# Quality Assurance Policy for Pharmaceutical Products

**Amended and restated on 15 November 2023***

* As per Board Decision GF/B50/DP06. Originally issued on 11 November 2009 (Board Decision GF/B20/DP13) and amended on 15 December 2010 (Board Decision GF/B22/DP09).

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## BASIC PRINCIPLE

1. Global Fund resources and Grant Funds may only be used to procure finished pharmaceutical products (FPP) in accordance with the standards prescribed in this Quality Assurance Policy for Pharmaceutical Products (the "Policy").

## DEFINITIONS

2. Capitalized terms and acronyms used in this Policy shall have the meaning given to them below unless the context requires otherwise.

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| **Common Technical Document for the Registration of Pharmaceutical Products for Human Use (CTD)** | means a common format for the submission of information to regulatory authorities in ICH member countries. |
| **Expert Review Panel (ERP)** | means a panel of technical experts independent of the Global Fund which, in accordance with its terms of reference, analyzes the potential risks and benefits of Finished Pharmaceutical Products and advises the Global Fund on use of Global Fund resources and Grant Funds for procurement of Finished Pharmaceutical Products for a time-limited period. |
| **Finished Pharmaceutical Product (FPP)** | means a medicine presented in its finished dosage form that has undergone all stages of production, including packaging in its final container and labelling. |
| **Fixed Dose Combination** | means a combination of two or more active pharmaceutical ingredients in a fixed ratio of doses. |
| **Good Manufacturing Practices (GMP)** | means the practices, which ensure that pharmaceutical products are consistently produced and controlled according to quality standards appropriate to their intended use and as required by marketing authorization. |
| **Grant Funds** | means the funds specified in a Grant Confirmation, which the Global Fund, subject to the terms and conditions set forth in the Grant Agreement, agrees to make available to the Grantee (or to its Principal Recipient designated in the Grant Confirmation) in the form of a grant for the implementation of the relevant program. |

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| **International Conference on Harmonization of Technical Requirements for the Registration of Pharmaceuticals for Human Use (ICH)** | is an initiative involving regulatory bodies and pharmaceutical industry experts that was established to make recommendations on ways to achieve greater harmonization in the interpretation and application of technical guidelines and requirements for product registration. ICH member countries are specified on the ICH website.[1] |
| **International Organization for Standardization (ISO)** | means the non-governmental organization, including national standards institutes of 167 countries, which sets standards, including generic standards (e.g., ISO 9000 series) or product-specific requirements for implementing a quality management system (e.g., ISO 13485 for medical devices). |
| **Medicine** | means an active pharmaceutical ingredient that is intended for human use. |
| **National Regulatory Authority (NRA)** | means the official regulatory authority of a country designated to administer the regulatory activities related to Medicines. |
| **NRA Recognized Laboratories** | means quality control laboratories for pharmaceutical products selected by NRAs according to their standards to conduct their quality control testing for pharmaceutical products. |
| **Pharmaceutical Inspection Cooperation Scheme (PIC/S)** | means the Swiss association of inspectorates which provides a forum for GMP training. The PIC/S is not subject to any international or domestic regulations. PIC/S member countries are specified on its website.[2] |
| **Product Formulation** | means an active pharmaceutical ingredient (or combination of ingredients), dosage form and strength. Note: different FPPs may exist for the same Product Formulation. |
| **Public Health Emergency of International Concern (PHEIC)** | means a formal declaration by the World Health Organization of an extraordinary event which is determined to constitute a public health risk to other States through the international spread of disease and to potentially require a coordinated international response.[3] |
| **Quality Control** | means all measures taken, including the setting of specification sampling, testing and analytical clearance, to ensure that starting material, intermediate, packaging material and FPPs conform with established specifications for identity, strength, purity and other characteristics. |
| **Recipient** | means any legal entity that receives Grant Funds and/or Global Fund resources. |

[1] https://www.ich.org/
[2] https://picscheme.org/
[3] WHO International Health Regulations (2005): https://www.who.int/publications/i/item/9789241580496

