Ensuring the Quality of Priority Medicines

Quality Assurance- Health Product Management Hub

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The Global Fund

Our Mission

Investing the world’s money to defeat AIDS, tuberculosis and malaria

Quality Assurance

Quality assurance is ensuring that the health products that are purchased (everything from medication to microscopes) and used by **Global Fund-supported programs** are safe, effective, of good quality and available to the patient.

Key stakeholders in quality assurance include:

- Manufacturers
- National regulatory authorities
- Quality control laboratories and pharmacovigilance centers
- National procurement systems
- International agencies
- Technical partners
- Health care providers

Content Overview

1. TGF QA Policy for Pharmaceuticals

2. TGF QA Policy for Diagnostics

3. Collaboration with GDF StopTB Partnership

4. TB Treatment and Global Fund Needs

5. Sustainability, Transition and Co-financing Policy

Global Fund Quality Assurance Policy for Pharmaceutical Products ("QA Policy"):

Implementers of programs for **AIDS**, **TB**, **HepB & C** or **Malaria** who want to use Global Fund grants to purchase medicines must ensure that those pharmaceutical products meet the Global Fund's quality standards as set out in the **Quality Assurance Policy for Pharmaceutical Products.**

1. Clinical criteria

- Medicines procured with Global Fund resources must be listed in WHO or national or institutional Standard Treatment Guidelines (STGs)
- If grant applicants or PRs select products not listed in at least one set of STGs, they must provide a technical justification

**PR: Principal Recipient*

2. Quality Criteria and Selection Process

- **All medicines must be**

➢ Authorized for use by drug regulatory authority in recipient country

- **In addition, ARVs, anti-TB, medicines to treat Hepatitis B and C and antimalarial medicines must be :**

➢ Prequalified by WHO (**Option A**) or authorized for use by a stringent regulatory authority (SRA) (**Option B**)

- OR (if fewer than two A/B products are available):

➢ Permitted for use based on the advice of the Expert Review Panel (**ERP**)

Expert Review Panel (ERP)

- A panel of experts hosted by WHO
- **Assesses the potential risks/benefits** associated with the use of FPPs that are not yet WHO-prequalified or SRA-authorized
- ERP provides **time limited** recommendations to The Global Fund
- GF decision **valid for a period of maximum 12 months**

3. ERP Process For Pharmaceutical Products

Invitation to Antiretroviral (HIV/AIDS), Antihepatitis B and C, Antituberculosis and Antimalarial Medicines Manufacturers to Submit an Expression of Interest for Product Evaluation by the Global Fund Expert Review Panel for Pharmaceutical Products

- List of **priority medicine**
- 2 ERP Cycles per calendar year
- The overall timeline of cycle is 22 weeks
- No additional data management within an ERP cycle

Timeline of the ERP process for Pharmaceutical Products

KEY DELIVERABLES

- Finalized list of Pharmaceutical products to include in the EoI
- EoI published on TGF website
- Manufacturer are invited to submit a Product Questionnaire
- Manufacturer are informed about the screening outcome of the Product Questionnaire
- ERP Review
- TGF receives the ERP Reports
- Inform Manufacturer about the outcome of the ERP Review
- Update TGF List of Pharmaceutical products

Acronyms: ERP : Expert Review Panel, EoI: Expression of Interest, TGF: The Global Fund

ERP –eligibility criteria for Priority Medicine

- **Criteria 1 products (medicines invited to PQ)**
  - Manufactured at GMP compliant facility
  - Submitted and accepted for assessment (PQ/SRA)

  Exceptions in problem areas:
  - *Acceptable level of GMP compliance based on GMP risk assessment*
  - *Commitment to submit dossier to PQ/SRA*

- **Criteria 2 products (medicines not invited to PQ)**
  (certain TB, Malaria and NTD medicines, amoxicillin)
  - Manufactured at a GMP compliant facility.
  - Submission to PQ/SRA not required.

