GDF QUALITY ASSURANCE (QA) POLICY FOR TB PRODUCTS

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TABLE OF CONTENTS

ACRONYMS

AIDS	Acquired Immune Deficiency Syndrome
CAB	Conformity Assessment Body
CoA	Certificate of Analysis
EMA	European Medicines Agency
ERP	Expert Review Panel
EU	European Union
FDA	Food and Drug Administration
FPP	Finished Pharmaceutical Product
GDF	Global Drug Facility
GDP	Good Distribution Practice
GMP	Good Manufacturing Practice
GLP	Good Laboratory Practice
GSP	Good Storage Practice
IMRDF	International Medical Devices Regulatory Forum
ICH	International Conference of Harmonization
ISO	International Organization for Standardization
IVD	In-Vitro Diagnostics
MD	Medical Devices
NRA	National Regulatory Authority
OoS	Out of Specification
PA	Procurement Agent
PIC/S	Pharmaceutical Inspection Cooperation Scheme
PSI	Pre-Shipment Inspection
QA	Quality Assurance
QC	Quality Control
QCA	Quality Control Agent
QMS	Quality Management System
SRA	Stringent Regulatory Authority
TB	Tuberculosis
WHO	World Health Organization
MQAS	Model Quality Assurance System for Procurement Agencies
WHO PQP	World Health Organization Prequalification Programme

DEFINITIONS

Antituberculosis Medicines: Medicines that are recommended for the prevention and treatment of TB as per the latest WHO treatment guidelines, and related medicines such as Vitamin Bit B6.

Common Technical Document for the Registration of Pharmaceutical Products for Human Use (CTD): A common format for the submission of information to regulatory authorities in International Conference of Harmonization (ICH) member countries.

Diagnostic Products: Products used for the screening, diagnosis, and/or surveillance and monitoring of TB. Diagnostic products include medical devices (MD), in-vitro diagnostics (IVD), and medical software, as well as laboratory equipment, reagents, chemicals, and consumables.

Finished Pharmaceutical Product (FPP): A medicine presented in its finished dosage form that has undergone all stages of production, including packaging in its final container and labeling.

Good Manufacturing Practices (GMP): 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 (ICH) of Technical Requirements for the Registration of Pharmaceuticals for Human Use: An initiative involving regulatory authorities and pharmaceutical industry experts that was established to make recommendations on ways to achieve greater harmonization worldwide to ensure that safe, effective, and high-quality medicines are developed, registered, and maintained in the most resource-efficient manner whilst meeting high standards. ICH member countries are specified on its website: http://www.ich.org.

International Medical Device Regulators Forum (IMDRF): A voluntary group of medical device regulators from around the world who have come together to build on the strong foundational work of the Global Harmonization Task Force on Medical Devices (GHTF). IMDRF aims to accelerate international medical device regulatory harmonization and convergence. More information is available on the IMDRF website: https://www.imdrf.org/.

International Organization for Standardization (ISO): An independent non-governmental organization with a membership of 167 national standard bodies which brings together experts to share knowledge and develop voluntary, consensus-based, market-relevant international standards that support innovation and provide solutions to global challenges. These include generic standards (e.g., ISO 9000 series) or product-specific requirements for

implementing a quality management system (e.g., ISO 13485 for medical devices). More information is available on the ISO website: https://www.iso.org/home.html.

In Vitro Diagnostic Product (IVD) Medical Device: A medical device, whether used alone or in combination, intended by the manufacturer for in-vitro examination of specimens derived from the human body solely or principally to provide information for diagnostic, monitoring, or compatibility purposes. IVD medical devices include reagents, calibrators, control materials, specimen receptacles, software, and related instruments or apparatus or other articles. IVD medical devices are used for the following test purposes: diagnosis, aid to diagnosis, screening, monitoring, predisposition, prognosis, prediction, and determination of physiological status.

Manufacturer: A company that carries out operations such as production, packaging, repackaging, labelling, and re-labelling of medicines and/or diagnostic products.

Medical Devices: An article, instrument, apparatus, or machine that is used in the prevention, diagnosis, or treatment of illness or disease; or, for detecting, measuring, restoring, correcting, or modifying the structure or function of the body for some health purpose. Typically, the purpose of a medical device is not achieved by pharmacological, immunological, or metabolic means. The full definition is available from the IMDRF website: https://www.imdrf.org/sites/default/files/docs/ghtf/final/sg1/technical-docs/ghtf-sg1-n071-2012-definition-of-terms-120516.pdf.