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| **Regional regulatory system** | means a system composed of individual regulatory authorities, or a regional body composed of individual regulatory authorities, operating under a common regulatory framework including or excluding a common legal framework. The common regulatory framework must at least ensure equivalence between the members in terms of regulatory requirements, practices, and quality assurance policies. |
| **Stringent Regulatory Authority (SRA)[4]** | means a regulatory authority which was, prior to 23 October 2015: (a) a member of the ICH ; or (b) an ICH Observer, being the European Free Trade Association (EFTA) as represented by Swiss Medic, Health Canada and World Health Organization (WHO) (as may be updated from time to time); or (c) a regulatory authority associated with an ICH member through a legally binding mutual recognition agreement including Australia, Norway, Iceland and Liechtenstein (as may be updated from time to time). |
| **WHO** | means the World Health Organization. |
| **WHO Emergency Use Listing (EUL)** | means WHO's risk-based procedure for assessing and listing unlicensed vaccines, therapeutics, and in vitro diagnostics with the ultimate aim of expediting the availability of these products to people affected by a public health emergency.[5] |
| **WHO Listed Authority[6] (WLA)** | means a regulatory authority or a Regional regulatory system which has been documented by WHO to comply with all the relevant indicators and requirements specified by WHO for the requested scope of listing based on an established benchmarking and performance evaluation process. |
| **WHO Prequalification Programme** | means the programme managed by WHO which prequalifies (a) medicines that are considered to be acceptable for procurement by the United Nations and specialized agencies; and (b) quality control laboratories for medicines. |

## INTERPRETATION

3. In this Policy, unless the context otherwise requires:

   (i) headings do not affect the interpretation of the Policy;

   (ii) the singular shall include the plural and vice versa;

   (iii) any phrase introduced by the terms "including", "include", "in particular", "such as", or any other similar expression shall be illustrative only and shall not limit the sense of the words preceding those terms; and

   (iv) reference to an undated ISO standard designates the latest version of that standard.

[4] This also includes a positive opinion under the Canada S.C. 2004, c. 23 (Bill C-9) procedure, or Art. 58 of European Union Regulation (EC) No. 726/2004 or United States FDA tentative approval.

[5] SRAs and WLAs may also implement similar procedures for the same purpose.

[6] Evaluating and publicly designating regulatory authorities as WHO listed authorities WHO Policy document – Geneva 2021. https://www.who.int/publications/i/item/9789240023444

## APPLICABLE LAWS AND REGULATIONS

4. Each Recipient shall ensure that the procurement of pharmaceutical products with Grant Funds and Global Fund resources is undertaken in compliance with all applicable national laws and regulations.

## CLINICAL STANDARDS

### Compliance with Standard Treatment Guidelines and Essential Medicines Lists

5. Global Fund resources and Grant Funds may only be used to procure medicines that appear in applicable national standard treatment guidelines or essential medicines list ("National STGs or EML"), or the WHO standard treatment guidelines or essential medicines list ("WHO STG or EML") or a WHO Rapid Communication.[7]

6. When submitting funding requests to the Global Fund, Recipients must ensure that they include a list of the medicines that they intend to procure with Grant Funds, together with a copy of the relevant National STG or EML or the WHO STG or EML. If a Recipient intends to procure medicine that is included in the relevant National STG/EML, but not included in the WHO STG or EML, or vice versa, the applicant shall provide a detailed technical justification for the selection of that medicine, which will be reviewed by the WHO disease program, at the discretion of the Secretariat.

7. If a Recipient proposes to use Grant Funds to procure medicines other than those already approved by the Global Fund, it shall provide the Global Fund with a brief description of the medicine and, if applicable, the technical justification for review as described in Section 6 above, for approval by the Global Fund.

### Adherence, Drug Resistance and Monitoring Adverse Effects

8. It is strongly recommended that Recipients implement mechanisms to encourage adherence to treatment regimens (including but not limited to providing medicines in Fixed Dose Combinations, once-a-day formulations and/or blister packs, use of WHO-endorsed digital adherence technologies (DATs) and providing peer education and support), to monitor and contain resistance, and to monitor adverse drug reactions according to existing international guidelines.[8] The cost of implementing such mechanisms may be included in the budget for the relevant Global Fund grant.

9. To help contain resistance to second-line tuberculosis medicines, all procurement of FPPs to treat Multi Drug Resistant Tuberculosis (MDR-TB) must be conducted through the Global Drug facility (GDF) of the Stop TB Partnership.[9]

[7] WHO may issue a Rapid Communication to indicate an update in progress to WHO treatment guidelines which may take additional time before finalization.

[8] For example, WHO, The Uppsala Monitoring Centre. The Importance of Pharmacovigilance. Safety Monitoring of medicinal products. Geneva: World Health Organization, 2002. Safety of Medicines. A guide to detecting and reporting adverse drug reactions. Geneva: World Health Organization, WHO/EDM/QSM/2002.2.

[9] Pursuant to Board Decision GF/B03/DP15 of 10 October 2002.

# ANTIRETROVIRALS, ANTI-TUBERCULOSIS AND ANTI- MALARIAL FPPs

## Quality Standards

10. Global Fund resources and Grant Funds may only be used to procure antiretrovirals, anti-tuberculosis and anti-malarial FPPs that meet the following standards and, in accordance with the selection process described in Sections 11 and 12 below:

    (i) Prequalified by the WHO Prequalification Programme; or
    (ii) Authorized for use by an SRA; or
    (iii) Authorized for use by a WLA;[10] or
    (iv) Recommended for use by the ERP.

