Identifying Opportunities to Align Regulatory Reliance Pathways Across the African Continent: Applying the novel ARCH (Assessing Reliance for Collaborative Harmonization) Archetype

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Abstract

Regulatory reliance pathways represent important mechanisms to facilitate authorization of medicines throughout the continent. Because these have been developed independently over time, they are heterogenous in their scope and characteristics. This diversity adds complexity to regional approaches to facilitating availability of medicines. An objective approach to characterising these pathways would help to understand similarities, best practices and opportunities for collaboration based on common approaches to reliance. Herein we have developed the first step in this characterization process by developing the globally applicable yet region-specific ARCH (Assessing Reliance for Collaborative Harmonization) Archetype. Of the 55 economies in Africa, our assessment using the profiles of facilitated regulatory pathways (FRPs) contained in the FRPath® Project (www.FRPath.org) identified 20 countries (36%) that have published clear descriptions of 43 pathways. By applying a modified Delphi approach, 5 key criteria were identified from 31 fields used to characterize each pathway. Two taxonomic set were created: Three criteria were considered key for Decision Support by the agency (Guidance or SOP available; CPP required; Assessment reports used) and two were found to be important Process Activities (Is this a reliance pathway; Target time). The confluence of the two taxonomic sets resulted in 96 pathway archetype groups. The most common Decision Support approach was where a Guidance or SOP was available, the CPP was required at some point in the process, and unredacted assessment reports were required. This accounted for 17 pathways from 12 countries: Botswana, Ghana, Egypt, Eritrea, Ethiopia, Kenya, Namibia, Nigeria, Rwanda, South Africa, Uganda, Zimbabwe. Five pathways from 5 countries (Ethiopia, Liberia, Tanzania, Zambia and Zimbabwe) were characterized by where a Guidance or SOP was available, the CPP was required at some point in the process, and redacted assessment reports or public assessment reports (PARs)were accepted.
The ARCH Archetype was found to provide a simple method to characterize reliance and other facilitated pathways in a region, thereby identifying common practices, potential best practices and opportunities for regional collaboration based on common approaches. Its use as a real-world approach to characterizing reliance pathways has been demonstrated.

Background

Regulatory reliance pathways represent important mechanisms to facilitate authorization of medicines throughout the continent. While reliance can be used for many regulatory activities including inspection observations and post-approval labelling changes, reliance-based pathways are critical to the efficient review and authorization of new innovative products, generics and biosimilars. The WHO GBT recognizes the importance of reliance by including it as a key sub-indicator (e.g. MA01.08). Reliance as a form of authorization, has been endorsed by the WHO, ICMRA, and the International Pharmaceutical Regulators Programme (IPRP) among others.

However, because these pathways have been developed independently over time, they are heterogenous in their scope and characteristics. This diversity adds complexity to regional and global approaches to facilitating availability of medicines. An objective approach to characterising these pathways would help to understand similarities, best practices and opportunities for collaboration based on common approaches to reliance.

Resources are available that offer flow diagrams and pictorial representations of some regulatory pathways. However, this study aimed to provide additional value to the currently available resources through the application of a novel systematic characterization archetype process to a robust set of pathway characteristics.

Objectives

(1) To provide a high-level overview and characterize the decision-making and regulatory process systems for facilitated and related reliance pathways through an analysis of the FRPath® database (www.frpath.org) and to categorize these according to a standard taxonomy;

(2) To categorize the diversity of the different pathways by identifying sub-groups with common elements of process (i.e., archetypes) that could be used to describe general characteristics common to the different systems within each archetype. These have been used to develop the globally applicable yet region-specific ARCH (Assessing Reliance for Collaborative Harmonization) Archetype.