Medicine: Any substance or pharmaceutical product for human or veterinary use that is intended to modify or explore physiological systems or pathological states for the benefit of the recipient. In this document, the terms medicine and pharmaceutical product (see below) are used interchangeably.

National Regulatory Authority (NRA): The national authority that is responsible for assuring the quality, safety, and efficacy of medicines, vaccines, blood products, and medical devices, including IVDs.

Pharmaceutical Inspection Cooperation Scheme (PIC/S): A non-binding, informal co-operative arrangement between regulatory authorities in the field of GMP of medicinal products for human or veterinary use. It is open to any authority having a comparable GMP inspection system. PIC/S presently comprises 54 participating authorities from all over the world. PIC/S member countries are specified on its website: www.picscheme.org.

Product Formulation: The active pharmaceutical ingredient (or combination of ingredients), dosage form, and strength of a pharmaceutical product. Multiple FPPs may exist for the same product formulation.

Quality Assurance: A wide-ranging concept covering all matters that individually or collectively influence the quality of a product. It is the totality of the arrangements made with the objective of ensuring that pharmaceutical products are of the quality required for their intended use.

Quality Control: All measures taken, including the setting of specification sampling, testing, and analytical clearance, to ensure that starting material, intermediate material, packaging material, and FPPs conform with established specifications for identity, strength, purity, and other characteristics.

Quality Management System: A management system encompassing the organizational structure, procedures, processes, resources, and systematic actions necessary to ensure adequate confidence that a product or service will satisfy given requirements for quality.

Quality Monitoring: All activities undertaken to ensure that medicines and diagnostic products continue to conform with the manufacturer's established quality specifications during the storage, distribution, and use of such product (e.g., lot testing, reporting of deficient products, surveillance) as part of a QA system.

Stringent Drug Regulatory Authority (SRA): A regulatory authority which is either (a) an ICH member, (b) an ICH observer, or (c) a regulatory authority associated with an ICH member through a legally binding mutual recognition agreement as before 23 October 2015. Refer to the list of current members, observers, and associated authorities as specified on the ICH website: www.ich.org.

Supplier: A person, business, or entity that provides products, materials, or services on request. Suppliers may be agents, brokers, distributors, manufacturers, or traders. Where possible, suppliers should be authorized by a competent authority.

WHO Prequalification Programme (WHO PQP): The programme managed by WHO which prequalifies medical products which are acceptable for procurement by the United Nations and specialized agencies and quality control laboratories for medicines.

1. INTRODUCTION

1.1 Preface

The Stop TB Partnership is a global multistakeholder partnership that seeks to achieve a world without tuberculosis (TB) by facilitating, catalyzing, and coordinating the work of its partners through its secretariat in Geneva. A key initiative of the Stop TB Partnership is the Global Drug Facility (GDF).

The mission of GDF, an ISO:9001 certified entity, is to ensure worldwide, equitable access to quality-assured and affordable antituberculosis medicines, diagnostics, and other supplies (hereafter referred to as 'TB products'). ***GDF seeks to achieve this mission by employing innovative business approaches, efficient knowledge management for evidence-driven leadership in market management, strategic procurement, and high-quality procurement and supply services to country clients.***

GDF facilitates the procurement of all medicines and diagnostic products that are recommended by WHO for the screening, prevention, diagnosis, treatment, and surveillance and monitoring of all forms of TB for adults and children. When procuring through GDF, countries are guaranteed to receive quality-assured TB products in accordance with the quality standards described within this policy document.

The GDF Quality Assurance (QA) policy is based on international and WHO guidelines applicable to medicines, medical devices, and in-vitro diagnostics management and is aligned with the QA policies of key United Nations organizations, the Global Fund, Unitaid, and other international agencies.

1.2 Purpose and Scope of the GDF Quality Assurance Policy

The GDF QA policy sets out the principles and requirements for the selection of TB products to be procured and supplied by GDF to recipient clients and countries.

The GDF QA policy applies to all TB products procured by GDF for the screening, prevention, diagnosis, treatment, and surveillance and monitoring of TB regardless of the source of funding (e.g., national budgets, donor funding).

