Guiding Principles for Donors Regarding Quality Assurance of Essential Medicines and Other Health Care Commodities

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A. Background

This document outlines the set of agreed guiding principles for the quality assurance of essential medicines and other health care commodities, which donors will require of countries, bilateral, multilateral and third- party procurers when they use donor funds to purchase essential medicines. These agreed guiding principles would help ensure consistency in requirements for quality standards of essential medicines procured with donor funding and will provide uniformity in the application of these standards. These principles have important considerations, including that manufacturers who invest in assuring that their products meet international quality standards are not disadvantaged but are instead incentivized to remain in these markets.

Donors realize that a disease cannot be treated with a poor-quality product and should not be treated with a product whose quality is uncertain. Any amount of poor-quality medicine is unacceptable because it increases morbidity and mortality[1], jeopardizes the credibility of health services and programs, and in the case of antimicrobials contributes to the development of antimicrobial resistance. In addition, one cannot extrapolate the clinical trial experience (in which quality-assured products are used) to the larger patient experience if non-quality-assured products are used.

This set of agreed guiding principles provides the framework to help assure the quality of finished pharmaceutical products that are procured with donor funds.

**This document sources content from the UK Department for International Development (DFID) Quality Assurance Policy for Reproductive Health Commodities, Jan 2013*

[1] Impact of poor-quality medicines in the 'developing' world Trends Pharmacol. Sci. 2010; 31(3): 99–101.

B. Guiding principles for quality assured standards of essential medicines when procured with donor funds

Donors recognize the importance of the quality of essential medicines that are procured by countries. The principles outlined below reinforce donor commitments to provide quality products. They align procurement practices with international quality standards[2] and harmonize across other large procurers of essential medicines. This approach sends a strong signal to manufacturers and procurers that demonstrated manufacturing quality, in compliance with internationally agreed quality standards, is of critical importance in assuring the quality of the products purchased. The guiding principles for quality assurance of essential medicines for procurement using donor funds include:

1. The requirement that **all** essential medicines purchased with donor funds be quality assured if quality assured version(s) of the products are available on the market. For the purposes of these guiding principles, essential medicines are those products included on the WHO essential medicines list (http://www.who.int/medicines/publications/essentialmedicines/en), as well as any other specific medicines that are purchased with donor funds (be they direct or budget support funds). A quality-assured product is one that has been either:

   - WHO prequalified (PQ)

   - OR, approved by an agency upon which WHO relies for its abridged prequalification assessment procedure, along with documentation that the product is suitable from a quality and labeling perspective (e.g., stability, language) for use in the intended geography.

2. In the absence of a quality-assured product being available for purchase (i.e., either WHO PQ or approval by an agency upon which WHO relies for its abridged prequalification assessment procedure), on a defined interim basis, under specific circumstances, product advised for purchase by a qualified Expert Review Panel (ERP), convened by WHO may be purchased.

3. As a last resort, in the absence of all the above), product may be procured from accredited sources such as internationally approved wholesalers.

   IN ADDITION

   - All products purchased using donor funds must also be approved for use by the national authority in recipient countries or allowed to be used in country under special provisions of the Ministry of Health (if applicable)

4. The definition of "WHO prequalified" is that the WHO Prequalification of Medicines Program has reviewed the product dossier (using either its full or abridged prequalification assessment process) and provided a pre-qualification listing/approval of the actual product being purchased (i.e., same manufacturing site, same formulation, and same manufacturing process/line, not a different version of the product). This definition also includes those products PQ listed after US PEPFAR tentative approvals and Article 58 positive opinions. See the list of WHO prequalified medicines at: https://extranet.who.int/prequal/content/prequalified-lists/medicines

[2] http://www.who.int/about/finances-accountability/procurement/quality-assurance/en/

5. The definition of "approved by an agency upon which the WHO relies for its abridged prequalification assessment procedure" is approval by a regulatory authority currently recognized by the World Health Organization (WHO) as an agency on which WHO Prequalification (PQ) is willing to rely when it prequalifies a product[3]. Such agencies were previously referred to as "stringent regulatory authorities" or SRAs. These agencies have shown that they consistently use recognized international procedures to assure manufacturing quality, including:

   - Independent assessments, by qualified experts, of the entire manufacturing process (to assure quality is "built in" throughout the manufacturing process),
   - Assurance of compliance with good manufacturing practice and quality manufacturing systems standards, equivalent to those used by WHO PQ.

