Invitation to Manufacturers

15th July 2024

Manufacturers of Antituberculosis Are Invited to Submit An Expression of Interest For Product Evaluation by the Global Fund Expert Review Panel

Opening Date:	15th July 2024
Closing Date:	Not applicable / Open call
Reference Number:	GF/ERP/Ad-Hoc/07-2024

01 Background

Summary of the Global Fund Quality Assurance Policy

The Global Fund to Fight AIDS, Tuberculosis and Malaria ("Global Fund") provides grants to support national and global efforts to increase access, care and treatment in approximately 140 countries.

The Global Fund Quality Assurance Policy for Pharmaceutical Products ("QA Policy"[1]) defines uniform and stringent quality requirements applicable to antiretrovirals (ARVs), antituberculosis, and antimalarial pharmaceutical products purchased with Global Fund resources. In principle, these pharmaceutical products can be funded using Global Fund resources if they are in compliance with national regulatory standards as applicable and if:

[1] https://www.theglobalfund.org/en/sourcing-management/quality-assurance/medicines/

- prequalified by the WHO Prequalification Programme; **and/or**
- authorized for marketing in a country with a stringent regulatory authority[2] (registration "for export only" is not sufficient) or approved/subject to a positive opinion under one of the following schemes: Canada S.C. 2004, c. 23 (Bill C-9) procedures, or Art. 58 of European Union Regulation (EC9 No. 726/2004) or US-FDA tentative approval; **or**
- authorized for use by a World Health Organization Listed Authority (WLA)[3]
- products of which the dossiers were reviewed and permitted for use for a time limited period by an independent panel of technical experts (the Expert Review Panel).

Information about the Expert Review Panel mechanism and process for procurement of Expert Review Panel-reviewed products is available at: https://www.theglobalfund.org/en/sourcing-management/quality-assurance/expert-review-panel/

In order to assist Global Fund grant recipients to identify the regulatory status of Pharmaceutical Products, the Global Fund has developed list of products classified according to the above quality assurance requirements. The current lists can be downloaded from: https://www.theglobalfund.org/en/sourcing-management/quality-assurance/medicines/

Summary of the Global Drug Facility Quality Assurance Policy

In Sept 2022, the Global Drug Facility (GDF) revised its quality assurance policy and procedures as part of a collaborative process to ensure harmonization with the policies of major multilateral financing mechanisms, including the Global Fund and other organizations (i.e. the United Nations Children's Fund (UNICEF), Médecins Sans Frontières, UNITAID, etc) involved in TB control and to:

- ensure global consistency on quality standards set for procurement and supply of anti-TB medicines, medical devices, and in-vitro diagnostic products;
- avoid duplication of effort and to ensure optimum utilization of available resources.

With the combined objectives to improve the safety, efficacy and quality of products procured by the GDF, the GDF quality assurance system is based on:

- recommendations by WHO/Stop TB Strategy;
- authorization for use by the recipient countries;
- recommendations by the WHO Prequalification of Medicines Programme (PQP);
- authorization for marketing by a stringent national medicine regulatory authority;
- positive opinion for procurement purposes by an Expert Review Panel, for a specified period where there are few or no WHO-prequalified or stringent regulatory approved products available; and

[2] https://www.theglobalfund.org/en/sourcing-management/quality-assurance/medicines/
[3] Evaluating and publicly designating regulatory authorities as WHO listed authorities WHO Policy document – Geneva 2021. https://www.who.int/publications/i/item/9789240023444.

- a quality monitoring program for supplied products, including independent risk-based approach quality control in place.

Summary of the Unitaid Quality Assurance Policy

Unitaid's mission is to maximize the effectiveness of the global health response by catalyzing equitable access to better health products for HIV/AIDS, tuberculosis and malaria in low and middle-income countries. Unitaid's approach is to utilize market interventions to improve public health. In so doing, Unitaid aims to promote "healthy", dynamic market conditions whereby manufacturers have incentives to invest and innovate, while at the same time supply quality public health products at affordable prices and in acceptable formulations that enable the maximum number of people to access them. By working through markets, Unitaid's interventions impact not only those countries receiving direct Unitaid support, but also other countries and organisations that can benefit from Unitaid's global price reductions, improvements in product quality, and innovation. In all cases, Unitaid seeks to find innovative, cost-effective and sustainable market solutions to public health problems. The ultimate goal of Unitaid is to improve the public health of people living in low- and middle-income countries through market-based interventions.

All medicines procured under Unitaid-funded projects are required to be in compliance with Unitaid's quality assurance policy, which stipulates similar standards as described above and in the relevant sections of the Global Fund quality assurance policy.

