish the national guidelines for lot release. The guidelines should define all required procedures, from the submission of the lots for release to the issuance of lot release certificates. All vaccines lots should be released by an NRA or NCL; however, in defined exceptional circumstances (e.g., a public health emergency), exemptions could be allowed.
Requirement:	Lot release regulatory framework and regulations for lot release of all vaccines.
Evidence to review:	The assessor should ask for and review: 1. Legal provisions for lot release; 2. Documented procedures and records to ensure that staff participating in lot release function contribute, as appropriate, to other regulatory functions; 3. Legal provisions and regulations that require lot release for all vaccines; 4. Legal provisions and regulations for exemptions from lot release exist; 5. Legal provisions and regulations defining fast-track mechanism for lot release; 6. List of products, if any, where the routine procedure for independent lot release may have not been followed.
References:	1. Guidelines for independent lot release of vaccines by regulatory authorities, (42), (https://www.who.int/biologicals/WHO_ECBS/en/ and http://apps.who.int/medicinedocs/en)
Framework:	"Structure/Foundation/Input"
Rating Scale:	➜ NOT IMPLEMENTED (NI): There is no legal basis for lot release. ➜ ONGOING IMPLEMENTATION (OI): The NRA is preparing to establish the legal basis, but there is no evidence of results from such activities. ➜ PARTIALLY IMPLEMENTED (PI): The legal basis was established recently and is at the implementation stage, so this practice is not consolidated yet. ➜ IMPLEMENTED (I): The NRA has the legal provisions and also consistently maintains documentation of related activities over time.
Limitations and remarks:	Scoring this sub-indicator as "not applicable NA" is excluded (i.e. this sub-indicator will always apply for all benchmarked NRAs).
Sub Indicator:	**LR01.02: Acceptance policy and criteria for lot release performed by another NRA are documented.**
Maturity Level:	2
Scope:	Vaccines

Description:	If the country does not have the capacity to perform lot release on its own, the assessor should determine whether the country recognizes certificates from the country of origin or from other competent NRAs and NCLs. Different processes are used for implementing this recognition. Examples of these processes include establishment of a list of countries that are acceptable to the importing country or creation of mutual recognition agreements. Establishment of mutual recognition agreements is a legal approach. Many NRAs and NCLs use such agreements to: enhance international regulatory cooperation in order to maintain high standards of product safety and quality; reduce the regulatory burden for NRAs and NCLs and manufacturers; and improve the free flow of goods and increase the accessibility of medical products globally. Reciprocal mutual recognition of release certificates involves a number of legal aspects that should be addressed. However, the key to successful mutual recognition is the building of mutual confidence among the interested parties. This requires strong collaboration and communication among the different NRAs and NCLs and a good level of transparency. Situations may exist where a two-way recognition of certificates or test results is not possible, owing to technical or other limitations. However, even in cases where reciprocity is not attainable, an NRA or NCL may still wish to recognize a release certificate from another NRA or NCL. This should be possible, provided the releasing NRA or NCL has clearly established procedures that are transparent and relevant to the NRA or NCL wishing to recognize the certificate or test results.
Objective:	The objective of this sub-indicator is to ensure that, in cases when a lot has already been released by another NRA or NCL, it may be possible for the NRA to accept that lot for release on the basis of the existing release certificate.
Requirement:	Recognition of other NRA's decision
Evidence to review:	The assessor should ask for and review: 1. Documented provisions and criteria for recognition of decisions, reports or certificates from other authorities; 2. Documentation for the recognition decision process including its rationale and reasoning; 3. List of NRAs or NCLs that are considered acceptable
References:	1. Guidelines for independent lot release of vaccines by regulatory authorities, (42), (https://www.who.int/biologicals/WHO_ECBS/en/ and http://apps.who.int/medicinedocs/en)
Framework:	"Structure/Foundation/Input"
Rating Scale:	➜ NOT IMPLEMENTED (NI): There is no evidence of the policies mentioned in the indicator. ➜ ONGOING IMPLEMENTATION (OI): The NRA is preparing to draft such policies or procedures, but there is no evidence of results from such activities. ➜ PARTIALLY IMPLEMENTED (PI): The policy was established recently and is at the implementation stage, so this practice is not consolidated yet. ➜ IMPLEMENTED (I): The NRA has such policies and procedures and also consistently maintains documentation of related activities over time.
Limitations and remarks:	▪ In some counties, the legal framework prevents the NRA or NCL from recognizing decisions from other NRAs. In such cases, this sub-indicator should be scored as non- applicable. ▪ The product's manufacturer should be involved in the establishment of an agreement for sharing product information, since there are issues of confidentiality that need to be addressed.
Indicator:	**LR02 Arrangement for effective organization and good governance.**
Objective:	The objective of this indicator is to establish that structures are in place at the organizational and governance levels to promote effective intra- and inter-NRA and NCL relationships and efficient management of information traffic.

	The quality, safety and efficacy of a medical product, such as a vaccine, are the responsibility of the manufacturer. The regulatory authority of the country is responsible for establishing procedures to ensure that this responsibility is met. The same requirements for regulatory oversight should apply to the production of all vaccines, regardless of whether they are intended for domestic use or for export.
Category:	01. Legal provisions, regulations and guidelines
Sub Indicator:	**LR02.01: There is a defined organizational structure with clear responsibilities to conduct independent lot release activities.**
Maturity Level:	2
Scope:	Vaccines
Description:	The assessor should verify that roles and responsibilities for all regulatory entities involved in the independent lot release are documented and implemented. It is critical that the roles and responsibilities of both the NRA and the NCL are clearly defined, particularly when they are separate entities. When all elements are available for final evaluation, a formal decision-making process should be in place to decide whether the lot can be released.
Objective:	The objective of this sub-indicator is to ensure there are appropriate structures in place, with clearly defined roles and responsibilities for each entity involved in lot release activities.
Requirement:	Roles and responsibilities in regard to lot release function
Evidence to review:	The assessor should ask for and review: 1. Written document defining organizational structure, with clearly-defined responsibilities, to conduct independent lot release activities; 2. Documented evidence designating the post holder responsible for signing lot release certificates; 3. Organization chart including the department, unit, group or post holder responsible for independent lot release.
References:	1. Guidelines for independent lot release of vaccines by regulatory authorities, (42), (https://www.who.int/biologicals/WHO_ECBS/en/ and http://apps.who.int/medicinedocs/en) 2. Quality management systems — Requirements. International Standard ISO 9001:2015. International Organization for Standardization, 2015, (4), (https://www.iso.org/iso-9001-quality-management.html)
Framework:	"Structure/Foundation/Input"
Rating Scale:	➜ NOT IMPLEMENTED (NI): There is no defined structure with clear responsibilities to conduct independent lot release activities. ➜ ONGOING IMPLEMENTATION (OI): The NRA is preparing to establish the legal basis, but there is no evidence of results from such activities. ➜ PARTIALLY IMPLEMENTED (PI): The legal basis was established recently and is at the implementation stage, so this practice is not consolidated yet. ➜ IMPLEMENTED (I): The NRA has defined a structure with clear responsibilities to conduct independent lot release activities and consistently maintains documentation of related activities over time.
Limitations and remarks:	Scoring this sub-indicator as "not applicable NA" is excluded (i.e. this sub-indicator will always apply for all benchmarked NRAs).
Sub Indicator:	**LR02.02: Documented procedures are implemented to ensure coordination and communication among all regulatory entities involved in independent lot release.**
Maturity Level:	3

Scope:	Vaccines
Description:	The assessor should review the adequacy of the implemented coordination mechanisms. Lot release is one component of a regulatory framework which includes marketing authorization (MA), good manufacturing practices (GMP) inspection, and post-marketing surveillance. The relationship between NRA and NCL varies from country to country, but in all cases, it is essential that the different entities of the regulatory structure interact and exchange information effectively. Good coordination and communication are needed, especially when different regulatory entities are involved in this process.
Objective:	The objective of this sub-indicator is to ensure that documented procedures, structures, and mechanisms are implemented for proper relationships within and among entities involved in lot release, quality control (QC) laboratory testing, MA and facilities inspection. These coordination mechanisms will ensure effective and efficient exchange of information for lot release activities.
Requirement:	Communication among all regulatory entities relevant to independent lot release.
Evidence to review:	The assessor should ask for and review: 1. Documentation that defines role and responsibilities; 2. Documentation for established communication channels (i.e., written documents that describe methodology and procedures); 3. Records of relevant communications; 4. Records of regulatory actions taken based on lot release findings
References:	1. Guidelines for independent lot release of vaccines by regulatory authorities, (42), (https://www.who.int/biologicals/WHO_ECBS/en/ and http://apps.who.int/medicinedocs/en)
Framework:	"Structure/Foundation/Input"
Rating Scale:	➜ NOT IMPLEMENTED (NI): There are no documented procedures to ensure coordination and communication among all regulatory entities involved in independent lot release. ➜ ONGOING IMPLEMENTATION (OI): The NRA is preparing to establish the procedure, but there is no evidence of results from such activities. ➜ PARTIALLY IMPLEMENTED (PI): The procedure was established recently and is at the implementation stage, so this practice is not consolidated yet. ➜ IMPLEMENTED (I): The NRA has documented procedures and also consistently maintains documentation of related activities over time.
Limitations and remarks:	Scoring this sub-indicator as "not applicable NA" is excluded (i.e. this sub-indicator will always apply for all benchmarked NRAs).
Indicator:	**LR03 Human resources to perform NRA lot release.**
Objective:	The objective of this indicator is to ensure that all entities within an NRA are adequately resourced with a trained, experienced and skilled workforce, and are empowered to fully perform the function of independent lot release. This will ensure that NRA lot release activities are performed in accordance with international best practices. The objective of this indicator is to evaluate the human resource capacity of the entities with respect to the number of personnel, the skills and experience of the personnel, and the overall composition the workforce, with the goal of evaluating whether the workforce possesses the specific expertise required to perform the NRA lot release function.
Category:	Resources (HR, FR, infrastructure and equipment)