   In addition, such agencies must have an effective enforcement mechanism for non-compliance with these quality assurance standards, including an effective post approval product quality surveillance system.

6. The use of an "Expert Review Panel" is only relevant in cases where there is not a quality-assured product (i.e., approved by an agency upon which WHO relies for its abridged prequalification assessment program or WHO PQ) available in a recipient country. Then, partners may request that an Expert Review Panel (ERP), consisting of experts in manufacturing quality, be convened to provide a risk assessment regarding the manufacturing quality of relevant products that have national regulatory approval in the recipient country. An ERP request is contingent upon the product being submitted for approval by an agency upon which WHO relies for its abridged prequalification assessment program or, if eligible, WHO PQ listing, and ERP approval is only valid for 12 months. This ERP mechanism is used by the Global Fund to provide interim reviews of products currently under review in the pre-qualification program. The ERP mechanism is convened by WHO (or a designee of the donor agency)[4].

7. Since WHO has identified over 10% of tested medicines in low to middle income countries as substandard or falsified[5], some level of product quality assurance is important. When no quality- assured product is available, and an ERP review is not possible, or the time lag for obtaining a quality assured product is long, procurement from accredited sources can be used. These accredited sources include international wholesalers that are recognized and/or accredited by other donors or international institutions which have requirements in place to require product testing to help assure that the product is not substandard or falsified (for example, international wholesalers that are audited and approved by the United States Agency for International Development [USAID] or the Directorate-General for European Civil Protection and Humanitarian Aid Operations [ECHO]). As with the ERP, the testing and recognition by these entities does not assure the product's quality, but it provides a high level of confidence that the product is not substandard or falsified. When this risk management approach is used, there should be an initial provisional limit for such purchases of no more than 12 months, and such products should be required to enter WHO PQ or an agency upon which WHO PQ relies for its abridged assessment procedure dossier review during this time. If at the end of the initial 12-month period, no quality-assured product has successfully undergone ERP evaluation or been approved by WHO PQ or an agency upon which WHO

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3 (i.e., currently the United States Food and Drug Administration, the European Medicines Agency and their member state NRAs, Health Canada, Swissmedic, the Japanese Pharmaceutical and Medical Device Agency, the Australian Therapeutic Goods Administration)
https://extranet.who.int/prequal/sites/default/files/documents/75%20SRA%20clarification_February2017_0.pdf?ua=1

4 https://extranet.who.int/prequal/sites/default/files/documents/73%20ERP_Feb2016_1.pdf

5 http://www.who.int/medicines/regulation/ssffc/publications/gsms-report-sf/en

PQ relies for its abridged assessment procedure, such tenders can be extended on an annual basis (but no longer than the three-year tender cycle).

8. The recognition that, in most cases, products also need to be registered locally for the product to be procured and used legally in the receiving country.

These guiding principles apply to both procurement by donor country offices and third parties receiving donor funding. Donors expect all bids to reflect these principles. Donors do not insist that third parties apply these principles to products procured with other funds, but strongly encourage them to do so.
Donors also require adherence to these principles when procurement is carried out by national governments in receipt of budget or sector support from donors.

Donors are working with several partners to improve the availability of essential medicines listed by WHO PQ and/or approved by agencies upon which WHO relies for its abridged prequalification process. This includes, for example, strengthening national health systems (quality assurance capacity building) and supporting regulatory harmonization efforts. This work aims to increase the range of quality-assured commodities available for procurement and ultimately enables the full implementation of the intention of the guiding principles outlined in this document.

The monitoring and impact of these guiding principles will be reviewed on an ongoing basis.

C. Frequently asked questions

1. To whom do these principles apply?

- Donor country offices. All essential medicines procured by or for country programs.

- Third parties. Where donors have agreements with third parties, any donor money used for procurement must only be used to procure products in compliance with these guiding principles. Products procured using other agencies' money are not bound by these guiding principles; however, all partners are encouraged to consider the criticality of manufacturing quality when making their procurement decisions.

- General and sector budget support. Where donors have agreements with countries to whom general and sector budget support is given, any donor money used for procurement must only be used to procure products in compliance with these guiding principles. Products procured using other agencies' money or countries' own funds are not bound by these guiding principles; however, all partners are encouraged to consider the criticality of manufacturing quality when making their procurement decisions.

2. Do these guiding principles apply retroactively?

No. Items that have already been procured or orders that have already been placed will be honored. However, any orders that current partners are preparing must comply with these principles, where this is possible, or have a transition plan.

