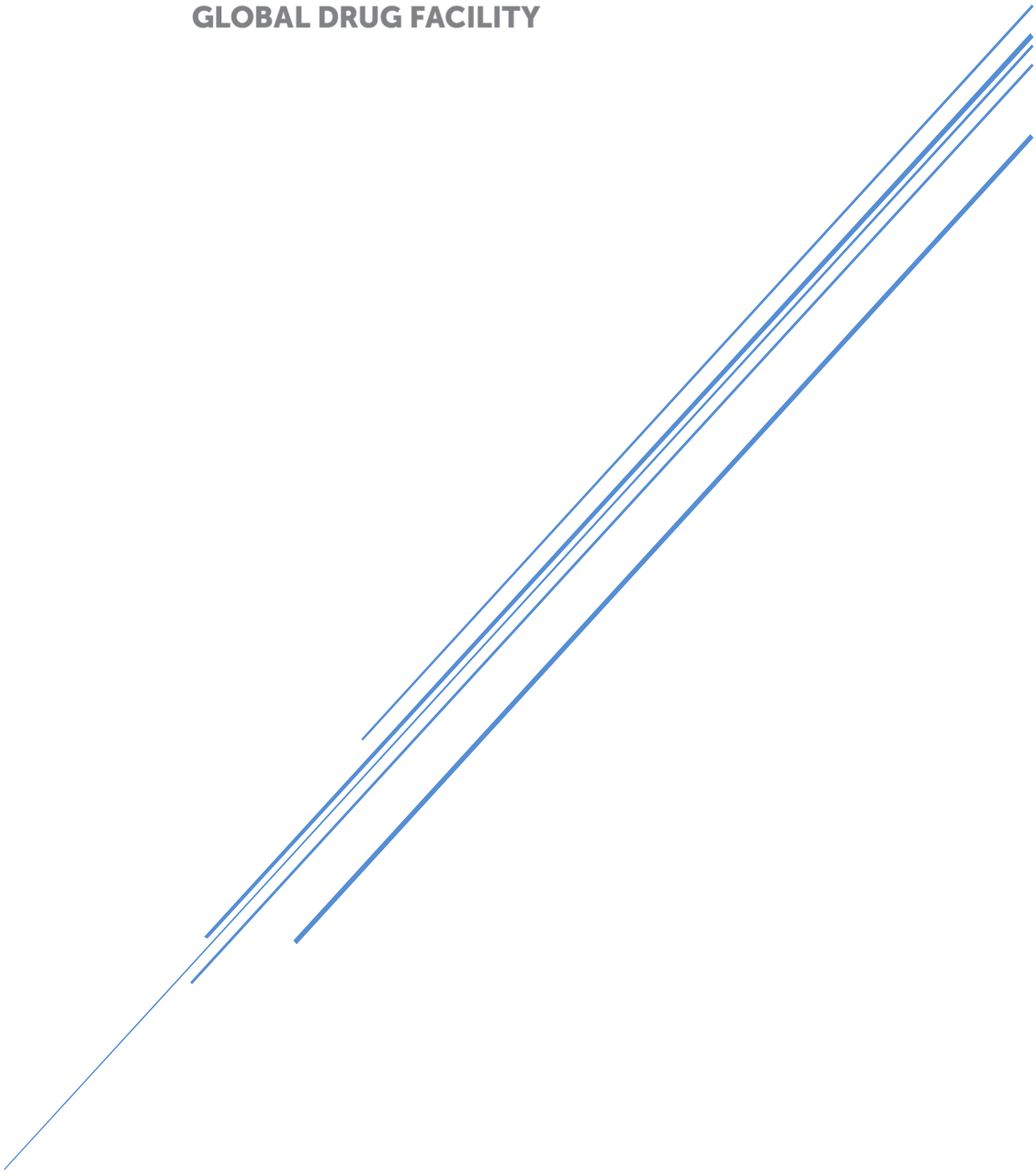
DRUG MONITORING PROGRAMME



1. Background

The Global Drug Facility (GDF) is an initiative of the Stop TB Partnership established to increase access to quality-assured tuberculosis (TB) medicines for DOTS implementation, a TB control strategy. GDF is hosted by the United Nations Office for Project Services (UNOPS) headquarters in Geneva and managed by the Stop TB partnership secretariat.

GDF, as a procurement arm of the Stop TB Partnership secretariat collaborates with selected and eligible procurement agents (PA), offers three core procurement services:

- Procurement for GDF Grants (first and second line anti-TB medicines, diagnostics and lab equipment for rapid tests) for countries, programmes and non governmental organizations (NGOs) that are donor-dependent for some or all of their drug supply,

- Direct Procurement (DP) Service for countries, programmes, NGOs and donors intending to buy first and second line anti-TB medicines, laboratory reagents, supplies and diagnostic equipment for rapid tests,

- Technical Assistance (TA) Service for Grant and DP recipients (first and second line anti-TB medicines) through assistance missions to strengthen in-country drug supply chain management, supply monitoring and forecasting, and capacity building.