Sub Indicator:	**LR03.01: Sufficient competent staff (i.e., education, training, skills and experience) are assigned to perform NRA lot release activities.**
Maturity Level:	3
Scope:	Vaccines
Description:	The assessor should verify that the human resources assigned to perform NRA lot release activities should be sufficient with respect to numbers and competent with respect to the requisite skills, education, experience and training. There should be technical documents and standard operating procedures (SOPs) that provide guidance on the required background for NRA lot release activities and that consider the requirements for educational background, competencies, skills, experience, and training. The assessor should verify that the NRA estimated the number of staff required to effectively and efficiently perform NRA lot release function and that the NRA actually recruited that number. In addition, the assessor should verify that these competency requirements are well-established and maintained by the NRA. Metrics and statistics on the different activities performed as well as performance indicators can be used for estimating the adequacy of the number of the assigned staff. The assessor should also verify that the competency of the assigned staff is built, maintained and improved through recruitment as well as continuous on-the-job training.
Objective:	The objective of this sub-indicator is to ensure the existing human resources for NRA lot release is sufficient, in terms of numbers, experience, and specific competencies, to perform all the activities along the entire NRA lot release chain.
Requirement:	Sufficient number of competent human resources in charge of NRA lot release activities.
Evidence to review:	The assessor should ask for and review: 1. Evidence that the number of staff members involved in each of the documented activities along the entire NRA lot release process flow is adequate. 2. Evidence that the systems and structures are in place to ensure appropriate placement of staff with respect to competence and skills. 3. Evidence that the system and structures have been implemented. The documentation should include the records to verify that the staff competence is appropriate for the job requirements. 4. Evidence that the professional profiles of the human resources engaged in NRA lot release activities are appropriate with respect to education, skills, and expertise, to perform a particular function along the NRA lot release chain. Documentation should include a list of the requisite skills and training for each position. 5. Recruitment plan.
References:	1. National drug regulatory legislation: guiding principles for small drug regulatory authorities. In: WHO Expert Committee on Specifications for Pharmaceutical Preparations: thirty-fifth report. Geneva: World Health Organization; 1999: Annex 8 (WHO Technical Report Series, No. 885), (1), (http://apps.who.int/medicinedocs/documents/s21964en/s21964en.pdf)
Framework:	Structure/Foundation/Input
Rating Scale:	➜ NOT IMPLEMENTED (NI): The NRA does not have enough competent staff (i.e., education, training, skills and experience) to perform NRA lot release activities ➜ ONGOING IMPLEMENTATION (OI): The NRA has recently developed a plan to recruit adequate competent staff; however, the plan has not been implemented. ➜ PARTIALLY IMPLEMENTED (PI): The NRA has initiated the implementation of the human resources development plan; however, there is need to complete the competency profile. ➜ IMPLEMENTED (I): The NRA has a sustained number of competent staff (i.e., education, training, skills and experience) assigned to perform NRA lot release activities

Limitations and remarks:	Assessment of the adequacy and appropriateness of the number of staff members is quite subjective and should be linked to some process or output indicators. When estimating staff adequacy, the assessor should consider the workload, backlog, and delays in delivery based on established timeframes. Scoring this sub-indicator as "not applicable NA" is excluded (i.e. this sub-indicator will always apply for all benchmarked NRAs).
Sub Indicator:	**LR03.02: Duties, functions, and responsibilities of the staff in charge of NRA lot release activities are established and updated in the respective job descriptions.**
Maturity Level:	3
Scope:	Vaccines
Description:	The assessor should verify that procedures are in place to maintain a current and updated structure for managing job descriptions for personnel participating in NRA lot release activities. In addition, job descriptions should address current staff duties, responsibilities and the requisite competencies. A job description with this format and content should be established and implemented for all staff. The management of job descriptions should be supported by a guidance document that provides direction on when and how to update the information, and where the information should be kept for easy access. The guidance document should present the appropriate duties and responsibilities that are assigned to each member of the organization involved in NRA lot release activities. Thus, the professional profiles of staff are reflected in their respective roles and responsibilities within the NRA. There should be procedures to guide responsible persons to document that duties, functions and responsibilities are revised and kept up to date. In addition, procedures should be available to guide the keeping and documenting of up to date work schedules and enforcing the implementation of the documented guidelines and procedures.
Objective:	The objective of this sub-indicator is to ensure that duties and responsibilities of the staff are clear and well defined, that job descriptions are kept up to date with current duties, functions and responsibilities, and that these activities are adequately documented.
Requirement:	Duties, roles and responsibilities of the staff relevant to NRA lot release activities.
Evidence to review:	The assessor should ask for and review: 1. Procedure and guidelines that guide placement of staff members within the NRA; 2. The professional profiles of staff (i.e., job descriptions) and documentation that they are related to their current roles and duties; 3. The professional profiles of the external experts and documentation that the profiles provide a composition that is complete and consistent with that prescribed in the legal provisions; 4. Procedures to guide the documentation of up to date duties and work schedules, and to enforce the implementation of the documented guidelines and procedures; 5. Job descriptions for designated staff.
References:	1. National drug regulatory legislation: guiding principles for small drug regulatory authorities. In: WHO Expert Committee on Specifications for Pharmaceutical Preparations: thirty-fifth report. Geneva: World Health Organization; 1999: Annex 8 (WHO Technical Report Series, No. 885), (1), (http://apps.who.int/medicinedocs/documents/s21964en/s21964en.pdf) 2. Quality management systems — Requirements. International Standard ISO 9001:2015. International Organization for Standardization, 2015 sub-clause 5.1.1, (4), (https://www.iso.org/iso-9001-quality-management.html) 3. Guiding principles for small national drug regulatory authorities. In: WHO Expert Committee on Specifications for Pharmaceutical Preparations: thirty-first report. Geneva: World Health Organization; 1990: Annex 6 (WHO Technical Report Series, No. 790), (5), (http://apps.who.int/medicinedocs/documents/s21964en/s21964en.pdf) 4. Effective drug regulation: A multicountry study. Geneva: World Health Organization; 2002, (7), (http://apps.who.int/medicinedocs/pdf/s2300e/s2300e.pdf)

Framework:	Structure/Foundation/Input
Rating Scale:	➜ NOT IMPLEMENTED (NI): There is no evidence of defined or established duties, functions, responsibilities, respective job descriptions and necessary required competencies. ➜ ONGOING IMPLEMENTATION (OI): The NRA has recently drafted or developed the role and responsibilities document but it has not yet been implemented. ➜ PARTIALLY IMPLEMENTED (PI): The NRA has initiated implementation of this requirement but it has not been defined or followed for all staff or the roles and responsibilities documents, including staff job descriptions, are not up to date. ➜ IMPLEMENTED (I): The NRA has defined and established all required duties, functions, and responsibilities, and respective job descriptions are up-to-date.
Limitations and remarks:	Scoring this sub-indicator as "not applicable NA" is excluded (i.e. this sub-indicator will always apply for all benchmarked NRAs).
Sub Indicator:	**LR03.03: Training plan developed, implemented and updated at least once a year for staff in charge of NRA lot release activities.**
Maturity Level:	3
Scope:	Vaccines
Description:	The assessor should verify that training plans are developed, implemented and updated at least once every year to reflect the current situation by considering education and experience of the staff. The training plan should be complemented with guidelines or similar documents that guide the development and implementation of training plans. The assessor should ensure that induction training for new staff as well as continued on- the-job training for staff is planned and implemented. There should be procedures to approve the training plan and the budget allocated for implementing and updating the training plan. The plans should present clearly defined training goals and should include training in certain topics and skills to address identified deficiencies. Learning objectives, training methods and activities, evidence of learning, and evaluation and assessment of training should be documented. This documentation should confirm that the learning objectives were achieved and were designed to address weaknesses within the entities. Procedures should be in place to ensure that a training plan is developed, implemented and updated at least once every year. The assessor should verify that there is a system in place for monitoring the implementation and effectiveness of the training plan and for documenting the skills acquired in training activities for internal and external experts.
Objective:	The objective of this sub-indicator is to ensure that a training plan for staff exists, and that it is implemented and updated annually. Through the training plan, NRA can be sure that competency of staff in charge of NRA lot release activities is maintained and enhanced.
Requirement:	Implementation of training plan
Evidence to review:	The assessor should ask for and review: 1. Guidelines for development, implementation and annual update (i.e., at least once per year) of the training plan. Guidelines should also provide for a mechanism to measure effectiveness of training. 2. Documentation for the system or structures used to approve the training plan and to evaluate the adequacy of the budget allocated to the training activities. 3. The current or existing staff training plan (or matrix) for staff. The assessor should assess this in in relation to the respective individual job descriptions. 4. SOP for developing and maintaining the training plan. 5. Evidence that the NRA has investigated and identified training needs. 6. List of trainings performed. 7. Example records for training activities.