3. What do I do if there isn't a product that is WHO prequalified or approved by an agency upon which WHO relies for its abridged prequalification assessment program or a commodity advised by an appropriate ERP available in the country in which I am working?

Donors would like these principles to come into effect immediately. Donors are aware that there are instances where there may be no product available that meets the procurement standards of this document, or where none of the otherwise acceptable products have NDRA approval. In cases where there are no otherwise acceptable products that are registered for use in recipient countries, partners may request that an appropriate ERP be convened to provide a risk assessment of the manufacturing quality of products that have national regulatory approval in the recipient country. If an ERP is not possible, partners and governments should procure health commodities through accredited sources that are recognized by established entities (other donors, for example, USAID, ECHO, UNDP, UNHCR, UNICEF) to have undergone quality testing, by entities such as international wholesalers, to help assure the products are not substandard or falsified.

4. **How do these principles consider the market realities and timing issues involved in transitioning to new suppliers (e.g., contract negotiations, national registration, and over branding, for example, with a social marketing brand)?**

Donors recognize that transitioning between suppliers is a resource-intensive task. Donors expect all bids to reflect these guiding principles and, as necessary, depending on specific circumstances at country level, include a transition procurement plan within its bid. Donors encourage all existing suppliers to international and national procurement agencies to make all efforts to ensure that products are submitted to WHO's Prequalification Program (if eligible), or to an agency upon which WHO relies for its abridged prequalification assessment program, or, as applicable, to an appropriate ERP, recognizing that an ERP recommendation is for a specific time limit with the expectation that the product will proceed to either WHO PQ or an agency upon which WHO relies for its abridged prequalification assessment program.

5. **What is the rationale behind these principles?**

- There are health commodities on the market in many recipient countries that have not undergone an internationally accepted quality assurance process but are nevertheless registered and available for purchase. These commodities may offer cost savings over those commodities that have been demonstrated to meet international standards of manufacturing quality. While these commodities appear to represent lower product costs, there may be significant public health and personal health risks associated with the procurement of these products. These products could result in significantly worse cost-effectiveness despite a seemingly lower up-front cost.

- In addition to the individual health risks posed to patients, there is a serious reputational risk to health services when ineffective, and potentially harmful, medicines are recommended by health workers who believe they are providing quality care with quality products to their patients. The use of donor funding for ineffective medicines can also undermine support for development assistance for health in both recipient and donor countries.

- These guiding principles also align donor procurement practices with international standards and with other large procurers of essential medicines. The principles reinforce the importance of manufacturing quality and send a strong signal to manufacturers that they too must demonstrate that their products meet international manufacturing quality standards to access the large markets that these donor organizations offer. Experience from The Global Fund to Fight AIDS, Tuberculosis and Malaria suggest that once a sufficient market share demands international quality standards, manufacturers will seek to gain the requisite WHO PQ listing or acceptable agency approval for their products.

6. **Isn't it better to increase access and choice rather than worry about quality?**

Access to poor-quality product and choice of poor-quality product does not improve access to medicines on which patients and practitioners can rely. Donors recognize that in the short term these guiding principles have the potential to create a perceived reduction in the access to, and choice of, health commodities for those who already have a high unmet need for these products. However, the need is for quality products and healthcare. The guiding principles will promote an increase in access to and choice of quality medical products.

7. **Could donors instead invest and assist national regulatory authorities to build capacity to assure the quality of medicines in their markets and develop strategies to encourage all manufacturers to comply with quality standards?**

The donor community has taken a pragmatic approach to use effective, existing mechanisms to deliver quality-assured essential medicines to low- and middle-income countries while in the long run assisting countries to take ownership and build capacity for regulating the pharmaceutical sector. Better control of markets may be achieved through harmonization initiatives, regulatory systems strengthening, including post-market surveillance, and possibly government incentives and a holistic approach to domestic manufacturing.

D. List of Abbreviations

DFID	–	UK Department for International Development
ECHO	–	Directorate-General for European Civil Protection and Humanitarian Aid Operations
ERP	–	Expert Review Panel
NDRA	–	National Drug Regulatory Authority
ODA	–	Overseas Development AID
PQ	–	Prequalification
QA	–	Quality Assured
RHSC	–	Reproductive Health Supplies Coalition
SRA	–	Stringent Regulatory Authority
UNICEF	–	United Nations Children's Fund
USAID	–	United States Agency for International Development
WHO	–	World Health Organization