02 Purpose

The purpose of this expression of interest is to invite submissions of product dossiers for review by the Expert Review Panel for which there could be supply bottlenecks, including the cases where there are less than two products of the same formulation available in the global market that are already WHO prequalified or approved by a stringent regulatory authority or WHO listed authority. This expression of interest may include, as well, some formulations even when there are two or more eligible products in the market, in cases where it has been determined that such products are eligible for distribution to a restricted number of countries only, or when it has been identified that the available production capacity of the qualified products cannot cover the demand.

03 Product formulations included in this expression of interest

The recommended active ingredients, dosage forms and strengths ("Formulations") listed in this document are included in the current WHO Model List of Essential Medicines and/or in the most recent WHO standard treatment guidelines for treatment and prevention of the three diseases.

Antituberculosis formulations included in this expression of interest are listed in Annex A.

WHO recommends and endorses the use of medicines in fixed-dose combinations. The Global Fund quality assurance policy strongly recommends that Principal 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, and providing peer education and support), to monitor and

contain resistance, and to monitor adverse drug reactions according to existing international guidelines. FDCs are considered as the preferred option when available.

04 Eligibility for submission[4]

Requirements under CRITERION-1:

The following criteria must be met in order for products to be accepted for External Review Panel review:

- the manufacturer of the product has submitted an application of the product to the WHO Prequalification Programme and it has been accepted by WHO for review; OR the manufacturer of the product has submitted an application for marketing authorization to a stringent regulatory authority or to WHO listed authority, and it has been accepted for review by the stringent regulatory authority or the WHO listed authority;
- AND the product is manufactured at a site that is compliant with all standards of good manufacturing practice that apply to the relevant product formulation, as verified after inspection by the WHO Prequalification Programme, OR a stringent regulatory authority, OR a WHO listed authority OR a regulatory authority participating in the Pharmaceutical Inspection Cooperation Scheme (PIC/S)[5].

Requirements under CRITERION-2:

The following criteria must be met in order for products to be accepted for an External Review Panel review:

- the product is manufactured at a site that is compliant with all standards of good manufacturing practice that apply to the relevant product formulation, as verified after inspection by the WHO Prequalification Programme OR a stringent regulatory authority OR a WHO listed authority OR a regulatory authority participating in the Pharmaceutical Inspection Cooperation Scheme (PIC/S),
- AND it is not listed in the WHO invitation to manufacturers to submit an expression of interest for product evaluation by the WHO Prequalification Programme.

05 Submission of documents for Expert Review Panel review under CRITERION-1

All manufacturers interested in submitting applications for review by the Expert Review Panel are requested to submit the following information and material for each product under consideration:

For each product awaiting WHO prequalification:

1. A covering letter expressing interest in submitting the product to the Expert Review Panel for review;
2. An acceptance letter from the WHO Prequalification Programme confirming that the submission for the product has been accepted for review, and stating the WHO reference number assigned by WHO to this specific product;

[4] Global Fund, https://www.theglobalfund.org/en/sourcing-management/quality-assurance/medicines/
[5] Pharmaceutical Inspection Cooperation Scheme (https://picscheme.org/en/picscheme)

3. Certification issued by the WHO Prequalification Programme confirming that the site and production line where the product is manufactured comply with all aspects of good manufacturing practice, or a letter describing arrangements made to obtain such certification and stating the date when it will be supplied;
4. A completed Pharmaceutical Product Questionnaire[6] (attached);
5. In lieu of annexes, reference can be made to the dossier submitted for WHO prequalification. Annexes should be submitted in case of any changes or updates;
6. Good quality photos of the sample : product itself (tablet, capsules, etc.), primary and secondary packaging.

For each product awaiting marketing authorization by a stringent regulatory authority or WHO listed authority:

1. A covering letter expressing interest in submitting the product to the Expert Review Panel for review;
2. An acceptance letter from a stringent regulatory authority or WHO listed authority confirming that the submission for the product has been accepted for review;
3. Certification, issued by a stringent regulatory authority OR a WHO listed authority OR a regulatory authority participating in the Pharmaceutical Inspection Cooperation Scheme (PIC/S), confirming that the site and production line where the product is manufactured comply with all aspects of good manufacturing practice, or a letter describing arrangements made to obtain such certification and stating the date when it will be supplied;
4. A completed Pharmaceutical Product Questionnaire[6] (attached), and all annexes as applicable;
5. Good quality photos of the sample : product itself (tablet, capsules, etc.), primary and secondary packaging.