References:	1. Effective drug regulation: A multicountry study. Geneva: World Health Organization; 2002, (7), (http://apps.who.int/medicinedocs/pdf/s2300e/s2300e.pdf) 2. Quality systems requirements for national good manufacturing practice inspectorates. In: WHO Expert Committee on Specifications for Pharmaceutical Preparations: thirty-sixth report. Geneva: World Health Organization; 2002: Annex 8 (WHO Technical Report Series, No. 902), (8), (http://apps.who.int/medicinedocs/documents/s22112en/s22112en.pdf)
Framework:	Process
Rating Scale:	➜ NOT IMPLEMENTED (NI): There is no systematic training program including training plan (or matrix). ➜ ONGOING IMPLEMENTATION (OI): The NRA has recently drafted or developed the training plan but there is no evidence of implementation. ➜ PARTIALLY IMPLEMENTED (PI): The NRA has developed and initiated the training plan implementation. However, the NRA has not fulfilled all required planned training or has been applying the plan for less than two years. ➜ IMPLEMENTED (I): The NRA has an updated training plan developed that is supported by adequate records to demonstrate effective plan implementation, including induction training for new staff and routine on-the-job training for recruited staff.
Limitations and remarks:	▪ Training plans must be updated regularly; ideally on an annual basis, but not less frequently that once every two years. ▪ Some regulatory functions may include many training activities that are not incorporated in the institutional training programme. Such training normally is offered by invitation. In this case, the assessor should recognize reports from non-routine NRA lot release-relevant training not included in the NRA training plan. ▪ Scoring this sub-indicator as "not applicable NA" is excluded (i.e. this sub-indicator will always apply for all benchmarked NRAs).
Sub Indicator:	**LR03.04: The NRA generates and maintains records of staff training activities and training effectiveness verification.**
Maturity Level:	3
Scope:	Vaccines
Description:	The assessor should verify that records of staff training that is performed or organized by the NRA are generated, maintained, regularly updated. This activity should be supported by guidelines that direct the NRA to generate and maintain records of staff training activities. Procedures should be in place to document and propose staff training needs and to allocate a budget for continuous staff capacity building and development. The assessor should check that there is an evaluation or assessment mechanism to verify the quality of learning, and to confirm that learning objectives are achieved. Documentation should include an inventory (i.e., soft and/or hard) system that records all impactful and non-impactful trainings and identifies all staff members who participated. A system to measure or estimate impact of trainings should be established.
Objective:	The objective of this sub-indicator is to ensure that training organized by the NRA or responsible regulatory authority is adequately documented and that the training records are adequately maintained and kept. Staff training records are considered an integral part of staff file and are a tool for measuring and tracking staff competency, development and adequacy.
Requirement:	Training records
Evidence to review:	The assessor should ask for and review: 1. Guidelines or similar documents that guide the NRA to generate and maintain records of staff training activities; 2. Evaluations of training effectiveness;

	3. The training inventory, and procedures for completing the inventory; 4. Examples of archived records of staff training, and procedures for the archiving system
References:	1. National drug regulatory legislation: guiding principles for small drug regulatory authorities. In: WHO Expert Committee on Specifications for Pharmaceutical Preparations: thirty-fifth report. Geneva: World Health Organization; 1999: Annex 8 (WHO Technical Report Series, No. 885), (1), (http://apps.who.int/medicinedocs/documents/s21964en/s21964en.pdf) 2. Quality management systems — Requirements. International Standard ISO 9001:2015. International Organization for Standardization, 2015 sub-clause 5.1.1, (4), (https://www.iso.org/iso-9001-quality-management.html) 3. Guiding principles for small national drug regulatory authorities. In: WHO Expert Committee on Specifications for Pharmaceutical Preparations: thirty-first report. Geneva: World Health Organization; 1990: Annex 6 (WHO Technical Report Series, No. 790), (5), (http://apps.who.int/medicinedocs/documents/s21964en/s21964en.pdf) 4. Effective drug regulation: A multicountry study. Geneva: World Health Organization; 2002, (7), (http://apps.who.int/medicinedocs/pdf/s2300e/s2300e.pdf)
Framework:	Output
Rating Scale:	➔ NOT IMPLEMENTED (NI): There is no evidence that the NRA generates and maintains records of staff training activities. ➔ ONGOING IMPLEMENTATION (OI): The NRA has recently initiated plans to generate, document and keep records of staff training activities, however they are not yet followed. ➔ PARTIALLY IMPLEMENTED (PI): The NRA has recently initiated plans to generate, document and keep records of staff training activities but they are not fully followed for all training activities or they have been established for less than two years. ➔ IMPLEMENTED (I): The NRA generates and maintains records of staff training activities.
Limitations and remarks:	▪ The assessor should note that some NRAs out-source training including staff capacity development activities. In this case the assessor should request the identity of the provider, as well as evaluations of the provider. The assessor may request the professional profiles of tutors or resource persons used to offer training. The assessor may also request records covering the archiving systems in place. ▪ Scoring this sub-indicator as "not applicable NA" is excluded (i.e. this sub-indicator will always apply for all benchmarked NRAs).
Indicator:	**LR04 Procedures established and implemented to perform NRA lot release.**
Objective:	The objective of this indicator is to ensure documented and implemented procedures to perform independent lot release. The lot release of vaccines by regulatory authorities is part of the regulation of vaccines and involves the independent assessment of each lot of a licensed vaccine before it is released onto the market. This assessment is based, at a minimum, on the review of manufacturer's summary protocols. Lot release may be supplemented by other documents such as the release certificates from the responsible NRA or NCL. In some circumstances, this information is also supplemented by product testing that is independent of the manufacturer's quality control testing. The summary protocol content should follow existing guidelines from the World Health Organization Technical Report Series or other internationally-accepted guidelines. If accepted guidelines are not available, the country should define the summary protocol template for the product. Current approaches to conducting lot release of vaccines include: review of the summary protocols only, review of the summary protocols combined with independent testing (i.e., either full or selected testing), and recognition and acceptance of lot release certificates from the responsible NRA or NCL. These approaches are not mutually exclusive and different approaches may be used for different products in the same country. It is the

	responsibility of the NRA or NCL to decide on an appropriate strategy for each vaccine, taking into consideration the nature of the vaccine, the post-marketing experience for the vaccine (including production history and safety profile), and the availability of other independent evidence of product quality.
Category:	07. Regulatory process
Sub Indicator:	**LR04.01: Independent lot release is based, at a minimum, on summary lot protocol review and the appropriate documentation exists.**
Maturity Level:	2
Scope:	Vaccines
Description:	The assessor should verify that summary lot protocols are mandatorily required for the lot release of vaccines. The assessor should make sure the NRA or NCL issue lot release certificates based, at a minimum, on the review of the summary lot protocols issued by the manufacturer. The protocol review should be performed by comparing the critical data of each lot (including testing data) to the licensed product specifications. The assessor should verify that the SOP for summary protocol review describes the steps and criteria required for a complete review of the summary protocol. The SOP should cover all review steps up to and including the final conclusion based on review of the summary protocol. When needed, these steps may include a request for corrections from the manufacturer and a review of corrected pages. In some cases, the NRA or NCL may elect to conduct an investigation before reaching a conclusion. The NRA or NCL should produce a formal written conclusion regarding the summary protocol review. A summary decision form should be filled out to verify that the product complied with approved specifications. This summary decision should be signed by the responsible staff. The assessor should determine whether the competent authority's approach to independent lot release is appropriately described in the NRA or NCL process charts. Procedures should cover the options used: release upon review of summary protocol only or release upon review of summary protocol plus independent testing by the NCL. The procedures should also define how and by whom the final decision is made. The summary decision form should define the specific option used and include a formal written conclusion. SOPs or documents are necessary to cover the essential elements.
Objective:	The objective of this sub-indicator is to ensure that summary lot protocols are mandatorily required, at a minimum, for vaccines lot release. The manufacturers' summary protocols summarize information taken from the production and QC to ensure that the lot meets the specifications in the approved MA. In addition, summary protocols submitted to the NRA or NCL should be approved by the person from the manufacturer who is designated as responsible for quality assurance or QC. In general, the format and content of the protocol is finalized and approved by the NRA or NCL during the review of the license application. The format of the protocol should be amended in response to changes in the approved production process. Amendments to the protocol should be approved by the NRA or NCL.
Requirement:	Documentation for national lot release
Evidence to review:	The assessor should ask for and review: 1. SOP or guideline for performing lot release; 2. List of required documents for performing lot release; 3. Relevant written and enforced SOPs developed as part of the quality management system for reviewing lot release protocols for each product; 4. Examples of lot release records; 5. Documented evidence of evaluation process.
References:	1. Guidelines for independent lot release of vaccines by regulatory authorities, (42), (https://www.who.int/biologicals/WHO_ECBS/en/ and http://apps.who.int/medicinedocs/en)

	2. WHO Expert Committee on Biological Standardization (ECBS), Vaccine-specific standardization, (135), (https://www.who.int/biologicals/vaccines/en/) 3. Guidelines for EU Official Control Authority Batch Release, European Directorate for the Quality of Medicines and Healthcare (EDQM), Council of Europe, (104), (https://www.edqm.eu/en/human-ocabr-guidelines)
Framework:	Process
Rating Scale:	➜ NOT IMPLEMENTED (NI): No procedures for lot release based, at a minimum, on summary protocol review are available. ➜ ONGOING IMPLEMENTATION (OI): The NRA is preparing the procedures but there is no evidence of results from such activities (i.e., reports or certificates). ➜ PARTIALLY IMPLEMENTED (PI): The procedure was established recently and is at the implementation stage, so this practice is not consolidated yet. ➜ IMPLEMENTED (I): The NRA has procedures for lot release based, at a minimum, on summary protocol review and consistently maintains documentation of the results over time.
Limitations and remarks:	Scoring this sub-indicator as "not applicable NA" is excluded (i.e. this sub-indicator will always apply for all benchmarked NRAs).
Sub Indicator:	**LR04.02: NRA or NCL staff involved in lot release have access to MA relevant files and updates.**
Maturity Level:	3
Scope:	Vaccines
Description:	The assessor should verify that the NRA or NCL staff involved in lot release has access to files and updates relevant to MA. NRA or NCL lot release should be performed only for medical products that have a valid MA in which specifications have been approved by the competent NRA or NCL of the country using the vaccine. In addition, the development and adoption of more effective test methods should be encouraged; however, any changes in testing should be approved by the NRA or NCL. If a different test method is used by the NRA or NCL, and if there is a discrepancy in test data between the manufacturer and the NRA or NCL, then the approved test method defined in the MA should be used to resolve the issue.
Objective:	The objective of this sub-indicator is to ensure that specifications as described in the MA are used to judge the test results. Also, there should be a mechanism in place to allow the testing staff of the NRA or NCL to be aware of the latest version of the approved MA specifications. In the decision-making process for MA, the responsible NRA or NCL staff should be involved in assessing the test methods, validity criteria and product specifications.
Requirement:	Access to MA data for lot release
Evidence to review:	The assessor should ask for and review: 1. SOPs that define how MA data are considered for lot release; 2. Records of relevant updated information that was communicated to NRA or NCL.
References:	1. Guidelines for independent lot release of vaccines by regulatory authorities, (42), (https://www.who.int/biologicals/WHO_ECBS/en/ and http://apps.who.int/medicinedocs/en)
Framework:	"Structure/Foundation/Input"
Rating Scale:	➜ NOT IMPLEMENTED (NI): No procedures to define how MA data are considered for lot release are available. ➜ ONGOING IMPLEMENTATION (OI): The NRA is preparing a procedure, but there is no evidence of results from such activities.

