GLOBAL FUND QUALITY ASSURANCE POLICY FOR PHARMACEUTICAL PRODUCTS (as amended and restated on 14 December 2010

BASIC PRINCIPLE

1. Global Fund grant funds may only be used to procure finished pharmaceutical products (FPP) in accordance with the standards prescribed in this policy.

GLOSSARY

2. Capitalized terms and acronyms used in this policy shall have the meaning given to them below.

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.

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 labeling.

Fixed Dose Combination (FDC) 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.

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 its website: http://www.ich.org.

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: www.picscheme.org.

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.

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.

Stringent Drug Regulatory Authority (SRA) means a regulatory authority which is (a) a member of the ICH (as specified on its website:); 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).

National Drug Regulatory Authority (NDRA) means the official drug regulatory authority of a country.

NDRA Recognized Laboratories means quality control laboratories for pharmaceutical products selected by NDRAs according to their standards to conduct their quality control testing for pharmaceutical products.

Medicine means an active pharmaceutical ingredient that is intended for human use.

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.

CLINICAL STANDARDS

Compliance with Standard Treatment Guidelines and Essential Medicines Lists

3. Global Fund grant funds may only be used to procure medicines that appear in current national or institutional standard treatment guidelines or essential medicines list ("National or Institutional STGs or EML"), or the World Health Organization (WHO) standard treatment guidelines or essential medicines list ("WHO STG or EML").

4. When submitting grant proposals to the Global Fund, applicants 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 or Institutional STG or EML or the WHO STG or EML. If an applicant intends to procure medicine that is included in the relevant National or Institutional STG/EML, but not included in the WHO STG or EML, or vice versa, the applicant is requested to provide a detailed technical justification for the selection of that medicine, which will be reviewed by the Technical Review Panel (TRP).

5. A Principal Recipient (PR) must submit a technical justification to the Global Fund if it would like to procure a medicine that (i) was not specified in the grant proposal approved by the Global Fund; and (ii) is included in the relevant National or Institutional STG/EML, but not included in the WHO STG or EML, or vice versa. The Secretariat may, if it deems necessary, refer that technical justification to the TRP for review.

Adherence, Drug Resistance and Monitoring Adverse Effects

6. It is strongly recommended that PRs implement mechanisms to encourage adherence to treatment regimens (including but not limited to providing medicines in FDCs, once-a-day formulations and/or blister packs, and providing peer education and support), to monitor and contain resistance, and to monitor adverse drug reactions according to existing international guidelines[1]. The cost of implementing such mechanisms may be included in the budget for the relevant Global Fund grant. To help contain resistance to second-line TB medicines and consistent with the policies of other international funding sources, all procurement of FPPs to treat Multi Drug Resistant Tuberculosis (MDR-TB) must be conducted through the Green Light Committee of the Stop TB Partnership hosted by the WHO (GLC).[2]

PROCUREMENT OF ANTIRETROVIRALS, ANTI-TUBERCULOSIS AND ANTI- MALARIAL FPPS

Quality Standards

7. Global Fund 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 8 and 9 below:

(i) Prequalified by the WHO Prequalification Programme or authorized for use by a Stringent Drug Regulatory Authority (SRA)[3]; or

(ii) Recommended for use by an Expert Review Panel (ERP), as described in Section 10 below.

Selection Process

8. If there are two or more FPPs available[4] for the same Product Formulation that meet the quality standards set out in Section 7(i), the PR may only use Global Fund resources to procure an FPP that meets either of those standards.

9. However, if a PR determines that there is only one or no FPP available[5] that meets either of the quality standards set out in Section 7(i) and it wishes to use Global Fund resources to procure an alternate FPP, it must request confirmation from the Global Fund that the PR's determination is accurate and that the alternate FPP meets the standard specified in Section 7(ii).

Expert Review Panel

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1 E.g. WHO, The Uppsala Monitoring Centre. The Importance of Pharmacovigilance. Safety Monitoring of medicinal products. Geneva: World Health Organization, 2002, available at http://www.who.int/medicinedocs/en/d/Js4893e/. Safety of Medicines. A guide to detecting and reporting adverse drug reactions. Geneva: World Health Organization, WHO/EDM/QSM/2002.2, available at http://www.who.int/medicinedocs/en/d/Jh2992e/

2 http://www.who.int/tb/strategy/en/

3 Or approved or subject to 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.

4 "Available" means the manufacture can supply the requested quantity of the FPP within not more than 90 days of the requested delivery date.

5 Refer to footnote 4.

10. Upon the Global Fund's request, an independent Expert Review Panel (ERP) composed of external technical experts will review the potential risks/ benefits associated with the use of an FPP that is not yet WHO-prequalified or SRA-authorized[6] and will make recommendation to the Global Fund.