Criteria for categorization of products and formulating ERP advise

The reviewed products will be classified into 4 categories:

- **Categories 1 and 2** can be considered, in principle, for time limited (12 months) procurement.
- **Category 3** can be considered only if there is no other option and the risks of not treating the disease is higher than the risk of using medicines not meeting all quality standards.
- **Category 4** cannot be considered under any circumstances

The following major product attributes will be used as a basis for comparing the products:

- **GMP status of the manufacturing site - one of the eligibility criteria**
- **FPP manufacturing process and FPP specification**
- **Stability data**
- **Evidence of therapeutic equivalence**
- **API source and API quality**

4. Global Fund List

•An overview of products and manufacturers classified according to the Global Fund QA Policy criteria
•Tool to assist countries:
➢ **to identify Global Fund QA-compliant products**
➢ **to make decisions for procurement selection**
•Not an exhaustive list - based on the information available to the Global Fund submitted by manufacturers

A classified product: WHO prequalification letter;
B classified product: SRA approval letter or market authorization/registration;
ERP-reviewed product- Cat 1 and 2 products are published based on the ERP report;

➢ List is updated regularly, usually at the end of the each month
Published on the Global Fund webpage:
https://www.theglobalfund.org/en/sourcing-management/quality-assurance/medicines/

5. Monitoring product quality

according to the QA Policy:

- The quality of FPPs procured with Global Fund grant funds must be monitored.

Principles of quality monitoring:

Concerns all products (including WHO-prequalified and SRA-authorized products)

Monitoring done all along the supply chain

Systematic random quality control testing (following a plan - not all products / lots will be tested)

- ✓ Pre-Shipment QC Testing before Procuring ERP approved Products
- ✓ **GDF is responsible for the QC testing activities for TB medicine procured through their services for the Global Fund**

Revised Global Fund Quality Assurance Policy for Diagnostic Products

37th Board meeting in Rwanda, May 2017

The development of the QA Policy

- developed in 2009 with experts support (regulators, association of manufacturers, WHO)
- approved by the Board in 2010 based on the Market Dynamics Committee recommendation
- updated in 2014, noting needs for future revisions for the phase-in of specific products

The QA Policy is based on 3 sets of requirements

- **Clinical standards** : ensure consistency with WHO guidance and national guidelines
- **Quality standards**: establish minimum standards and additional standards for specific products
- **Quality of use**: refer to guidance for ensuring quality use and adequate outcome

Rationale for proposed policy revisions

- Alignment with new or updated WHO guidelines for key products
- Alignment with the Global Fund Policy on co-infection and co-morbidities (COIMs)

**Link to the Policy : https://www.theglobalfund.org/media/5885/psm_qadiagnostics_policy_en.pdf*

Revisions related to changes/updates to normative guidance and policies

HIV self testing	WHO guidelines encourage countries to pilot/explore self-testing to scale up testing Global Fund supports operational research on HIV Self testing **Proposed revisions to the policy include specific quality requirements for HIV self testing RDTs (section 8)**
Procurement eligibility mRDTs	As of 31 Dec 2017, WHO Prequalification Programme will determine procurement eligibility Proposed revisions to the policy reflect alignment with these changes (section 8)
PMS on IVDs	In 2015, WHO guidance on Post-Market Surveillance of IVDs that describe measures to ensure on-going compliance of Diagnostics Proposed revisions to the policy include this WHO guidance (section 13)
G6PD testing	WHO recommends G6PD testing in regions with high prevalence of G6PD deficiency prior to primaquine treatment. **Proposed revisions include quality requirements for G6PD tests**
Co-infections	Proposed revisions include quality requirements for In-vitro diagnostics (IVDs) for Hepatitis B and C, Syphilis co-infections (section 8)

3. TGF's & GDF Stop TB partnership on QA Activities

- **Partnership** to optimize access to quality assured TB health products, through efficient procurement and supply management, technical assistance and capacity strengthening in the ***Global Fund*** countries
- The Global Drug Facility (STBP-GDF) is the designated **procurement mechanism** for ***Global Fund Principal Recipient*** to procure TB medicine and diagnostics.
- Compliance to ***Global Fund*** Quality Assurance policies
  - Clinical Criteria
  - Quality criteria
  - Monitoring Quality
  - Collaborate in cases where non-compliance quality defect or adverse effect/event occurs.

Manufacturer should always report back to the Quality assurance team of TGF any information related to a non-compliance or an ADR

TB New Treatment Guideline- MDR/XDR TB

→The Shorter MDR-TB Regimen

REGIMEN COMPOSITION

4-6 Km-Mfx-Pto-Cfz-Z-Hhigh-dose-E / 5 Mfx-Cfz-Z-E

Km=Kanamycin; Mfx=Moxifloxacin; Pto=Prothionamide; Cfz=Clofazimine; Z=Pyrazinamide; Hhigh-dose= high-dose Isoniazid; E=Ethambutol

- Use of **Bedaquiline**
- Use of **Delamanid** for children and adolescent between 6 and 17 years old.