	➔ PARTIALLY IMPLEMENTED (PI): The procedure was established recently and is at the implementation stage, so this practice is not consolidated yet. ➔ IMPLEMENTED (I): The NRA has procedures to define how MA data are considered for lot release, and also consistently maintains documentation of the results of related activities over time.
Limitations and remarks:	Scoring this sub-indicator as "not applicable NA" is excluded (i.e. this sub-indicator will always apply for all benchmarked NRAs).
Sub Indicator:	**LR04.03: Analysis of lot-to-lot consistency is conducted.**
Maturity Level:	3
Scope:	Vaccines
Description:	The assessor should verify that statistical analyses are conducted once sufficient data have been accumulated. Alert limits (i.e., warning limits) and action limits should be defined on the basis of statistical assessments and trend analyses of test data. In general, when data are distributed normally, ±2 and ±3 standard deviations from the mean are set for the alert limits (i.e., warning limits) and action limits respectively. The variability and precision of the test should be considered when defining the limits. Care should be taken in interpreting such limits when they are based on small datasets. Trend analyses of key parameters may be requested from manufacturers or from the responsible NRA or NCL. More complex statistical approaches can be used for trend analyses when sufficient data and expertise are available, particularly when data are not normally distributed. In addition, a set of data from a certain period (e.g., 6 months or 1 year) should be analyzed statistically and compared to data from the previous period, in order to detect any significant differences, shifts, or trends. In order to conduct an appropriate trend analysis, it is important to have data from an adequate number of release batches for each product. When the NRA or NCL does not receive consecutive lots, or when it receives only a small number of production lots, interpretation of trends may require additional information (e.g., yearly biological product reports).
Objective:	The objective of this sub-indicator is to ensure that all critical quantitative data from QC testing, especially from potency testing, from the manufacturer or other sources are used for trend analysis as an essential part of lot release.
Requirement:	Data monitoring
Evidence to review:	The assessor should ask for and review: 1. Procedures and mechanisms employed to ensure lot-to-lot consistency. 2. Documentation that these procedures are performed by NRA or NCL on regular basis.
References:	
Framework:	Output
Rating Scale:	➔ NOT IMPLEMENTED (NI): No procedures for analysis of lot-to-lot consistency are available ➔ ONGOING IMPLEMENTATION (OI): The NRA is preparing a procedure for analysis of lot-to-lot consistency but there is no evidence of results from such activities. ➔ PARTIALLY IMPLEMENTED (PI): The procedure was established recently and is at the implementation stage, so this practice is not yet consolidated. ➔ IMPLEMENTED (I): The NRA has such procedures and also consistently maintains documentation of related activities over time.
Limitations and remarks:	▪ Information obtained from lot-to -lot consistency analyses could be used to establish criteria for testing by the NCL.

- Scoring this sub-indicator as "not applicable NA" is excluded (i.e. this sub-indicator will always apply for all benchmarked NRAs).

Indicator:	**LR05 Mechanism for information-sharing exists to promote transparency and accountability.**
Objective:	The objective of this indicator is to ensure that the mechanisms for independent lot release, including requirements and timelines, are made public in a clear and transparent way. In addition, these mechanisms could contribute to informing the public about any risks, e.g., with respect to access, availability or shortages of some medical products subject to national lot release. Public transparency of decision-making and resource-management is one of the principles of truth and accountability.
Category:	08. Transparency, accountability and communication
Sub Indicator:	**LR05.01: Results of lot release process are publicly available.**
Maturity Level:	4
Scope:	Vaccines
Description:	The assessor should verify the existence of a list of product batches that pass or fail NRA lot release. In addition, the assessor should verify that the NRA or NCL has the required authority and an available process to publish the list of product batches that passed or failed NRA lot release. At a minimum, a publicly available website (or another form of communication) should be available to publish the list of product batches that passed NRA lot release. The assessor should determine the frequency at which this information is updated.
Objective:	The objective of this sub-indicator is to ensure that processes and procedures for lot release decision-making, as well as the list of product batches that pass or fail NRA lot release, are documented and available to the public. Transparency enhances public trust, permits the timely application of corrective measures, prevents public use of unqualified products, and promotes the timely identification of potential vulnerabilities due to possible acts of corruption.
Requirement:	Results of lot release process available
Evidence to review:	The assessor should ask for and review: 1. List of product batches that pass or fail NRA lot release; 2. Published list of product batches released; 3. List of product batches released compared with the list of product batches failed; 4. Guideline or SOP that defines the process to publish the list of product batches that passed or failed NRA lot release.
References:	1. Good governance for medicines: Model framework. Updated version 2014. WHO, (110), (https://www.who.int/medicines/areas/governance/ggm_modelframe_updated/en/) 2. Guidelines for independent lot release of vaccines by regulatory authorities, (42), (https://www.who.int/biologicals/WHO_ECBS/en/ and http://apps.who.int/medicinedocs/en)
Framework:	Output
Rating Scale:	➔ NOT IMPLEMENTED (NI): No results of lot release process are available. ➔ ONGOING IMPLEMENTATION (OI): The NRA is preparing a procedure but there is no evidence of results from such activities. ➔ PARTIALLY IMPLEMENTED (PI): The procedure or the list was established recently and is at the implementation stage, so this practice is not yet consolidated. ➔ IMPLEMENTED (I): The NRA has the list with results of lot release process and consistently maintains documentation of related activities over time.

Limitations and remarks:	In some countries, the legal framework does not allow publishing for the public results of product batches that fail lot release. Nevertheless, in case of emergency or risk, the NRA or NCL should inform public in timely manner. There may be specific situations to take into consideration, e.g., during recalls or when specifications are different in country of origin than in country of use.
Sub Indicator:	**LR05.02: Follow-up and communication with involved parties, including the manufacturer, on issues of data quality.**
Maturity Level:	3
Scope:	Vaccines
Description:	The assessor should verify the establishment and implementation of communication procedures with involved parties, including the manufacturer, on issues of data quality. Good communication with the manufacturer of the product is an important element in developing an effective system. NCLs should discuss with the manufacturer the transfer of assays, if required. This should begin as early as possible in the MA process, to allow for transfer, qualification, and validation of the methodology prior to application of the method for lot release testing of the first lot. It is also necessary to establish documented and approved procedures and guidelines for performance of lot release testing, both for internal use and for transparency with regard to partners, including other NCLs and the manufacturer of the product. A procedure to communicate QC and national lot release issues should be developed by the NRA or NCL. These procedures may include formal notifications by memorandum or letter, email communications, or minutes of telephone discussions. Manufacturers' responses should be reviewed and documented when making the decision on the lot. This response can include submission by the manufacturer of a corrected page or revision of the summary protocol. These corrections should then be properly traced by the NRA or NCL as per good documentation practices. Depending upon the nature and severity of the discrepancies or errors, the manufacturer may be asked to perform an investigation to determine the root cause of the issues, and to initiate any corrective and preventive actions required to avoid similar problems in the future. A feedback mechanism from the NCL to the NRA, the GMP inspectorate and the MA staff is highly advisable, in order to coordinate and optimize regulatory actions (e.g., encouraging license variations or refinements in product specification based on trend analyses).
Objective:	The objective of this sub-indicator is to ensure that any discrepancies, errors or out-of- specification results found in the summary protocol submitted are documented and verified before they are communicated to the manufacturer. The manufacturer should be notified when an out-of-specification result is confirmed, and exchanges should ensue to try to identify the cause of the discrepancy.
Requirement:	Follow-up and communication on issues of data quality
Evidence to review:	The assessor should ask for and review: 1. Evidence that the NRA or NCL has a suitable mechanism to follow up and communicate on issues related to data quality with all involved parties such as the manufacturer, importer, wholesaler or user of the products. 2. Written documents that describe the process; 3. Records of any actions.
References:	1. Guidelines for independent lot release of vaccines by regulatory authorities, (42), (https://www.who.int/biologicals/WHO_ECBS/en/ and http://apps.who.int/medicinedocs/en)
Framework:	Process
Rating Scale:	➔ NOT IMPLEMENTED (NI): No procedures or reports are available regarding follow-up and communication with involved parties, including the manufacturer, on issues of data quality.