Methods

We began by assessing the entirety of the FRPath database, which at the time of this work included 290 unique pathways. These included facilitated pathways of all types (reliance-based, priority, conditional, emergency use, etc) from 84 countries, global and regional initiatives, representing the single most comprehensive standardized database of FRPs available. The details for pathways from African countries were extracted. Regional regulatory initiatives (e.g. Zazibona, EAC) were not included in this analysis. For each pathway, we reviewed the details of 31 characteristic fields. Through a group collaboration using a modified Delphi approach, we agreed on a list of ten potential key characteristics. Each author was given 100 tokens that they could assign, in any whole amount, to any one or more of the list of potential characteristics. The tokens for each characteristic were summed. The top 5 characteristics were identified and confirmed by the authors. (Table 1)

The characteristics were subsequently used to identify two taxonomic sets. Three criteria were considered key for Decision Support by the agency (Guidance or SOP available; CPP required; Assessment reports used) and two were found to be important Process Activities (Is this a reliance pathway; Target time). The confluence of the two taxonomic sets resulted in 96 possible pathway archetype groups. The subgroups for each taxonomic set were labelled by a non-descriptive non-ranking letter. This allowed us to develop the globally applicable yet region-specific ARCH (Assessing Reliance for Collaborative Harmonization) Archetype. Each pathway was assigned to a specific archetype block.

Observations

- **Of the 55 economies in Africa, we identified 20 countries (36%) that have published some form of a description of 43 pathways.**
- **Insufficient details were found to conduct an ARCH Analysis for the following 11 pathways: Algeria: Autorisation Temporaire d'Utilisation (ATU); Botswana: Expedited/Fast-track procedure; Ethiopia: Registration of Low-Risk Medicines; Kenya: Fast track for locally manufactured and priority medicines; Kenya: Emergency Use Application (EUA); Rwanda: Authorization for Emergency Use for Medicinal Products, Medical Devices and IVDs; Rwanda: Priority Review (Biological Products); South Africa: Registration of Candidate COVID-19 vaccines; The Gambia: Abridged Review; Togo: Homologation procedure; Tunisia: Prioritization Request.**
- **Therefore, there were sufficient details to characterize 29 pathways fully and 3 partially (32 total). (Table 2)**
- **Although the confluence of the two taxonomic sets resulted in 96 pathway archetype groups, not all groups had pathways reflective of those combinations.**
- **The most common Decision Support approach was where a Guidance or SOP was available, the CPP was required at some point in the process, and unredacted assessment reports were required. This accounted for 17 pathways from 12 countries: Botswana, Ghana, Egypt, Eritrea, Ethiopia, Kenya, Namibia, Nigeria, Rwanda, South Africa, Uganda, Zimbabwe.**
- **Five pathways from 5 countries (Ethiopia, Liberia, Tanzania, Zambia and Zimbabwe) were characterized by where a Guidance or SOP was available, the CPP was required at some point in the process, and redacted assessment reports or public assessment reports were accepted.**
- **Regulatory flexibility was observed in some countries by the availability of multiple FRPs. Countries with 4 pathways were Ethiopia, South Africa, and Tanzania and with 3 pathways were Botswana, Ghana, Kenya, Namibia, Rwanda and Zambia.**

Table 1. Criteria selected using a modified Delphi approach

Characteristics	Category	Criteria
Guidance or SOP available	decision support	Yes, no
CPP required	decision support	No, yes (at submission or prior to final decision)
Assessment reports	decision support	Redacted + PARs, unredacted
Is this a reliance pathway	process	Yes, no
Target time (TT) range	process	<30; 31-60; 61-90; 91-120; 121-150; 151->180