Essential medicine for patients under 18 years of age with multidrug- or rifampicin-resistant (MDR/RR-TB) and extensively drug-resistant (XDR-TB) disease.

TB New Treatment Guideline- Pediatrics

New fixed-dose combinations for the treatment of TB in children

The FDCs are recommended :

- for the first line treatment of TB
- to replace previously used medicines for children weighing less than 25 kg

The formulations now available are :

- **For the intensive phase of TB treatment:**

Rifampicin 75 mg + Isoniazid 50 mg + Pyrazinamide 150mg

- **For the continuation phase of TB treatment:**

Rifampicin 75mg + Isoniazid 50 mg

GF Needs in term of TB Formulation

Shorther MDR-TB Regimen

Global Fund encourage countries to switch to new regimen

- The uptake of new regimen will increase significantly in the next months

Lake in TB Pediatrics → only one supplier of RH and RHZ, which is ERP approved

As per today the uptake of new pediatrics FDC is slower than it should be

- Countries want to finish their stocks of “old” formulations
- Some countries are reluctant to procure a product that is not WHO PQ

We would like to emphasizes that the ERP approval is time limited and made on a exceptional basis before getting WHO PQ approval

- For 2nd line TB medicine we would like to have products with a longer shelf life

Sustainability, Transition and Co-financing Policy

- TGF determines a Country's **eligibility for funding** according to the World Bank's income classification* and disease burden indicator for HIV, TB and malaria as defined in the eligibility policy

- TGF strongly recommend that all UMIC regardless of disease burden and all LMIC with low/moderate disease burden get prepared for the reduction or finalization of GF support

- For that purpose, TGF recommends defining a strategy to provide the overall pathway to transition, including a **phased plan for domestic take-up** of GF financed activities

- According to the 2016 Global Fund Sustainability, Transition and Co-financing policy, once a country disease component becomes ineligible for Global Fund funding, **it may receive up to three years of transition funding before the financing ends**

**For the purposes of Global Fund eligibility, income classification is determined by using an average of available GNI per capita data over the latest three-year period*

Sustainability, Transition and Co-financing Policy

Global Fund Definition of Sustainability

Ability of a health program or country to both maintain and scale up services coverage to a level, in line with epidemiological context, that will support efforts for elimination of the three diseases, even after the removal of funding by the Global Fund and other donors.

Global Fund Definition of Transition

The process by which a country, or a country disease component, moves towards fully funding and implementing its health program, independent of Global Fund support while continuing to sustain the gains and scaling up as appropriate.

*The Global Fund considers a transition to be **successful** where national health programs are able to maintain or improve equitable coverage and uptake of services through resilient and sustainable systems for health after Global Fund support has ended.*

Sustainability, Transition and Co-financing Policy

Global Fund Definition of Co-financing

Co-financing is defined as all domestic public resources and domestic private contributions that finance the health sector and national strategic plans supported by the Global Fund

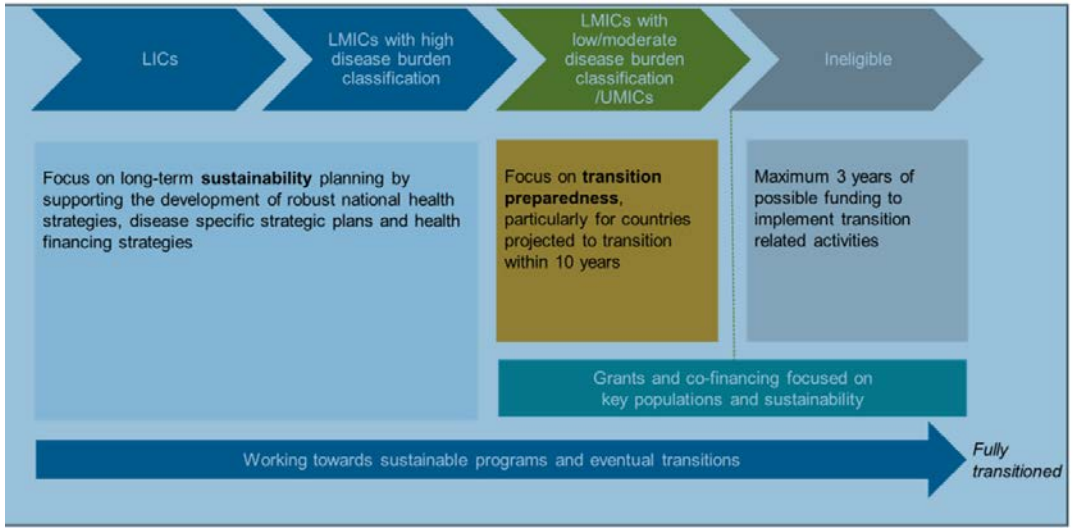
- Domestic public resources can include government revenues, government borrowings, social health insurance, and debt relief proceeds