11. The Global Fund will maintain an up-to-date list of all FPPs that have been recommended by the ERP. This list will be made publicly available on the Global Fund's website. If, pursuant to Section 9, a PR requests to procure an FPP that does not appear on the list, the Global Fund shall request the ERP to review the relevant FPP.

12. The Global Fund will also make the terms of reference and rules of procedure for the ERP publicly available.

Eligibility Criteria for ERP Review

13. FPPs are eligible for review by the ERP if the following conditions have been met:

(i)
- (a) the manufacturer of the FPP has submitted an application for pre-qualification of the product by the WHO Prequalification Programme and it has been accepted by WHO for review; OR
- (b) the manufacturer of the FPP has submitted an application for marketing authorization to an SRA, and it has been accepted for review by the SRA,

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
- (c) a regulatory authority participating to the Pharmaceutical Inspection Cooperation Scheme (PIC/S).[7]

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/benefits in accordance with paragraph 10 of this Policy 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 will indicate which of the ERP-recommended FPPs were eligible for review as a result of this paragraph.

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[6] Refer to footnote 3.

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

Time Limitation

14. 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-authorized[8], whichever is the earlier.

15. In accordance with Section 9, the PR 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, but the term of the contract must not exceed 12 months (that is, the PR cannot place an order for FPPs under the contract more than 12 months after it is executed).

16. 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 or SRA-authorized[9] within the ERP Recommendation Period. The Global Fund may refer more than one request for such an extension to the ERP.

PROCUREMENT OF ALL OTHER FPPs

Quality Standards

17. All FPPs, other than antiretrovirals, anti-tuberculosis and anti-malarial FPPs, need only to comply with the relevant quality standards that are established by the National Drug Regulatory Authority (NDRA) in the country of use.

Selection Process

18. PRs must select FPPs, other than antiretrovirals, anti-tuberculosis or antimalarial FPPs, in accordance with NDRA requirements.

NATIONAL DRUG REGULATORY AUTHORITY AUTHORIZATION

19. Global Fund resources may only be used to procure FPPs that have been authorized for use by the NDRA in the country where they will be used in accordance with its standard practices for drug registration or other forms of authorization (such as authorizations for marketing or importation).

20. For FPPs that have been prequalified by the WHO Prequalification Programme, NDRAs 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.

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[8] Refer to footnote 3.
[9] Refer to footnote 3.

21. For FPPs that have been authorized for use by an SRA[10], NDRAs 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 fulfill national requirements.

PROCUREMENT PRACTICES TO ASSURE QUALITY

22. In addition to the Global Fund's existing polices for procurement practices, PRs 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[11] (as amended from time to time).

23. PRs 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.

MONITORING PRODUCT QUALITY

24. 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. PRs 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

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

26. Such samples must be sent to NDRA laboratories or NDRA Recognized Laboratories or WHO Prequalified Laboratories or Global Fund contracted laboratory(ies) for quality control testing.

27. To ensure the NDRA Laboratories or NDRA Recognized Laboratories have adequate capacity for full pharmacopoeial testing, they must meet one of the following criteria:

(i) Prequalified by WHO Pre-qualification Programme, or

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[10] Refer to footnote 3.

[11] 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). Annex 6. In: *WHO Expert Committee on Specifications for Pharmaceutical Preparations*, Fortieth report, Geneva, World Health Organization, 2006, (WHO Technical Report Series, No 937), and Interagency Publication by WHO, UNICEF, UNIDO, UNDP and World Bank WHO/PSM/PAR/2007.3.

(ii) Accredited in accordance with ISO17025.

28. The Global Fund will, based on the advice of WHO, provide protocols and standard operating procedures that may be used for quality control testing and reporting of results.

29. The Global Fund will request Local Fund Agents to verify whether PRs have complied with the process described in Sections 25 and 26.

30. Technical assistance aimed at strengthening NDRA Laboratories or NDRA Recognized Laboratories may be included in Global Fund proposals.

For FPPs Recommended for Use by the ERP

31. When a PR procures an FPP that has been recommended for use by the ERP, the Global Fund will make the necessary arrangements for randomly selected samples of the FPP to be tested for quality control purposes, in accordance with advice provided by the ERP, prior to the delivery of that FPP by the manufacturer to the PR or other designated recipient. The PR will ensure that its contract with the manufacturer affords the Global Fund and its authorized agents with access rights that would allow for such sampling to be undertaken. The cost of the sampling and testing of the FPP will be borne by the Global Fund.

TRANSITIONAL PROVISIONS

32. If a PR entered into a contract with a supplier on or before 30 June 2009 for the procurement of FPPs that complied with the Global Fund's previous QA Policy, but do not comply with this policy, the PR must notify the Global Fund of the details of this contract. The Global Fund may, after consultation with the PR, require the PR to take reasonable steps to discontinue procurement of FPPs under such contract, with a view to making a smooth transition to compliance with this policy at the earliest opportunity. In any event, the PR may not seek to extend or renew such a contract after 30 June 2009.