	➔ ONGOING IMPLEMENTATION (OI): The NRA is preparing a procedure for this but there is no evidence of results from such activities. ➔ PARTIALLY IMPLEMENTED (PI): The procedure was established recently and is at the implementation stage, so this practice is not consolidated yet. ➔ IMPLEMENTED (I): The NRA has such procedures and also consistently maintains records of the results of related activities over time.
Limitations and remarks:	For imported lots, communication with the NRA of the producing or releasing country may be required. For producing or releasing countries, communication with the country inspectorate may be required. Such information exchange can help to evaluate the corrective and preventive actions introduced by the manufacturer. When needed, confidentiality issues should be taken into consideration during the communication process. In some countries, communications among government, manufacturer and NRA are used, for planning purposes, for all batch release processes and not only for product analysis. Scoring this sub-indicator as "not applicable NA" is excluded (i.e. this sub-indicator will always apply for all benchmarked NRAs).
Indicator:	**LR06 Mechanism in place to monitor regulatory performance and output.**
Objective:	The objective of this indicator is to ensure the implementation of a system or mechanism for monitoring regulatory performance and output of the independent lot release function.
Category:	09. Monitoring progress and assessing outcomes and impact
Sub Indicator:	**LR06.01: Lot release records, reports and certificates available.**
Maturity Level:	3
Scope:	Vaccines
Description:	The assessor should verify that there is requirement to issue a certificate of release for all vaccines that have undergone lot release. This release certificate is issued by the responsible NRA or NCL on the basis of, at a minimum, a review of the lot summary protocol for the relevant lot. The assessor should verify that lot-to-lot consistency is appropriately analyzed and documented by the NRA or NCL on regular basis.
Objective:	The objective of this sub-indicator is to ensure that all documentation related to independent lot release is available and readily accessible to internal staff whenever needed. A general lot release process chart that outlines the lot approval process and identifies the persons responsible for each activity should be available. Documentation supporting compliance with approved specifications (i.e., summary protocol review and test reports, if applicable) should also be available.
Requirement:	Documentation system
Evidence to review:	The assessor should ask for and review: 1. SOP describing the acceptance criteria for NCL test results; 2. Records of all the individual test results from the certificates of analysis (i.e., for all lots that have undergone lot release); 3. Records of evaluation of lot release including reports and certificates;
References:	1. Guidelines for independent lot release of vaccines by regulatory authorities, (42), (https://www.who.int/biologicals/WHO_ECBS/en/ and http://apps.who.int/medicinedocs/en)
Framework:	Output

Rating Scale:	➔ NOT IMPLEMENTED (NI): No lot release records, reports or certificates are available. ➔ ONGOING IMPLEMENTATION (OI): The NRA is preparing a procedure for lot release but there is no evidence of results from such activities (i.e., reports or certificates). ➔ PARTIALLY IMPLEMENTED (PI): The procedure was established recently and is at the implementation stage, so this practice is not yet consolidated yet. ➔ IMPLEMENTED (I): The NRA has procedures, records, reports and certificates for lot release and also consistently maintains documentation of related activities over time.
Limitations and remarks:	Scoring this sub-indicator as "not applicable NA" is excluded (i.e. this sub-indicator will always apply for all benchmarked NRAs).
Sub Indicator:	**LR06.02: Corrective actions taken in case of deviations due to laboratory error.**
Maturity Level:	3
Scope:	Vaccines
Description:	The assessor should review that appropriate corrective actions are taken by the NCL in case of deviations (i.e. significant discrepancy between NCL testing results and manufacturer results due to laboratory or operator error and not due to product quality). Depending upon the nature and severity of the discrepancies or errors, the NCL may be asked to perform an investigation to determine the root cause of the issues, including steps for corrections, corrective actions and/or preventive actions to avoid recurrence or similar problems in the future.
Objective:	The objective of this indicator is to confirm that corrective and preventive actions are taken, necessary improvements are made, and the effectiveness of the actions is confirmed. The NRA or NCL should determine opportunities for improvement and implement any necessary actions in case of a deviation. These should include improving products and services to meet requirements as well as addressing future needs and expectations. Responsive actions can include corrections, corrective actions, preventive actions, continued improvements, innovations, and re-organizations.
Requirement:	Corrective and preventive actions system
Evidence to review:	The assessor should ask for and review: 1. Evidence for availability of procedures for corrections, corrective actions and preventive actions; 2. Examples of corrections, corrective actions and preventive actions. 3. Evidence for implementation of corrections, corrective actions and preventive actions.
References:	1. Guidelines for independent lot release of vaccines by regulatory authorities, (42), (https://www.who.int/biologicals/WHO_ECBS/en/ and http://apps.who.int/medicinedocs/en) 2. Quality management systems — Requirements. International Standard ISO 9001:2015. International Organization for Standardization, 2015, (4), (https://www.iso.org/iso-9001-quality-management.html)
Framework:	Process
Rating Scale:	➔ NOT IMPLEMENTED (NI): No procedures or reports regarding corrections, corrective actions and continued improvements are available. ➔ ONGOING IMPLEMENTATION (OI): The NRA is preparing a procedure for this, but there is no evidence of results from such activities. ➔ PARTIALLY IMPLEMENTED (PI): The procedure was established recently and is at the implementation stage, so this practice is not consolidated yet. ➔ IMPLEMENTED (I): The NRA has such procedures and also consistently maintains documentation of related activities over time.

Limitations and remarks:	A selected sample of yearly biological product reports should be reviewed as well. This is a report that is submitted annually to the NRA or NCL by manufacturers and that contains production information on both bulk and final lots. The report should include test methods and results, reasons for any recalls and corrective actions taken, and any pertinent post-marketing information. Scoring this sub-indicator as "not applicable NA" is excluded (i.e. this sub-indicator will always apply for all benchmarked NRAs).
Sub Indicator:	**LR06.03: Regulatory action taken in case of product non-compliance.**
Maturity Level:	3
Scope:	Vaccines
Description:	The assessor should verify that in case of non-compliances, the NRA or NCL should confirm, through appropriate laboratory investigation, that the non-compliant results reflect the quality of the lot tested and is not due either to an analytical error by the NCL or to the influence of variables unrelated to the product. Once confirmed, the manufacturer should be notified as soon as possible with prompt exchanges of information to try to identify the cause of the discrepancy through manufacturer investigation. Test reports, including the results and outcomes of all of testing performed, should be prepared. These test reports should be used in the final evaluation and decision-making process for the lot (or lots) under consideration. A feedback mechanism from the NCL to the NRA, the GMP inspectorate, and the MA staff is highly advisable in order to coordinate and optimize regulatory actions (e.g., batch recall, product withdrawal, MA revocation, encouraging license variations, or refinements in product specifications based on trend analyses). For imported lots, communications between the NRAs or NCLs of the producing and releasing country may be required. For producing and releasing countries, communications with the country inspectorate may be required. Such information exchange can help to evaluate the corrective and preventive actions introduced by the manufacturer.
Objective:	The objective of this sub-indicator is to ensure that the NRA or NCL has an implemented procedure dealing with the actions to be taken when test results do not comply with the specifications. These procedures should also cover the appropriate regulatory actions to be taken.
Requirement:	Non-compliance action
Evidence to review:	The assessor should ask for and review: 1. Written documents that describe regulatory actions (e.g., revoking of authorization, recalling of product, or stopping of importation) to be taken in case of non-compliance. 2. Records of actions.
References:	1. Guidelines for independent lot release of vaccines by regulatory authorities, (42), (https://www.who.int/biologicals/WHO_ECBS/en/ and http://apps.who.int/medicinedocs/en) 2. Quality management systems — Requirements. International Standard ISO 9001:2015. International Organization for Standardization, 2015, (4), (https://www.iso.org/iso-9001-quality-management.html)
Framework:	Process
Rating Scale:	➜ NOT IMPLEMENTED (NI): No procedures or reports regarding regulatory actions taken in cases of non- compliance are available. ➜ ONGOING IMPLEMENTATION (OI): The NRA is preparing a procedure for this, but there is no evidence of results from such activities. ➜ PARTIALLY IMPLEMENTED (PI): The procedure was established recently and is at the implementation stage, so this practice is not consolidated yet. ➜ IMPLEMENTED (I): The NRA has such procedures and also consistently maintains records of the results of related activities over time.

Limitations and remarks:	Scoring this sub-indicator as "not applicable NA" is excluded (i.e. this sub-indicator will always apply for all benchmarked NRAs).
Sub Indicator:	**LR06.04: Performance indicators for national lot release activities are established and implemented.**
Maturity Level:	4
Scope:	Vaccines
Description:	The assessor should verify the existence and implementation of performance indicators for different activities included under the national lot release functions. Specifically, the system should define key performance indicators (KPIs) along the entire national lot release activity chain and all indicators should be adequately justified. For the purpose of clarity and consistency, established KPIs should be supported with guidelines for monitoring and maintenance of the KPIs. The guidelines in turn should be supported by SOPs and tools that define the procedures to be used for monitoring and evaluating the performance indicators and that define procedures and timelines for reviewing and revising the indicators. Examples of performance indicators for national lot release activities include, but are not limited to: number of released lots per year, number of rejected lots per year, and average number of days to reach a decision on the release of the received batches. Established KPIs might be qualitative, quantitative or combination of both. In general, quantitative indicators are preferred to avoid bias or misinterpretation. However, qualitative indicators are also accepted. Qualitative indicators may or may not include scoring or scaling to render them semi-quantitative and thus more informative. The assessor should ensure that indicators are measured on a regular basis to monitor progress and advancement. In addition, the assessor should verify measured indicators are analyzed to identify trends or abnormalities. Justifications for any identified abnormalities should be provided; when necessary, process optimizations should be introduced to avoid recurrence.
Objective:	The objective of this sub-indicator is to ensure that a system, mechanism, or procedure exists to require the NRA to establish performance indicators along the entire national lot release chain. Additionally, the objective is to ensure that KPIs are actually contributing to monitoring of regulatory performance, to measuring effectiveness of national lot release regulatory activities, and to making any necessary adjustments or optimizations.
Requirement:	KPIs for national lot release activities
Evidence to review:	The assessor should ask for and review: 1. Documents supporting the system, mechanism, or procedure compelling the NRA to establish and implement performance indicators along the entire national lot release activity chain. 2. Evidence that the performance indicators have been established and implemented, and that the members of staff involved in the national lot release function are aware of the indicators and the guidelines and SOPs used for monitoring and evaluating their performance. 3. The current performance indicators for national lot release activities 4. Analyses of the measured indicators along with the investigations done to identify trends or abnormalities. 5. Documentation for follow-up of any observed abnormalities, including justifications for any identified abnormalities as well as any process optimizations introduced to avoid recurrence.
References:	1. Quality management systems — Requirements. International Standard ISO 9001:2015. International Organization for Standardization, 2015, (4), (https://www.iso.org/iso-9001-quality-management.html) 2. World Health Organization. European Observatory on Health Systems and Policies. Performance measurement for health system improvement: experiences, challenges