- Domestic private contributions include verified contributions from domestic corporations and philanthropies that finance national strategic plans

To enhance sustainability and preparedness for transition TGF has implemented new Co-Financing requirement *

**https://www.theglobalfund.org/en/funding-model/funding-process-steps/co-financing/*

Sustainability, Transition and Co-financing Policy

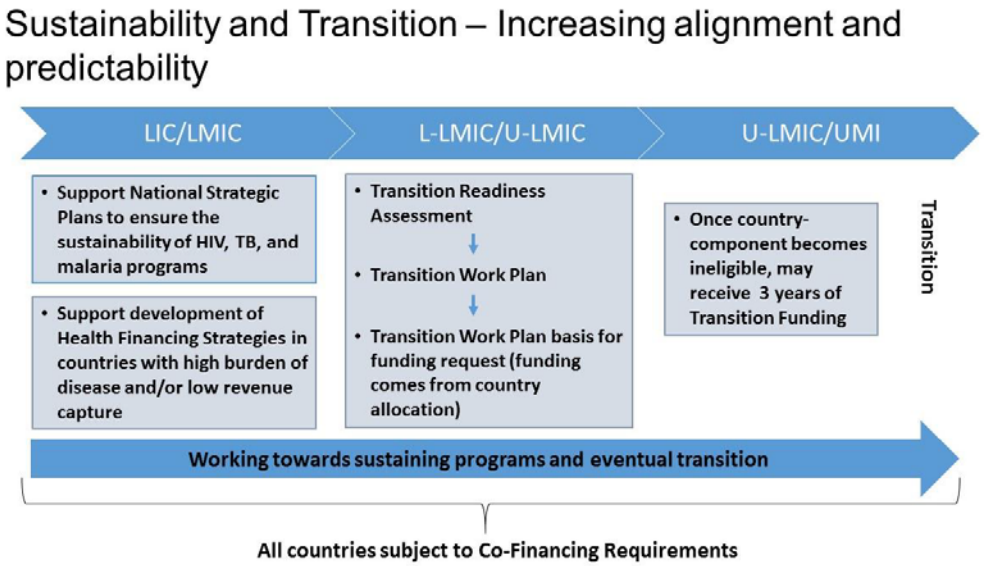


National Strategies and Health Financing Strategies: National Health and Disease-Specific Strategic Plans (NSPs) provide the overall strategic direction for a country's health and disease specific programs over a defined period of time (usually 5 years).

For the **current 2018 fiscal year**,

- low-income economies (LIC) are defined as those with a GNI per capita, calculated using the World Bank Atlas method, of $1,005 or less in 2016;
- lower middle-income economies (LMIC) are those with a GNI per capita between $1,006 and $3,955;
- upper middle-income economies (UMI) are those with a GNI per capita between $3,956 and $12,235

Sustainability, Transition and Co-financing Policy



- **National systems are not necessarily government systems.**
- **National systems may also include instances where the government contracts with non-governmental organizations (NGOs)**

Countries in view of transition need to **invest in the appropriate System for Health** and **implementing GF activities through National Systems*** as well as implementing Health Financing Strategies to **progressively increase domestic financing** for health and for the 3 diseases.

Table 2: Transition Projections*

Newly ineligible since 2014-16 allocation and may receive transition funding in 2017-2019	Projected to become ineligible in 2017-2019 based on country move to UMI status and may receive transition funding in 2020-2022	Projected to become ineligible based on country move to UMI status in 2020-2022 and may receive transition funding in 2023-2025
Albania (HIV, TB) Algeria (HIV) Belize (TB) Botswana (malaria) Bulgaria (TB) Cuba (HIV) Dominican Republic (TB) Paraguay (TB, malaria) Panama (TB) Sri Lanka (malaria) Suriname (TB) Turkmenistan (TB)	Armenia (HIV, TB) El Salvador (TB, malaria) Kosovo (HIV, TB) Philippines (malaria) Sri Lanka (HIV, TB)	Bolivia (malaria) Egypt (TB) Guatemala (TB, malaria)
Countries projected to move to High Income status and become ineligible ***(High Income countries are not eligible for transition funding)***		
Projected to become ineligible over 2017-2019	*Projected to become ineligible over 2020-2022*	*Projected to become ineligible over 2023-2025*
Malaysia (HIV) Panama (HIV)	Costa Rica (HIV) Romania (TB)	Kazakhstan (HIV, TB) Mauritius (HIV)