1.3 Effective Date

This GDF QA policy takes effect on 15 September 2022 and supersedes GDF's policy of July 2010.

1.4 Policy Statement

GDF attaches significant importance to the quality of the products that are procured and delivered to countries for screening, prevention, diagnosis, treatment, and surveillance and

monitoring of TB. Through its stakeholder coordination, market, procurement and supply management, technical assistance, and quality monitoring programme approaches, GDF plays a key role in supporting countries to reliably access affordable TB products that meet internationally accepted quality standards.

1.5 Roles and Responsibilities

The selection of qualified and eligible TB products, manufacturers and suppliers, and services providers, the monitoring of product quality, and the compliance of manufacturing sites with the applicable ISO norms and QMS requirements, and GMP standards are essential parts of GDF's QA system.

Within GDF, the product QA team—which works independently but in collaboration with all other GDF teams—is responsible for the QA policy definition, development of related procedures, and satisfactory QA policy implementation during the tendering, contracting, and implementation of contracts with manufactures/suppliers and services providers.

All GDF staff involved in the procurement and supply management of TB products shall perform their activities in accordance with this QA policy.

1.6 GDF's Quality Assurance Principles

With GDF's mission to facilitate worldwide, equitable access to TB products, the GDF QA system is based on the following principles:

a) The product, technology, or approach procured contributes to ending TB.

b) The product, technology, or approach procured is recommended by WHO in either a Rapid Communication or a WHO standard TB guideline for screening, prevention, diagnosis, treatment, and surveillance and monitoring of TB.

c) The product, technology, or approach procured and delivered to countries is authorized for use or has been given a waiver by the recipient country.

d) The product, technology, or approach is procured, managed, delivered, and monitored in accordance with international and WHO norms and standards for procurement and supply management of health products and in compliance with the applicable norms and standards.

1.7 Applicable Quality Standards and Norms

GDF bases its QA system for procurement and supply management of TB products on the following quality standards and norms:

- WHO TB rapid communications and guidelines, and WHO essential medicines

lists,

- WHO, Stringent Regulatory Authority (SRA), and PIC/S Good Manufacturing Practices (GMP),
- WHO, SRA, and PIC/S Good Distribution Practices (GDP), including Good Storage Practices (GSP)
- Interagency Guidelines: A Model Quality Assurance System for Procurement Agencies (MQAS)
- WHO policies on essential medicines, diagnostics, medical devices, and other health products
- Monographs set by WHO International Pharmacopeia (Pharm Int), the United States Pharmacopoeia (USP), the British Pharmacopeia (BP), and the European Pharmacopeia (EP)
- ICH guidelines
- International Medical Devices Regulatory Forum (IMDRF) documents
- Relevant and applicable ISO and other standards and norms

1.8 Confidentiality Commitment

In line with the need for harmonization of QA policies and qualification processes, exchanges of information on products and suppliers between GDF and key partners will be governed by signed confidentiality agreements and, where required, authorizations from the proprietors of the information.

GDF has created and maintains a product database which contains all the information related to product quality, efficacy, and safety. This database is managed by GDF QA personnel. Non-confidential product information (e.g., technical specifications of products, approved artworks for medicines supplied via GDF) is made available to interested parties upon request, including GDF clients, technical partners, procurement agent and quality control agents (QCA).

2. QUALITY ASSURANCE REQUIREMENTS FOR ANTITUBERCULOSIS MEDICINES

2.1 Quality Criteria for Procurement Eligibility of Antituberculosis Medicines

To be eligible for GDF procurement, finished pharmaceutical products (FPPs) shall be:

(A) Prequalified by WHO PQP[1] or authorized for use by an SRA,[2] defined as either an ICH member country, observer, or any country whose regulatory authority is associated with an ICH member through a legally binding mutual recognition agreement.

In the absence of an FPP meeting the standard (A) described above, the FPP may be approved for procurement by GDF if:

(B) Recommended for procurement through a quality/clinical risk assessment process managed by the WHO-coordinated Expert Review Panel (ERP).[3] A FPP recommended by the ERP for a limited period shall meet the following conditions:

a) The FPP is manufactured at a site compliant with GMP standards that apply for the relevant product formulation[4] as verified after inspection by:

i. WHO PQP (refer to https://extranet.who.int/pqweb/medicines).
or
ii. An SRA, defined as above.
or
iii. Inspectors of a regulatory authority participating in the Pharmaceutical Inspection Cooperation Scheme (PIC/S).[5]

b) The manufacturer of the FPP has submitted an application/dossier for prequalification of the product by the WHO PQP or for marketing authorization to an SRA and the application/dossier has been accepted for assessment either by WHO PQP or an SRA.[6]

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[1] For more information on WHO PQP, see https://extranet.who.int/pqweb/.