	and Prospects, (125), (https://www.who.int/management/district/performance/PerformanceMeasurementHealthSystemImprovement2.pdf) 3. World Health Organization. European Observatory on Health Systems and Policies. Health System Performance Comparison: an agenda for policy, information and research, (126), (http://www.euro.who.int/__data/assets/pdf_file/0009/244836/Health-System-Performance-Comparison.pdf) 4. Quality management -- Quality of an organization -- Guidance to achieve sustained success, ISO 9004:2018, International Organization for Standardization (ISO), (115), (https://www.iso.org/standard/70397.html)
Framework:	Output
Rating Scale:	➜ NOT IMPLEMENTED (NI): There are no KPIs for national lot release activities. ➜ ONGOING IMPLEMENTATION (OI): The NRA has recently drafted KPIs for national lot release activities but they have not yet been reported. ➜ PARTIALLY IMPLEMENTED (PI): The NRA has developed KPIs for national lot release activities and has been applying them for less than two year or they have not covered all critical steps. ➜ IMPLEMENTED (I): The NRA has established and implemented KPIs for national lot release activities. The indicators are reviewed regularly, and appropriate actions are taken, and decisions made.
Limitations and remarks:	When they refer to outcomes, indicators may be ambiguous and difficult to interpret, as outcomes are the result of many factors that are difficult to disentangle. When they refer to processes, indicators are often too specific, as they may focus on a particular intervention or condition or they may quickly become outdated as business models develop. Different methodologies are used to measure the NRAs performance on national lot release activities. In this case, the assessor should verify that adequate supporting documents are available. The assessor should consider that developed performance indicators should be Specific, Measurable, Achievable, Realistic, and Time- bound (i.e., “SMART”). Scoring this sub-indicator as “not applicable NA” is excluded (i.e. this sub-indicator will always apply for all benchmarked NRAs).

Glossary and Definitions

The definitions given below apply to the terms as used in different fact sheets of the World Health Organization (WHO) global benchmarking tool (GBT) for evaluation of national regulatory system of medical products. These terms may have different meanings in other contexts.

Accountability
The result of the process which ensures that health actors take responsibility for their obligations and are made answerable for their actions.

Advisory/Scientific committee
See expert advisory body

Benchmarking
A formal process of evaluation of a process or system, preferably quantitative, but sometimes necessarily qualitative.

Benchmark
A measurement or point of reference at the beginning of an activity which is used for comparison with subsequent measurements of the same variable.

Commitment
In accounting usage, commitments refer to a stage in the expenditure process at which contracts or other forms of agreement are entered into, generally for future delivery of goods or services. A liability will not be recognized until delivery of the item, but the government is contractually committed to meeting the obligation once delivery is made. The term is also used in a more general, non-contractual sense to mean firm promises of the government made in policy statements.

Competency
Competency combines knowledge, skills and attitude. Competencies describe how the work is to be carried out while objectives indicate what must be accomplished. They also provide a sound basis for consistent and objective performance standards by creating a shared language for what is needed and expected by the organization.

Clinical Trials Oversight (CT)
NRAs should have the legal mandate to authorize regulate and, if necessary, terminate clinical trials (CTs). The necessary requirements, guidelines, procedures and forms should be developed to be in line with country and region-specific guidelines as well as major international CT guidance including guidelines from the Declaration of Helsinki, the Nuremberg code, International Council on Harmonization, and World Health Organization Good Clinical Practices. CT oversight is aimed at protecting the safety and rights of humans participating in CTs, ensuring that trials are adequately designed to meet scientifically sound objectives, and preventing any potential fraud and falsification of data.

NRAs are responsible at two stages for the critical evaluation of the documentation supporting clinical studies: when CTs are being proposed for authorization and when the results are submitted in an application for marketing authorization. CT protocols should be reviewed and approved by Independent Ethics Committees before the trial commences. A CT review committee should review the protocols and should have the authority, when necessary, to require protocol revisions. The CT review committee should be composed of members who have the appropriate medical and scientific knowledge, experience and skills and who are free of conflicts of interest.

In order to ensure the quality and safety of investigational products, the investigational products should be manufactured in compliance with GMPs for investigational medical products, and the supporting preclinical

studies should be in compliance with Good Laboratory Practices. Additionally, the importation, storage, use, and/or destruction of investigational products should follow national requirements. Qualified and experienced inspectors should carry out on-site inspections of the CT sites to verify compliance with Good Clinical Practices, ethical principles and regulatory requirements, and to provide assurance of the quality and reliability of the data obtained. The oversight activities should be conducted with due concern for confidentiality.

The legal provisions should allow the NRA to recognize and/or rely on relevant CT decisions, reports and information from other NRAs or from designated regional and international bodies. In special circumstances (e.g., for public health interest), the legal provisions should allow the NRA to elect not to follow the routine CT procedures. Transparency in the entire oversight process is fundamental to ensuring the safety of patients and to ensuring that no product with unacceptable benefit to risk balance will be made available to the public.

Decentralization
Political reform designed to promote local autonomy; decentralization entails changes in authority and financial responsibility for health services. Hence, decentralization can have a large impact on health service performance. There are several forms of decentralization affecting the health sector in different ways: (i) decentralization, which transfers authority and responsibility from the central level of the Ministry of Health (MOH) to its field offices; (ii) delegation, which transfers authority and responsibility from the central level of the MOH to organizations not directly under its control; (iii) devolution, which transfers authority and responsibility from the central level of the MOH to lower level autonomous units of government; and (iv) privatization, which involves the transfer of ownership and government functions from public to private bodies. These bodies may consist of voluntary organizations and for-profit and not-for-profit private organizations, with varying degree of government regulation. (http://www.who.int/health- laws/topics/governance-decentralisation/en/)

Effectiveness
The extent to which a specific intervention, procedure, regimen or service, when deployed in the field in routine circumstances, does what it is intended to do for a specified population.

Efficacy
The extent to which a specific intervention, procedure, regimen or service, produces the intended result under ideal conditions.

Efficiency
The capacity to produce the maximum output for a given input.

Emergency
Emergency is a term describing a state. It is a managerial term, demanding decision and follow-up in terms of extra-ordinary measures (Oxford Pocket Dictionary, 1992). A “state of emergency” demands to “be declared” or imposed by someone in authority, who, at a certain moment, will also lift it. Thus, an emergency is usually defined in time and space, requires threshold values to be recognized, and implies rules of engagement and an exit strategy. Conceptually, it relates best to Response.

Entities
In this document, entities refer to different composition units within the NRA (e.g., divisions, departments, or sections), or to different institutions, organizations, or bodies which are involved in the national regulatory system.

Ethics committee (also called research ethics committee or independent ethics committee)
An independent body (i.e., an institutional, regional or national review board or committee), constituted of medical professionals and non-medical members, whose responsibility is to verify that the safety, integrity and human rights of the subjects participating in a particular trial are protected and to consider the general ethics of the trial thereby providing public reassurance. Ethics committees should be constituted and operated so that their tasks can be executed free from bias and from any influence of those who are conducting the trial.

Event
A specific identifiable happening or occurrence, e.g., the taking of a medicine or the experience of an adverse effect.

Expert advisory body
An advisory board or committee of experts, including academic experts and practicing health care professionals.

Falsified medical products
Medical products that deliberately and fraudulently misrepresent their identity, composition or source.

Findings
See inspection observation

Good governance
See governance

Good Clinical Practice (GCP)
A standard for the design, conduct, performance, monitoring, auditing, recording, analysis and reporting of clinical trials or studies. The standard provides assurance that the data and results that are reported are credible and accurate.

Good review practices
Documented best practices for any aspect related to the process, format, content and management of a medical product review.

Governance
Governance includes (i) the exercise of political, economic and administrative authority in the management of a country's affairs at all levels, comprising the complex mechanisms, processes, relationships and institutions through which citizens and groups articulate their interests, exercise their rights and obligations and mediate their differences. (ii) the traditions and institutions by which authority in a country is exercised for the common good, including the processes by which those in authority are selected, monitored and replaced; the capacity of the government to effectively manage its resources and implement sound policies; and the respect of citizens and the state for the institutions that govern economic and social interactions among them; (iii) the process of creating an organizational vision and mission (i.e., what it will be and what it will do) in addition to defining the goals and objectives that should be met to achieve the vision and mission; of articulating the organization, its owners and the policies that derive from these values; (iv) policies concerning the options that its members should have in order to achieve the desired outcomes; and adopting the management necessary for achieving those results and a performance evaluation of the managers and the organization as a whole. See stewardship.

Guidelines or guidance documents
Non-statutory advisory publications intended to assist those parties affected by legislation to interpret and apply requirements.

Impact
Impact includes (i) the total, direct and indirect, effects of a programme, service or institution on a health status and overall health and socioeconomic development; (ii) the positive or negative, long-term or medium-term effects produced by a programme or intervention; and (iii) the degree of achievement of an ultimate health objective.

Independent ethics committee (IEC)
See Ethics committee.

Input
A quantified amount of a resource put in a process.

Inspection observation
A finding or statement of fact made during an inspection and substantiated by objective evidence. Such findings may be positive or negative. Positive observations should take the form of a description of the processes that the firm is carrying out particularly well and that may be considered as examples of particularly good practice. Negative observations are findings of noncompliance with requirements.

Investigational product
Any pharmaceutical product (i.e., a new product or a reference product) or placebo being tested or used as a reference in a clinical trial.

Key performance indicators (KPIs)
Factors that are under the control of the organization and are critical for its sustained success subject to performance measures

Legislation
The first stage of the legislative process, in which laws are passed by the legislative body of government with regard to a subject matter (e.g., control of pharmaceuticals). Laws define the roles, rights and obligations of all parties involved in the subject matter in general terms (see regulations).