** In October 2016*

- The country components projected to transition from Global Fund support, grouped by the allocation period in which they are projected to receive their last allocation:

  Country components that have recently become ineligible and will be eligible to receive a Transition Funding grant in the 2017-2019 allocation period are also listed below.

In total, 24 countries are projected to transition in at least one component by 2025, with 13 countries projected to transition fully away from Global Fund financing.

Link to references

QA policy for Pharmaceuticals & ERP Process

https://www.theglobalfund.org/en/sourcing-management/quality-assurance/

https://www.theglobalfund.org/media/5894/psm_qapharm_policy_en.pdf

https://www.theglobalfund.org/en/sourcing-management/quality-assurance/expert-review-panel/

https://www.theglobalfund.org/en/sourcing-management/updates/2017-02-08-opportunity-for-evaluation-of-selected-medicines/

QA policy for Diagnostics & ERPD Process

https://www.theglobalfund.org/en/sourcing-management/quality-assurance/diagnostic-products/

https://www.theglobalfund.org/media/5885/psm_qadiagnostics_policy_en.pdf

https://www.theglobalfund.org/en/sourcing-management/updates/2017-01-30-opportunity-for-evaluation-of-diagnostic-products/

Eligibility & Transition

https://www.theglobalfund.org/en/funding-model/funding-process-steps/eligibility-transitions/

https://www.theglobalfund.org/media/5601/core_eligiblecountries2017_list_en.pdf

https://www.theglobalfund.org/media/5641/core_projectedtransitions2016_list_en.pdf

https://www.theglobalfund.org/media/4227/bm35_06-eligibility_policy_en.pdf

https://www.theglobalfund.org/media/5648/core_sustainabilityandtransition_guidancenote_en.pdf

Annexes

UMI countries Albania (HIV, TB), Algeria (HIV, TB), Angola (HIV, TB, malaria), Azerbaijan (HIV, TB), Belarus (HIV, TB), Belize (HIV, TB), Botswana (HIV, TB, malaria), Bulgaria (TB), Colombia (HIV), Costa Rica (HIV), Cuba (HIV), Dominica* (HIV, TB), Dominican Republic (HIV, TB), Ecuador (HIV), Gabon (HIV, TB, malaria), Georgia (HIV, TB), Grenada* (HIV, TB), Iran (HIV), Iraq (TB)***, Jamaica (HIV), Kazakhstan (HIV, TB), Malaysia (HIV), , Marshall Islands* (HIV, TB), Mauritius (HIV), Mongolia (HIV, TB)**, Namibia (HIV, TB, malaria), Panama (HIV, TB), Paraguay (HIV, TB, malaria), Peru (HIV, TB), Romania (TB), Saint Lucia* (HIV, TB), Saint Vincent and the Grenadines* (HIV, TB), Serbia (HIV), South Africa (HIV, TB), Suriname (HIV, TB, malaria), Thailand (HIV, TB, malaria), Tonga* (HIV, TB), Tunisia** (HIV), Turkmenistan (TB), Tuvalu* (HIV, TB)

LMI countries with low or moderate disease burden classification : Armenia (HIV, TB), Bangladesh (HIV), Bhutan (HIV, malaria), Bolivia (malaria), Cabo Verde* (malaria), Egypt (TB), El Salvador (TB, malaria), Guatemala (TB, malaria), Honduras (TB, malaria), Kiribati* (HIV), Kosovo (HIV, TB), Lao PDR (HIV), Micronesia, Fed. Sts. (HIV), Nicaragua (TB, malaria), Philippines (malaria), Samoa* (HIV, TB), São Tomé and Principe* (HIV), Solomon Islands* (HIV), Sri Lanka (HIV, TB, malaria), Sudan (HIV, TB), Swaziland (malaria), Syrian Arab Republic (HIV, TB), Timor-Leste (HIV), Uzbekistan (malaria), Vanuatu* (HIV), Palestine(HIV, TB), Yemen, Rep. (TB)