[2] For more information on SRA and WHO Listed Authorities see https://www.who.int/initiatives/who-listed-authority-reg-authorities/ SRAs as before 23 Oct 2015. For new members of the European Union (EU), only pharmaceutical products which were delivered a market authorization after EU integration are considered as approved by SRA, 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 (EC9 No. 726/2004) or United States FDA tentative approval.

[3] For more on the ERP process, see https://extranet.who.int/pqweb/sites/default/files/documents/73_ERP_Feb2019_new%20templ.pdf.

[4] Requirement fulfilled if the scope of the audit covers the specific dosage form as confirmed by either WHO PQP/SRA or ERP experts.

[5] For more information on PIC/S, see http://www.picscheme.org/. For any new PIC/S members, GDF will consult with relevant WHO/QSM experts on the level of equivalence of the GMP inspection with those of old members of PIC/S countries or as before 23 Oct 2015.

[6] A written proof of such submission and acceptance issued by WHO PQP or the relevant SRA authority will be required.

c) The procurement of an ERP-recommended FPP shall be valid for a period of no more than 12 months from the time of the ERP recommendation or until the FPP is either WHO prequalified or SRA authorized (whichever is the earliest) unless otherwise advised by the ERP recommendation letter.

2.2 Selection Principles Among Antituberculosis Medicines with Different Quality Assurance Status

FPPs prequalified by WHO PQP or authorized for use by an SRA are considered equivalent in terms of QA standards, but not with ERP-recommended FPPs. Thus, if there are two or more FPPs available for the same formulation that are prequalified by WHO PQP or authorized for use by a SRA, the selection for procurement/market allocation of an ERP-recommended FPP shall not be considered, except in cases where the production capacity of the available WHO-prequalified or SRA-authorized FPPs is not sufficient to cover the estimated quantities within the required timeframe.

3. QUALITY ASSURANCE REQUIREMENTS FOR DIAGNOSTIC PRODUCTS

GDF, within the scope of this QA policy, defines 'diagnostic products' as the products used for the screening, prevention, diagnosis, and surveillance and monitoring of TB. Diagnostic products include medical devices (MD), in-vitro diagnostics (IVD),[7] and software as a medical device (SaMD) as defined by IMDRF,[8] as well as laboratory equipment, reagents, chemicals, and consumables.

3.1 Quality Criteria for Manufacturers of Diagnostics Products

a) Medical devices, IVDs, and medical software shall be manufactured by a manufacturer with a valid and certified Quality Management System (QMS), in accordance with the requirements of the current version of ISO 13485 or an equivalent QMS standard, and covering the relevant categories of products, locations, and facilities where the relevant activities are performed as assessed by a competent conformity assessment body (CAB) recognized by the regulatory authority of one of the founding members of GHTF/IMDRF (i.e., EU, USA, Canada, Australia, and Japan).

b) Diagnostic products other than those listed in Section 3.1(a) above (For example, pipettes, test tubes, balances and general laboratory consumables) shall be manufactured by a manufacturer compliant with a valid and certified QMS, as per the current versions, in accordance with all applicable requirements of the ISO 9000 series or an equivalent QMS standard, covering the relevant categories of

[7] Definitions can be found at https://www.imdrf.org/sites/default/files/docs/ghtf/final/sg1/technical-docs/ghtf-sg1-n071-2012-definition-of-terms-120516.pdf.

[8] For SAMD specifically, definitions can be found at https://www.imdrf.org/sites/default/files/docs/imdrf/final/technical/imdrf-tech-131209-samd-key-definitions-140901.pdf.

products, locations, and facilities where the relevant activities are performed as assessed by a competent CAB.

c) Diagnostic products shall be manufactured by manufacturers with a valid manufacturing license for the relevant category of products, issued by the National Regulatory Authority (NRA) in the country of manufacture.