Laboratory Testing (LT)
The laboratory testing regulatory function is intended to ensure that the NRA is able to assess the quality of medical products by performing quality tests on them in certain situations. For example, this testing can be a requirement to corroborate manufacturer's test results as a part of the evaluation for marketing authorization or for a variation to a marketing authorization. Testing can be a requirement for lot release for certain products depending upon national regulations. Testing also may be needed for products for which there has been a complaint or a report or for products that are under investigation due to an adverse event. As part of the market surveillance function, laboratory testing is utilized for checking and confirming the quality of medical products placed on the market and for detecting substandard and falsified medical products. In order to do this product testing, the NRA must have access to suitable laboratories where these tests can be performed.

If a country is able to provide all the resources needed, a laboratory under the responsibility of the NRA or a governmental laboratory represents the best choice. Commonly, this governmental laboratory is a national control laboratory (NCL). As an alternative option, the regulatory system may have access to external laboratories, either inside or outside the country, to perform the required tests on behalf on the NRA. When external laboratories are used, regulatory decisions and actions remain at the discretion of the NRA and the NRA retains accountability.

A well-functioning laboratory for medical products testing is an important resource for the national regulatory system. The staff generally has expertise in different life science disciplines and can help in other regulatory activities, for example, the assessment and review of marketing authorization applications and the review of clinical trial data.

When the regulatory laboratory testing activities are decentralized to one or more internal or external laboratories, the NRA or NCL must ensure that a continuous information exchange mechanism is established so the central authority can issue guidance and the decentralized entity can report back with the information needed for making decisions.

Licensing Establishments (LI)
In order to protect public health, licensing activities are of outstanding importance and are considered fundamental, together with inspections activities, for guaranteeing the quality, safety and efficacy of medical products used within or exported out of the country. The NRA is responsible for coordinating licensing activities and should be supported by published and readily available legal provisions, regulations and guidelines which ensure that licensing of facilities throughout the supply chain is based on compliance with Good Practices (GXPs) and that the NRA is empowered to issue, suspend or revoke licenses for premises and establishments.

Premises, facilities, establishments and companies throughout the supply chain should possess a license to operate issued by the NRA. These facilities include, but are not limited to, manufacturers, distributors, wholesalers, importers, exporters and retailers. The process of issuing licenses should be based on the implementation of and compliance with quality standards of GXP. An inspection for confirmation of compliance with GXP is required in order to grant or re-grant a license or approval of a substantial modification.

An updated list or database of all licensed facilities should be published and publicly available.

The GXPs considered most relevant for this function are good manufacturing practices and good distribution practices, including good cold chain management practices. Good clinical practices and good vigilance practices, which are generally excluded from this function, are addressed, however, in other functions.

A general limitation to this function occurs when there is no domestic manufacturing of medical products. In this case, the function cannot apply to manufacturers, because none exist in the country. Nevertheless, the function will always apply to distribution practices, including wholesaling. Another general limitation applies to those countries that depend on the regulatory inspection function, without licensing, to ensure compliance to GXPs at the premises, facilities, establishments and companies throughout the supply chain. In the latter case, the whole function might not apply; however, the assessor of this establishment licensing function should liaise with the assessor of the regulatory inspection function to verify that proper and appropriate controls are in place despite the absence of any licensing activities in the country.

Market Surveillance and Control (MC)
Market surveillance and control function plays a crucial role in assuring medical products consumer safety since its objective is to ensure compliance of the products placed on the market with pre-set criteria for quality, safety and efficacy (i.e., verify compliance with marketing authorization and GXP guidelines). Market surveillance and control function activities are primarily concerned with four themes: (1) control of import activities, (2) prevention and detection of and response to substandard and falsified medical products, (3) market surveillance program for monitoring the quality of medical products throughout the supply chain, and (4) control of promotional, marketing and advertising activities. The aforementioned activities may or may not be undertaken by a single entity (e.g., organization, division, or department).

A general limitation to one of the market surveillance and control function activities exists in countries where advertisement is not allowed or is restricted to specific medical products (e.g. over-the-counter medical products). However, in all cases, control of marketing and promotional materials (i.e., in its wider meaning that includes promotion to healthcare professionals) will always apply.

Medical products
In this document, a term that includes medicines and vaccines.

NRA Lot Release (LR)
NRA lot release (also called official authority batch release) is a non-common regulatory function that does not apply to all medical products. Lot release is a system specifically established for the regulatory release of specified biological products. The goal of the regulatory function is to ensure the quality, safety and efficacy of biological products through a regulatory release system. Lot release is done on a lot-by-lot basis and takes into account the nature and inherent variability of these products.

NRAs should have the legal mandate to perform independent lot release. They should develop and implement the necessary policies, guidelines, procedures and forms in line with WHO and major international guidelines.

In the case of vaccines, different approaches are currently used for conducting lot release. The options include: review of the summary protocols only, review of the summary protocols combined with independent testing (i.e., either full or selected testing), and recognition and acceptance of lot release certificates from the responsible NRA or NCL. The NRA or NCL has the responsibility to decide on an appropriate strategy for each

vaccine subject to NRA lot release. The decision should take into consideration the nature of the vaccine, the post-marketing experience for each product (including production history and safety profile), and the availability of other independent evidence of product quality.

National Regulatory System (RS)
The National Regulatory System (RS) provides the framework that supports the WHO recommended regulatory functions. The NRA is the institution in charge of assuring the quality, safety, and efficacy of medical products as well as ensuring the relevance and accuracy of product information. A sustainable, well-functioning regulatory system will ensure an independent and competent oversight of medical products.

Non-conformity
Refers to a failure to comply with requirements. A requirement is a need, expectation or obligation. It can be stated or implied by an organization, its customers or other interested parties. There are many types of requirements. These include quality requirements, customer requirements, management requirements, product requirements, process requirements and legal requirements. Whenever an organisation fails to meet one of these requirements, a nonconformity occurs.

Observations
See inspection observation

Output
The quantity and quality of activities carried out by a programme.

Performance indicators
Measurable values used to quantify quality objectives to reflect the performance of an organization, process or system, also known as “performance metrics” in some regions.

Performance monitoring
The continuous process of collecting and analysing data to compare how well a project, program, or policy is being implemented against expected results.

Post-Marketing
The stage when a drug is approved and generally available on the market.

Promotion
All informational and persuasive activities by manufacturers and distributors, the intended effect of which is to induce the prescription, supply, purchase and/or use of medicinal products. Ethical criteria for drug promotion, WHO, 1988. For the purposes of this manual, promotion includes advertising.

Public health emergency of international concern (PHEIC)
Defined in the International Health Regulation (2005) as “an extraordinary event which is determined, as provided in these Regulations:

- to constitute a public health risk to other States through the international spread of disease; and
- to potentially require a coordinated international response”.

This definition implies a situation that is serious, unusual or unexpected, carries implications for public health beyond the affected State’s national border, and may require immediate international action.

Recognition
The routine acceptance by the NRA in one jurisdiction of the regulatory decision of another NRA or other trusted institution. Recognition indicates that evidence of conformity with the regulatory requirements of country A is sufficient to meet the regulatory requirements of country B. Recognition may be unilateral or multilateral, and may be the subject of a mutual recognition agreement.

Regulations
The second stage of the legislative process (the first stage being legislation, see above). Regulations are specifically designed to provide the legal machinery to achieve the administrative and technical goals of legislation.

Registration and Marketing Authorization (MA)
The issuance of marketing authorizations (MAs, also referred as product licensing or registration) is critical to any NRA. MA refers to a procedure for approval of a medical product for marketing after it has undergone a process of evaluation to determine the safety, efficacy and quality of the product and the appropriateness of the product information. The objective of this regulatory function is to provide a system which ensures that only medical products which have been duly authorized by the NRA are allowed to be manufactured, imported, distributed, sold or supplied to end-users. The process of assessment for MA includes the review of data on quality, safety and efficacy submitted by the applicant. The same standards should be applied to imported and locally manufactured medical products. Nevertheless, the evaluation of the complex data used to support market authorization of new or novel medical products may require specialized resources and experience not available in the NRA; therefore, countries with limited resources may wish to give priority to well-established products.

In the evaluation of well-established products, the NRA may elect to prepare its own report, rely on evaluation reports prepared by other national authorities, rely on decisions made by another NRA, or use a combination of these approaches. GMP inspections or certifications should be part of the MA requirements. A legal provision should exist that allows the NRA to grant MA of either unlimited or limited duration. In the earlier case, measures should be in place to ensure continued adherence of the medical product to quality, safety, and efficacy standards (e.g. through a vigilance system). In the latter case, MA should be renewed at a predefined time interval.

Mechanisms should exist to ensure that information on MA applications, including authorized, suspended, rejected or completed applications, is published to promote transparency and information sharing among stakeholders. Regular publication of MA decisions is helpful to procurement and distribution networks and to other NRAs. Mechanisms and procedures should be in place to monitor and ensure that all activities within the MA function are checked to reduce errors and to reasonably ensure that the processes are consistent and will provide assurance of high-quality outputs. Such approaches would lead to consistency in the performance of the MA regulatory function and to reliability of the regulatory outputs.

Regulatory framework
The collection of laws, regulations, guidelines, and other regulatory instruments through which a government controls medical products manufacture, clinical evaluation, marketing, promotion and post-marketing safety benchmarking.

Reliance
The act whereby the regulatory authority in one jurisdiction may take into account and give significant weight to (i.e., totally or partially rely upon) evaluations performed by another regulatory authority or trusted institution in reaching its own decision. The relying authority remains responsible and accountable for decisions taken, even when it relies on the decisions and information of others.

Research ethics committee
See ethics committee.