06 Submission of documents for External Review Panel review under CRITERION-2

All manufacturers interested in submitting applications for review by the External Review Panel under *Eligibility Criterion 2* are requested to submit the following information and material for each product under consideration:

1. A covering letter expressing interest in submitting the product to the External Review Panel for review;
2. Certification issued by the WHO Prequalification Programme confirming that the site and production line where the product is manufactured comply with all aspects of good manufacturing practice, or a letter describing arrangements made to obtain such certification and stating the date when it will be supplied;

and/or

[6] As available at the Global Fund website:
https://www.theglobalfund.org/media/4325/psm_interagencyfinishedpharmaceuticalproduct_questionnaire_en.docx

3. Certification, issued by stringent regulatory authority OR a WHO listed authority OR a regulatory authority participating in the Pharmaceutical Inspection Cooperation Scheme (PIC/S), confirming that the site and production line where the product is manufactured comply with all aspects of good manufacturing practice, or a letter describing arrangements made to obtain such certification and stating the date when it will be supplied;
4. A completed Pharmaceutical Product Questionnaire[7];
5. Good quality photos of the sample : product itself (tablet, capsules, etc.), primary and secondary packaging.

07 Confidentiality

All information provided by manufacturers will be received by the Global Fund and shared with the External Review Panel members for the purpose of facilitating their review of the submission and provision of advice to the Global Fund.

Information provided by manufacturers, review findings and advice provided by the External Review Panel in connection with this expression of interest will be shared with and used by the Global Fund, GDF, Unitaid and the following partners: Médecins sans Frontières, UNICEF, and the United States Agency for International Development (USAID) as the basis for procurement decisions.

08 Eligibility

Completeness of the documents submitted to Global Fund Secretariat for External Review Panel review is determined by the Global Fund quality assurance specialist. All the documents listed in the instructions for submission (in annex) must be included by the applicant. Incomplete submissions will not be forwarded to the External Review Panel.

The eligibility of the submissions for External Review Panel review will not be considered by the Global Fund Secretariat. It is the External Review Panel's responsibility to review and to judge the eligibility and whether or not to perform the risk-benefit assessment of the products submitted.

For any product found not to comply with the required standards during previous External Review Panel review, all documentation requested should be re-submitted in full.

09 Instructions for submission

Documentation should be submitted by electronic means ONLY via file transfer (because of new IT policy security, please liaise in advance with the contact address above of this EoI to ensure file transfer software is acceptable to Global Fund). Files should be named to reflect their content as mentioned in this letter (e.g. "Covering Letter.pdf"). For ease of reference, electronically submitted annexes to the questionnaire should be named according to the letters on the list of annexes on page 17 of the questionnaire

[7] As available at the Global Fund website:
https://www.theglobalfund.org/media/4325/psm_interagencyfinishedpharmaceuticalproduct_questionnaire_en.docx

(e.g. "A.pdf" for information on the formulation of the product). **Please keep the naming of the annexes as short as possible (e.g. "A.pdf").**
In regards of the technical evaluation, it is mandatory to submit good photos of the sample of the finished product offered.

The deadline for the Submission is : Not applicable /Open tender.

Submissions should be sent to the following Address of the TGF QA team:
Sandrine.cloez@theglobalfund.org

Should you have any further questions, please send an e-mail to the following email address: Sandrine.cloez@theglobalfund.org

Annex A - Antituberculosis formulations

Preferred standard packaging specifications: for all the solid dosage products the preferred standard packaging specifications are Blister.

Formulations included under eligibility (CRITERION-1):

Fixed-dose combinations:

a) Rifapentine / Isoniazid / Moxifloxacin, 300 mg / 75 mg / 100mg tablet

b) Rifampicin / Isoniazid / Pyrazinamide / Ethambutol, 150 mg / 75 mg / 400 mg / 275 mg [8]
c) Rifampicin / Isoniazid / Ethambutol, 150 mg / 75 mg / 275 mg [8]
d) Rifampicin / Isoniazid, 150 mg / 75 mg [8]

[8] For FPPs described in section b), c) and d), manufacturer may propose an existing WHOPQ FPP manufactured using a new Active Pharmaceutical Ingredient (API) source if the API Master File (APIMF) has been submitted for prequalification and has been accepted for assessment by WHOPQ. In such cases, the submission to ERP can follow principles outlined in the prequalification variation guide (Variation number 8e1). Additionally, the applicant must confirm that no other changes have been introduced to the prequalified product.

END

Additional consulted reference guidelines:

WHO guidelines (15 December 2022) consolidated Guidelines on Tuberculosis, Module 4: Treatment - Drug-Resistant Tuberculosis Treatment
https://www.who.int/publications/i/item/9789240063129

WHO guidelines (18 March 2022) consolidated guidelines on tuberculosis Module 5: Management of tuberculosis in children and adolescents
https://www.who.int/publications/i/item/9789240046764