3.2 Quality Criteria for Suppliers of Diagnostic Products.

If the supplier is not the manufacturer of the product, the supplier shall, as a minimum:

a) Have a valid and certified QMS, as per the current versions, in accordance with ISO 9001, or an equivalent QMS standard for the management and distribution of diagnostic products.

b) Where the supplier is involved in repackaging of diagnostic products (kitting), a valid license from the NRA authorizing them to undertake such activities as well as a certificate of Good Distribution Practice (GDP) shall be required.

3.3 Quality Criteria for Diagnostic Products

To be eligible for GDF procurement, diagnostic products shall meet the following:

a) For **IVDs**, the product shall:

i. Be recommended by the WHO Global TB Programme.[9]
or
ii. Have regulatory approval and marketing authorization issued by one of the regulatory authorities of the founding members of GHTF/IMDRF (i.e., EU, USA, Canada, Australia, and Japan) when stringently assessed as high-risk classification.
or
iii. Be prequalified by WHO PQP.
or
iv. Be recommended by the Expert Review Panel for Diagnostics (ERPD)[10] for a time-limited period (pending full assessment through one of the processes listed in i., ii., or iii.).
and
v. Have a Declaration of Conformity in accordance with IMRDF[11] and/or ISO

[9] For more information on WHO's Global Tuberculosis Programme (GTP), see https://www.who.int/teams/global-tuberculosis-programme/.
[10] For more information on ERPD, see https://extranet.who.int/pqweb/vitro-diagnostics/expert-review-panel-diagnostics.
[11] For more information on IMDRF's Declaration of Conformity, see https://www.imdrf.org/sites/default/files/docs/ghtf/final/sg1/technical-docs/ghtf-sg1-n78-2012-conformity-assessment-medical-devices-121102.pdf.

17050.[12]

and

vi. Be compliant with the quality requirements/specifications against test methods set for them as prescribed by the relevant ISO standards and/or compendia as applicable. To demonstrate this, a Certificate of Analysis shall be availed.

b) For **medical devices and medical software**, and depending on the product risk classification,[13,14,15] the product or technology shall as applicable:

i. Be recommended by the WHO Global TB Programme.

or

ii. Have regulatory approval and marketing authorization issued by one of the regulatory authorities of the founding members of GHTF/IMDRF (i.e., EU, USA, Canada, Australia, and Japan) as applicable.

or

iii. Be prequalified by WHO PQP.

or

iv. Have a CAB certificate/s as applicable.

and

v. Have a Declaration of Conformity in accordance with IMRDF and/or ISO 17050.

and

vi. Be compliant with the quality requirements/specifications and test methods set for them as prescribed by the relevant ISO standards and/or compendia as applicable. To demonstrate this, a Certificate of Analysis shall be availed.

c) Products for **general laboratory use** (e.g., general lab equipment, chemicals, laboratory-related consumables) shall:

i. Have a Declaration of Conformity in accordance with IMRDF and/or ISO 17050 where applicable.

and

ii. Be compliant with the quality requirements/specifications and test

[12] ISO/IEC 17050-1 specifies general requirements for a supplier's Declaration of Conformity in cases where it is desirable or necessary that conformity of an object to the specified requirements be attested. ISO/IEC 17050-2 specifies general requirements for supporting documentation to substantiate a supplier's Declaration of Conformity, as described in ISO/IEC 17050-1.

[13] For principles of IVD medical devices classification, see https://www.imdrf.org/sites/default/files/docs/imdrf/final/technical/imdrf-tech-wng64.pdf.

[14] For principles of general medical device classification, see https://www.imdrf.org/sites/default/files/docs/ghtf/final/sg1/technical-docs/ghtf-sg1-n15-2006-guidance-classification-060627.pdf.

[15] Regulatory controls should be proportional to the level of risk associated with a medical device. The level of regulatory control should increase with increasing degree of risk, taking account of the benefits offered by use of the device.

methods set for them as prescribed by the relevant ISO standards and/or compendia as applicable. To demonstrate this, a Certificate of Analysis shall be availed.

d) In the case of new products where no other quality-assured products exist, for emergency purposes GDF may accept products approved under Emergency Use Listing by WHO or by one of the regulatory authorities of the founding members of GHTF/IMDRF (i.e., EU, USA, Canada, Australia, and Japan).