Table 2 Assignment of Pathways using the ARCH Archetype

	(L) GUIDANCE or SOP	NO	NO	YES	YES	NO	NO	YES	YES
	(AA) CPP	NO	NO	YES	YES	YES	YES	NO	NO
	(Z) ASSESSMENT	REDACTED + PAR	UNREDACTED	REDACTED + PAR	UNREDACTED*	REDACTED + PAR	UNREDACTED	REDACTED + PAR**	UNREDACTED
M	(V) RELIANCE	NO	None	None	None	Ghana: Alternative/Non-Routine Authorization Application Pathways - VERIFICATION ROUTE	None	None	None	Ghana: Emergency Use Authorization (EUA) of Medical Products
	(S) Target Time	<30							
A	(V) RELIANCE	NO	None	None	None	None	None	None	None	Tanzania: Emergency Use Authorization of Medicinal Products Tanzania: Orphan Medicines
	(S) Target Time	31-60							
F	(V) RELIANCE	NO	None	None	None	Eritrea: Fast Track/Priority Registration South Africa: Reliance-Based Evaluation Pathways - RECOGNITION South Africa: VERIFIED REVIEW Zambia: Verification Review (Type 1)	None	Mozambique: Verification Review	None	Botswana: Non-Routine Assessment of Products for Public Health Emergencies
	(S) Target Time	61-90							
R	(V) RELIANCE	NO	None	None	Liberia: Registration of Medicine Zambia: Fast-Track/Priority Review	Nigeria: Registration of Imported Drugs in Nigeria	None	None	None	None
	(S) Target Time	91-120							
	(V) RELIANCE	NO	None	None	None	None	None	None	None	None
	(S) Target Time	121-150							
V	(V) RELIANCE	NO		Namibia: Verification Review	None	Namibia: Expedited Fast-Track Registration Procedure Zimbabwe: Expedited or Fast-track Registration Procedure	None	None	None	None
	(S) Target Time	151->180							
D	(V) RELIANCE	YES	None	None	Ethiopia: Fast Track for Locally Manufactured and Priority Medicines	Botswana: Medicine Registration Exemption	None	None	None	None
	(S) Target Time	<30							
	(V) RELIANCE	YES	None	None	None	Egypt:Biologics Reliance Pathways (decree 820/2016)	None	None	None	None
	(S) Target Time	31-60							
N	(V) RELIANCE	YES	None	None	None	Kenya: Reliance for Regulatory Decision Making in Kenya South Africa: Reliance-Based Evaluation Pathways - ABRIDGED REVIEW	None	None	None	None
	(S) Target Time	61-90							
K	(V) RELIANCE	YES	None	None	None	Uganda: NDA Abridged Evaluation Process	None	None	None	None
	(S) Target Time	91-120							
E	(V) RELIANCE	YES	None	None	Tanzania: Fast Track Evaluation	None	Tanzania: Abridged Review	None	None	None
	(S) Target Time	121-150							
S	(V) RELIANCE	YES		Namibia: Abridged Review	Zambia: Abridged Review (Type 2)	Ghana: Abridged Review Rwanda: Priority Review	None	Mozambique: Abridged Review	None	None
	(S) Target Time	151->180							

Nigeria: Licensing or Access to COVID-19 Vaccines (no TT)
Ethiopia: Conditional Medicines Approval (no TT)

Ethiopia: Emergency Use Authorization of COVID-19 Vaccine (no TT)

Conclusions

Herein we have developed the first step in the development of the globally applicable yet region-specific ARCH (Assessing Reliance for Collaborative Harmonization) Archetype.

We have applied the ARCH Archetype to African countries for which transparent information about their pathways is available; this mapping allows a systematic approach to understanding the common characteristics of reliance pathways, how they can be optimized based on possible best practices and provides practical insights for those involved with regulatory system strengthening initiatives.

Study Limitations

The primary limitation was the lack of transparent descriptions about the individual pathways. Even where a publicly available process document or SOP was available, these often were high-level and did not provide details of the process sufficient for use by a submitting organization or for another agency to understand the process involved. The FRPath Project offers free access to regulators around the world to its database and includes a mechanism for agency input into each profile. We therefore encourage the ongoing, active contribution by agencies to this unique database.

Acknowledgements

The FRPath project is an educational activity of the nonprofit Erudee Foundation (www.erudee.org). This work was underwritten by the Foundation and by a grant from the Bill and Melinda Gates Foundation. Access to the full FRPath database is available at no cost to regulatory agencies worldwide. Passwords can be requested at https://portal.bmgf.erudee.org/request. Presented at the 6th Biennial Scientific Conference on Medical Products Regulation in Africa (SCoMRA VI), Cairo, Egypt. December 2023. This poster can be accessed at www.frpath.org/resources. Contact: Liberti@usc.edu