Regulatory Inspection (RI)
Inspection of establishments across the medical product supply chain is an essential regulatory function. The supply chain includes manufacturers, distributors, re-packagers, re-labelers, importers, agents, traders, wholesalers and retailers of medical products. The purpose of regulatory inspections is to ensure that operations at these establishments are carried out in accordance with approved standards, norms, and guidelines and are in compliance with the national medical products legislation and regulations. These, in turn,

should be consistent with WHO recommendations and other internationally recognized guidelines. The scope of the function applies to different GXPs and is not limited to GMPs. Good Distribution Practices and GCPs also come under the scope of this function. Good Vigilance Practices are not addressed in this function but are addressed under the vigilance function.

NRAs should have the legal mandate to inspect and enforce GXPs throughout the supply chain, to make decisions concerning the issuance, suspension or withdrawal of establishment licenses, and to issue authorizations or certifications for the activities performed by these establishments. Additionally, the NRA should develop policies, regulatory actions and procedures on the handling of medical products with suspected quality defects and medical products identified as substandard and falsified. Commonly, inspectors perform several types of inspections: pre-licensing or post-licensing, pre-approval or post-approval, announced or unannounced, and domestic or overseas inspections.

Inspection activities should be conducted based on a risk management approach. Inspections reveal weaknesses and deficiencies, as well as actual or potential errors in the production, quality control, storage or distribution of medical products. Therefore, inspection activities are fundamental for guaranteeing the quality, safety and efficacy of medical products used by the population. An appeal system that is independent of the body that made the initial decision should be available.

The credibility of the inspection depends on the transparency and clarity of the process, on the absence of conflicts of interest, and on the availability of regulations, directives, guidelines and procedures related to the quality management and assurance system of the inspectorate. The system also is highly dependent on the technical competence and integrity of the inspectors. The inspectorate must also ensure confidentiality of the information obtained in the course of its inspection activities.

Networking with other international bodies and NRAs is an important method for acquiring, sharing, and exchanging information relevant to the quality and safety of medical products; in turn, this information contributes to informed science-based decisions. The inspectorate of the NRA should follow uniform procedures incorporating quality system principles.

A general limitation for this function exists in countries where no domestic manufacturing capacities exist. In this case, domestic regulatory inspections based on GMP are not applicable; however Good Distribution Practices would always apply. Similarly, GCP inspections might not apply in countries where no clinical trials are conducted. Even in the absence of a domestic pharmaceutical manufacturer, a GMP inspection function is needed. GMP compliance is always a requirement for granting marketing authorization for a medical product. In this case, GMP compliance can be assured through overseas inspections or desk assessments, which may or may not include verification of documentation. Thus, even if there is no domestic manufacturer, there will be a need for a function which can ensure the GMP compliance of foreign pharmaceutical manufacturers either by physical inspection or desk review (e.g., taking into consideration the GMP certificates from a stringent regulatory authority).

Regulatory system (national regulatory authority or NRA)
The system composed of entities responsible for the registration, marketing authorization and other regulatory functions concerning medical products. The number of regulatory entities responsible for different regulatory functions may vary from one country to another (i.e., NRA may or may not be a single entity). The terms national medicines regulatory authority and drug regulatory authority are also used, however less encouraged, for designating the NRA.

Safety signal
See signal

Signal
A hypothesis of a risk with a medicine, with various levels of evidence and arguments to support it. The complexity of the signal detection process cannot easily be captured in a single, precise definition. In addition to

detecting previously unknown risks with medicines, signal detection should aim to find and communicate any important and relevant information that adds to previous safety knowledge about a medicine, including also risk factors and at-risk groups, details of severity, time at risk, and duration of adverse effects.

Stakeholders
An individual, group or an organization that has an interest in the organization and delivery of health care.

Stewardship
The very essence of good government, the careful and responsible management of the well-being of the population. Stewardship includes: health policy formulation (i.e., defining the vision and direction of health system), regulation (i.e., setting fair rules of the game with a level playing field) and intelligence (i.e., assessing performance and sharing information). See governance.

Substandard and falsified products (SF)
See Substandard medical products and falsified medical products

Substandard medical products (also called "out of specification")
Authorized medical products that fail to meet either their quality standards or their specifications, or both.

Summary of product characteristics (SPC)
Product information as approved by the regulatory authority, and which may have different names globally (e.g., also known as the 'product label'). The summary of product characteristics serves as the basis for production of information for health personnel as well as for consumer information on labels and leaflets of medicinal products and for control of advertising (see also Product information).

Transparency
Defining policies and procedures in writing and publishing the written documentation and giving reasons to the public.

Unregistered or unlicensed medical products
Medical products that have not undergone evaluation and approval by the national or regional regulatory authority for the market in which they are marketed, distributed or used, and for which marketing, distribution and use is subject to permitted conditions under national or regional regulation and legislation.

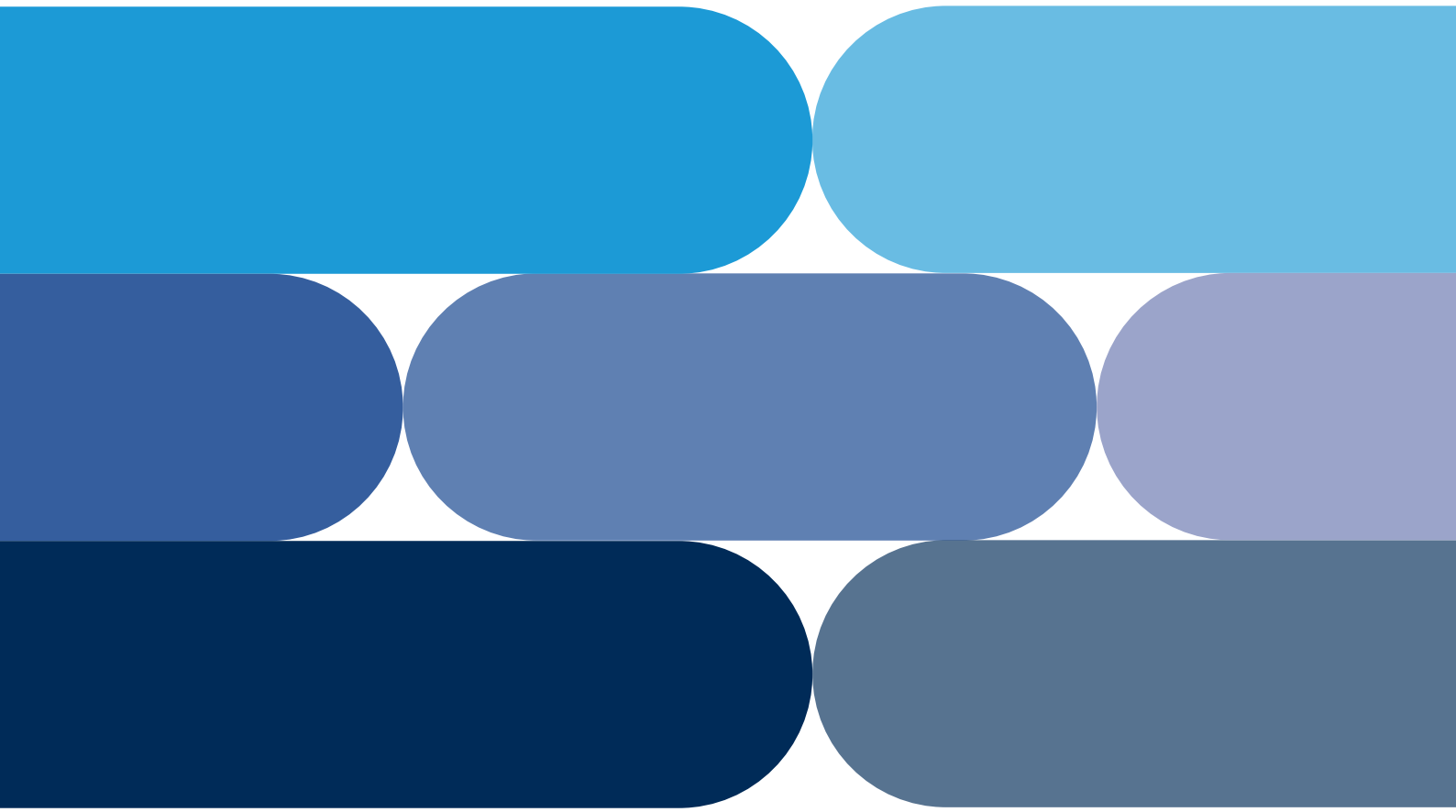
Vigilance (VL)
Medical products vigilance, defined as the science and activities relating to the detection, assessment, understanding and prevention of adverse effects or any other medical product-related problems, is extremely important for guaranteeing that safe and effective medical products of high quality are used within the country. Vigilance activities should be established in the countries based on a risk management approach.

A reporting system should be established to monitor the safety of medical products. One important activity within that function is to monitor and assess side effects and other product-related safety issues (e.g., adverse drug reactions for medicines and adverse events following immunization for vaccines). While common side effects are likely to be detected during pre-approval clinical trials (phases I. II and III), rare events are more likely to be observed after the marketing of medical products. Other unexpected events may also be due to errors and thus could occur at any time during product development and marketing. Side effects may differ with respect to severity, causes and public health consequences. Hence, it is advised that each country establish its own vigilance system. A vigilance system, in general, monitors all kinds of patient harm potentially related to medical products, be it due to inadequate product quality, inappropriate use (e.g., medication errors) or intrinsic adverse effects.

Serious effects (e.g., adverse events following immunization) often lead to public concerns and could erode the confidence in medical products and the overall regulatory and health systems. If not dealt with adequately, such concerns could have significant negative implications on the public health. A post-marketing vigilance system of medical products is therefore essential.

Networking with other international bodies and regulators is a logical method for acquiring, sharing, and exchanging the relevant information on medical products safety. This information, in turn, contributes to informed science-based decisions. To facilitate networking and exchange of information with other international bodies and regulators, harmonization across countries of the vigilance systems and safety reporting requirements in accordance with internationally agreed standards, is expected.

Vigilance events
See event



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