## Selection Process

11. If there are two or more FPPs available[11] for the same Product Formulation that meet the quality standards set out in Section 10 (i), (ii), or (iii), Recipients may only use Grant Funds or Global Fund resources to procure an FPP that meets one of those standards.

12. However, if a Recipient determines that there is only one or no FPP available[12] that meets either of the quality standards set out in Section 10 (i), (ii), or (iii), and the Recipient wishes to use Grant Funds or Global Fund resources to procure an alternate FPP, it must request confirmation from the Global Fund that the Recipient's determination is accurate and that the alternate FPP meets the standard specified in Section 10 (iv).

## Expert Review Panel

13. Upon the Global Fund's request, the ERP will review the potential risks and benefits associated with the use of an FPP that is not yet WHO-prequalified, SRA-authorized, or WLA authorized and will make recommendation to the Global Fund.

14. The Global Fund maintains an up-to-date list of all FPPs that have been recommended by the ERP which is publicly available on the Global Fund's website. If a Recipient requests to procure an FPP that does not appear on the list, the Global Fund requests the ERP to review the relevant FPP.

15. The Global Fund makes the terms of reference and rules of procedure for the ERP publicly available.

16. FPPs are eligible for review by the ERP if the following conditions are met:

    (i)
        (a) the applicant has submitted an application for prequalification of the product by the WHO Prequalification Programme and it has been accepted by WHO for review; OR
        (b) the applicant has submitted an application for marketing authorization to an SRA or a WLA, and it has been accepted for review by the SRA or the WLA,

[10] If the scope of listing includes the marketing authorisation function as published and regularly updated in the WHO website.
[11] 'Available' means the manufacturer can supply the requested quantity of the FPP within not more than 90 days of the requested delivery date.
[12] See Footnote 11.

AND

(ii) the FPP is manufactured at a site that is compliant with the standards of Good Manufacturing Practice (GMP) that apply for the relevant Product Formulation, as verified after inspection by:
   (a) the WHO Prequalification Programme; OR
   (b) an SRA or a WLA; OR
   (c) a regulatory authority participating to the Pharmaceutical Inspection Cooperation Scheme (PIC/S).[13]

Provided that the criterion in Paragraph (ii) above is met, FPPs that do not meet the criteria in Paragraph (i) above are also eligible for review by the ERP for associated potential risks and benefits if the Product Formulation is not listed in the WHO invitation to manufacturers to submit an expression of interest for product evaluation by the WHO Prequalification Programme. The list of ERP-recommended FPPs that is made publicly available indicates which of the ERP-recommended FPPs were eligible for review as a result of this paragraph.

17. If the ERP recommends the use of an FPP, the ERP's recommendation shall be valid for a period of no more than 12 months ("ERP Recommendation Period"), or until the FPP is WHO-prequalified or SRA-or WLA authorized, whichever is earlier.

18. In accordance with Section 122, the Recipient may enter into a contract with a supplier for the procurement of an FPP recommended for use by the ERP at any time until the expiry of the ERP Recommendation Period; however, the term of the contract must not exceed 12 months. For clarity, the Recipient cannot place an order for FPPs under the contract more than 12 months after it is executed.

19. However, the Global Fund may, in its sole discretion, request the ERP to consider extending the ERP Recommendation Period for up to an additional 12 months if the FPP is not yet WHO-prequalified, SRA authorized, or WLA authorized within the ERP Recommendation Period. The Global Fund may refer more than one request for such an extension to the ERP.

## ALL OTHER FPPs

### Quality Standards

20. All FPPs, other than antiretrovirals, anti-tuberculosis and anti-malarial FPPs, need to only comply with the relevant quality standards that are established by the NRA in the country of use.

### Selection Process

21. Recipients must select FPPs, other than antiretrovirals, anti-tuberculosis or antimalarial FPPs, in accordance with NRA requirements.

## NATIONAL REGULATORY AUTHORITY AUTHORIZATION

22. Global Fund resources and Grant Funds may only be used to procure FPPs that have been authorized for use by the NRA in the country where they will be used in accordance with its

[13] List of PIC/S members is available on the PIC/S website: https://picscheme.org/

standard practices for drug registration or other forms of authorization (such as authorizations for marketing or importation or waivers).

23. For FPPs that have been prequalified by the WHO Prequalification Programme, NRAs are encouraged to expedite the process for authorizing the use of such FPPs by accepting the prequalification approval letter and supporting documentation, including WHO prequalification report and the manufacturer's summary of information relating to the quality, safety, and efficacy of the FPP, together with all necessary information to perform quality control testing of products and necessary reference standards.