3.4 Additional Requirements

a) Where the supplier is not the manufacturer of the product, the supplier shall have authorization from the manufacturer to supply the product on their behalf.

b) Product information relating to product safety (e.g., safety data sheets, shelf-life) shall be availed as applicable.

c) For products requiring special transport and storage conditions as recommended by the manufacturer, these shall be required to be monitored during transportation and records maintained.

4. NATIONAL REGULATORY AUTHORITY AUTHORIZATION

GDF monitors the status of registration of antituberculosis medicines in countries per supplier. For FPPs not registered, GDF encourages suppliers to register their FPPs in supplied countries or obtain any other forms of authorization (such as authorization for marketing, waiver for importation, and/or authorization for use) by the National Regulatory Authority (NRA).

For FPPs prequalified by the WHO PQP: GDF encourages countries' NRAs and suppliers to use the WHO collaborative procedure for accelerated registration[16] to expedite the process of authorization for use in countries. Where such authorization has not been granted by the NRA yet, a waiver or exceptional permission to import/use the product shall be obtainable.

For SRA-authorized FPPs: GDF encourages countries' NRAs and suppliers to expedite the process for authorizing the use of such FPPs 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 (QC) testing of products and necessary reference standards, in order to fulfill national requirements. Where such authorization has not been granted by the NRA yet, a waiver or exceptional permission to

[16] For more information on the WHO collaborative procedure for accelerated registration, see https://extranet.who.int/pqweb/vitro-diagnostics/collaborative-procedure-accelerated-registration.

import/use the product shall be obtainable.

For diagnostic products: Diagnostic products shall be authorized for marketing and use in the destination country by the relevant NRA in accordance with local requirements for registration or other forms of authorization including authorization for special use. Where such authorization has not been granted by the NRA yet, a waiver or exceptional permission to import/use the product shall be obtainable.

5. QUALITY ASSURANCE REQUIREMENTS FOR PROCUREMENT AND QUALITY CONTROL AGENTS

5.1 Quality criteria for Procurement Agent (PA)

GDF contracts services of a Procurement Agent through a competitive process for a specific time duration as per the signed agreement.

The list of PA activities includes support to GDF on tendering for anti-TB products and related supplies, contracting manufacturers and suppliers, ensuring purchase of selected products, managing of products transportation and insurance to the destination, and coordinating product recalls where needed. The PA is also responsible for contracting the QCAs on behalf of GDF, coordinating the pre-shipment inspection (PSI), sampling and quality control testing activities.

The PAs should follow GDF's QA Policy and the related Procedures, the WHO applicable standards and the ISO relevant norms to undertake the above listed activities.

The minimum requirements for the PA eligibility are:

- the PA shall have a licence and be compliant with the WHO Good Distribution Practices (GDP) including Good Storage Practices (GSP).

- the PA shall be compliant with the WHO Model Quality Assurance System for Procurement Agencies for the activities performed on behalf of GDF; specific attention will be given to the batch-tracking system and recall procedures.

Within its QA system, PAs should have a written procedure on how to recall promptly and effectively any delivered product known or suspected to be defective, with a designated person(s) responsible.

A recall could be initiated by one or several GDF beneficiary countries, a manufacturer and/or marketing authorization holder, or a PA itself. In any case, communication must be set between GDF and PA QA responsible staff as soon as one party is informed of a quality alert linked to a product supplied by GDF. The PA will work with the product supplier to carry out appropriate recall procedure.

5.2 Quality criteria for quality control agent (QCA)

a) For Antituberculosis Medicines

GDF selects quality control agents (QCAs) through a competitive bidding process and signs long-term agreements (LTAs) with awarded QCAs via its contracted procurement agent to conduct pre-shipment inspections (PSIs) and batch sampling where applicable, review manufacturer certificates of analysis (CoA) for each FPP batch procured and perform QC testing of FPP batch(es) as per the randomized established protocol.

Since 2010, GDF and the Global Fund have organized joint tenders for the selection of QCAs with the aim of harmonizing QA/QC activities, standardizing QA/QC processes and procedures, reaching cost-efficiency through the pooling of QA/QC activities and sharing of results, and improving transparency.

The QCAs selected by GDF and the Global Fund to perform PSI and QC testing must comply with the following quality standards:

- WHO prequalification[17]
- ISO 17025 and 15189 certifications by an internationally recognized accreditation body
- ISO 17020 certification by an internationally recognized accreditation body (i.e., for inspection agencies)
- A Good Laboratory Practices (GLP) certificate issued by an SRA
- Comply with other quality standards that may become relevant during the contract validity period

b) For Diagnostic Products

To perform PSI and/or QC testing, GDF uses QC agencies that comply with the following requirements and standards as applicable:

- Selected and contracted out by the client/destination country
- Selected and contracted by UNOPS (the GDF hosting organization) or other UN agencies
- Recognized as a WHO TB Supranational Reference Laboratory for QC testing and

[17] For more information on prequalification for QC testing, see https://extranet.who.int/pqweb/medicines/medicines-quality-control-laboratories-list.

other tests as specified by GDF

6. GDF QUALITY MONITORING PROGRAM

The monitoring of the quality of antituberculosis medicines and diagnostic products procured by GDF is an essential part of the GDF's QA system.

GDF uses the services of the QCAs (mentioned in Section 5 above) to perform the quality monitoring of TB products.

For products supplied to a country receiving financial support from external donors (e.g., the Global Fund), GDF coordinates the monitoring activities with such funding institutions to avoid duplication of efforts.

6.1 Pre-Shipment Inspection

For FPPs: Pre-shipment inspections (PSIs) are organized by GDF and its procurement agent in accordance with the criteria set up in the GDF quality monitoring program and related procedures or when required by countries. PSIs are performed by GDF's selected QCA.

For diagnostics products: PSIs are organized as per country request and performed by QCAs contracted by a country, or by UNOPS (the GDF hosting organization), or by other UN agencies in line with GDF operational procedure.

6.2 Quality Control Testing Before Delivery

For FPPs: Sampling and QC testing are organized by GDF and its procurement agent and performed by its selected QCA laboratories as per the randomized established protocol in accordance with GDF's quality monitoring program and related procedures.

For diagnostics products: Sampling and QC testing are organized by GDF when required and performed by its selected WHO TB Supranational Reference Laboratories.

In cases of non-compliant testing results for FPPs and diagnostics products (i.e., confirmed out of specifications (OoS) by GDF's contracted QCA laboratories):

- For Global Fund-funded orders/products, GDF will inform the GF QA team and request for a complaint investigation.
- For non-Global Fund-funded orders/products, GDF will proceed as per GDF operational procedure.

An OoS investigation must not delay order arrival to a country's TB programme. In case of delays, GDF will ask the manufacturer to replace the batch at the manufacturer's own cost to meet the programme's needs.

6.3 Post-Delivery Quality Surveillance

Quality monitoring activities can also be organized post-delivery by recipient countries as part of their medicine and diagnostic products monitoring programmes. Some countries conduct systematic laboratory testing once medicines or diagnostic products are received by customs, kept in quarantine, or stored in warehouses at different points in the supply chain.

6.4 Handling of Product Complaints

Customer, partners, or other sources can report a product complaint to GDF. Currently, two reporting systems exist at GDF to submit this. The customer can fill out a non—compliance or complaint form which is available on the GDF website[18] or submit feedback via a GDF customer satisfaction survey. GDF conducts customer satisfaction surveys on a regular basis to collect customers' feedback on their level of satisfaction with GDF's processes, products, and performance.

All complaints concerning potentially defective products procured through GDF are reviewed carefully by GDF QA staff so that appropriate actions can be taken, including potential recall. Product complaints received are duly recorded and investigated by GDF as per its internal procedures.

All complaints related to the quality of TB products which are WHO PQP approved and/or ERP recommended are shared with WHO PQP, ERP, and the funding agency. As for SRA-authorized products, the manufacturer/supplier is required to inform the relevant regulatory authority as per its requirements.

7. PRODUCT VARIATIONS

Any product and marketing authorization-related changes that were submitted for approval to a regulatory agency such as WHO PQP or an SRA by the supplier or manufacturer shall be communicated to the GDF QA team as soon as possible. GDF will rely on the assessment results of such variations by WHO PQP or an SRA.

For products found acceptable through quality/clinical risks assessment (i.e., the ERP or ERPD processes), changes would have to be submitted to the ERP Secretariat managed by the Global Fund QA team.

8. REVISION OF THIS POLICY AND PROCEDURES

This policy supersedes all previous versions and will be revised periodically.

[18] The complaint form can be found at https://www.stoptb.org/suppliers/quality-assurance.