24. For FPPs that have been authorized for use by an SRA or a WLA, NRAs are encouraged to expedite the process for authorizing the use of such FPPs in the relevant country by accepting the executive summary of the Common Technical Document for the Registration of Pharmaceutical Products for Human Use (CTD) or sections of the CTD relating to the quality, safety, and efficacy of the FPP, together with all necessary information to perform quality control testing of products and necessary reference standards, to fulfil national requirements.

## PROCUREMENT PRACTICES

25. In addition to the procurement principles and related obligations in the Global Fund's Grant Regulations (as amended from time to time), Recipients must ensure that all FPPs are procured in accordance with principles set forth in the Interagency Guidelines: A Model Quality Assurance System for Procurement Agencies.[14]

26. Recipients are responsible for monitoring the performance of suppliers with respect to product and supply chain quality and must submit information to the Global Fund on supplier performance as defined by the Global Fund.

## TRANSPORTATION, STORAGE AND DISTRIBUTION

27. Recipients shall comply or ensure compliance with WHO or internationally recognized guidance for good transportation, storage, and distribution practices applicable to FPPs.

## MONITORING PRODUCT QUALITY

28. The quality of FPPs procured with Global Fund Grant Funds must be monitored. The cost of conducting Quality Control activities may be budgeted for in the Global Fund grant. Recipients must submit to the Global Fund the results of Quality Control tests, which may be made publicly available by the Global Fund.

### For All FPPs

29. In collaboration with NRAs, Recipients must ensure that random samples of FPPs are obtained at different points in the supply chain – from initial receipt of the FPPs in the country to delivery to end-users/patients - for the purpose of monitoring the quality of such FPPs (including Quality Control testing).

[14] A model quality assurance system for procurement agencies: Recommendations for quality assurance systems focusing on prequalification of products and manufacturers, purchasing, storage and distribution of pharmaceutical products. Interagency Publication by WHO, UNICEF, UNIDO, UNDP and World Bank WHO/PSM/PAR/2007.3

30. Such samples must be sent to NRA laboratories or NRA Recognized Laboratories or WHO Prequalified Laboratories or Global Fund contracted laboratories for Quality Control testing.

31. To ensure the NRA Laboratories or NRA Recognized Laboratories have adequate capacity for full pharmacopeial testing, they must meet one of the following criteria:

    (i) Prequalified by WHO Prequalification Programme, or

    (ii) Accredited in accordance with ISO 17025.

32. The Global Fund will make publicly available WHO or internationally recognized guidance that may be used for Quality Control testing and reporting of results.

33. The Global Fund will request Local Fund Agents to verify whether Recipients have complied with the process described in Sections 29 and 30.

34. Technical assistance aimed at strengthening NRA Laboratories or NRA Recognized Laboratories may be included in funding requests.

### For FPPs Recommended for Use by the ERP

35. When a Recipient procures an FPP that has been recommended for use by the ERP, the Global Fund will make any necessary arrangements to implement risk mitigations, including for Quality Control, in accordance with advise provided by the ERP, prior to the delivery of the FPP by the manufacturer to the Recipient. The Recipient will ensure that its contract with the manufacturer affords the Global Fund and its authorized agents with access rights that would allow for such arrangements to be undertaken. The cost of such arrangements will be borne by the Global Fund.

## EMERGENCIES

36. To provide support to countries facing a Public Health Emergency of International Concern (PHEIC), as declared by WHO Director General per International Health Regulations,[15] the Global Fund Board may approve the use of Global Fund resources and Grant Funds to procure FPPs that are:

    (i) Approved pursuant to the WHO Emergency Use Listing (EUL) procedures; or

    (ii) Approved pursuant to any other emergency procedure set up by one SRA or WLA.

## MONITORING POLICY IMPLEMENTATION

37. The Strategy Committee oversees the implementation of this Policy.

38. In order to ensure implementation of this Policy, the Global Fund will provide guidance, training and a reporting mechanism to permit monitoring and oversight.

39. During implementation, the Global Fund Secretariat may need to review and address issues identified related to the quality of health products on an order-by-order basis (e.g., non-conformities with product specifications or non-compliance with product authorizations). The Secretariat will investigate, conduct a risk-based assessment and implement appropriate measures in consideration of patient safety, supply security and programmatic implications.

[15] International Health Regulations, WHO, 2005. https://apps.who.int/iris/rest/bitstreams/1031116/retrieve

## TRANSITIONAL ARRANGEMENTS

40. Authorization given by SRA as per Section 10 (ii) becomes not relevant for the purposes of this Policy when the regulator becomes WLA listed. In that instance, implementation of Sections 10, 13, 16, 17, 19, 24 and 36 of this Policy will only be on the basis of the regulator's WLA status going forward.