In 2008, GDF initiated a revision and expansion of its Quality Assurance Policy and Procedures as part of a collaborative process to ensure harmonization with the policies of two major multi-lateral financing mechanisms (i.e. The Global Fund and UNITAID), and other organizations (i.e. The Union; UNICEF, Médecins Sans Frontières, UNDP, WHO) involved in TB control and in particular to:

- ensure global consistency on quality standards set for procurement and supply of anti-TB medicines, laboratory reagents and supplies and diagnostic equipment for rapid test,
- avoid duplication of efforts.

From March 2009, GDF has been an active partner of the Global Fund Quality Control Initiative, using the same consignment inspection, sampling and testing capabilities and publishing jointly Request for Proposals for the selection of the common Quality Control Agents (QCA) aimed at:

- Harmonization of activities
- Standardization of process and procedures
- Cost efficiency through the pooling of activities and sharing of results
- Transparency and competition

In July 2009, the Global Fund and GDF launched a Request for Proposal (RfP) for the selection of agents for the provision of the pre-shipment inspection, batch sampling and testing services. Such joint RfP will be published every 3 -5 years to minimize cost per required services and to standardize all quality reporting and recording requirements among particpating partners.

2. Selected Agents for Pre-Shipment Inspection, Batch Sampling and Testing Services

Two companies were selected to carry out the above:

2.1. A QCA for PSI to perform consignment inspection and sampling services in support of GDF products

2.2. A QCA to carry out Quality Control (QC) Testing including CoA review including the critical review

3. Scope of the work of this programme:

1. Consignment inspection at the specified locations and sampling (batch and product)
2. Quality Control Testing including review of Certificates of Analysis(CoA)

3. Process Management
4. Quality Control Test Reporting
5. Providing technical advice on the above mentioned activities, if and when required.

4. Drug Quality Monitoring Programme

4.1. Consignment Pre-shipment Inspection (PSI)

4.1.1. Pre-shipment (PSI) is carried out at (i) the manufacturer's site or (ii) at the procurement agent storage facility (if required, post-shipment inspection of the consignment will be carried out at the destination/user country on arrival) according to latest versions of respective:

- GDF list of prequalified products and eligible manufacturers with relevant characteristics[1] to be provided by GDF QA Officer
- Standard Operating Procedure (SOPs),
- Packaging and labelling instructions,
- Approved artworks

4.1.2. PSI dates are agreed between GDF, the PA and the QCA.
4.1.3. If the consignments comply a Clean Report of Findings (CRF) is issued by the QCA.
4.1.4. Samples are sent to the designated QCA laboratories for testing.

All consignments are subject to PSI unless instructions indicate otherwise. PSI is currently waived for shipments whose value is below 2000 USD and the Procurement Agent is expected to check the product packaging integrity and shelf life before shipment and advise the country/programme and GDF procurement focal persons accordingly.

4.2. Sampling

4.2.1. Random sampling for testing done at the time of PSI as described below is applicable to all GDF orders:

i. For WHO PQP: Sampling for testing is done on the first 5 batches of a product and then 10 percent of the subsequent batches of the same product.
ii. For ERP reviewed products: Sampling for testing of the first 5 batches of a product and then 20 percent for the subsequent batches of the same product
iii. No sampling is required for SRA-authorized medicines, unless specifically requested by GDF QA.

4.3. Quality Control Testing and CoA Review

Products as sampled in section 4.2. above are shipped to the respective QCA laboratories for testing.

4.3.1. Quality control testing methods

4.3.1.1. The methods for independent analysis commissioned by GDF are selected in the following order:

i. The latest editions of International Pharmacopoeia (IP), British Pharmacopoeia (BP) and United States Pharmacopoeia (USP) should be followed to perform the analysis.
ii. If needed, approved additional in-house methods for specific parameters will also be followed. In such cases the manufacturer will submit to GDF/QCA the complete analytical method and validation data.
iii. If there is no monograph available in any of the three pharmacopoeia listed above, the approved manufacturer's specifications and validated methods are used as

[1] INN; strength; dosage form; packing type and size; manufacturer, manufacturing site; shelf-life; storing conditions

supported by the manufacturer's validation data. A method transfer will be performed.

iv. Implementation of the manufacturer's method will be done as per chart agreed with the Global Fund (Contract number 20012982).

4.3.1.2. The QCA will perform all tests as indicated in the contract with the Global Fund under the analytical methods and parameters tested. In general, the following tests should be performed and reported on:

- Appearance
- Identification, assay and impurity control (related substances)
- Dissolution and or disintegration for tablets and capsules
- Content uniformity or weight variation for tablets and capsules
- pH and microbial limits for the solutions if in the specification
- Sterility and bacterial endotoxin test, if applicable (e.g. for injectables)

4.3.1.3. Tests will be interpreted according to compendial specifications.

4.3.1.4. Based on the parameters required to be tested, the QCA will determine the quantity of dosage units or multi dose packs adequate to cover the testing requirements.

4.3.1.5. If the results of parameters tested are not within the expected specifications, the batch is considered to be Out of Specification (OoS). Procedures and reporting in case of OoS are described in the corresponding SOP.

The above set-up of the PSI, sampling and randomization testing scheme may be modified by GDF at any given time.

4.3.2. Review of Certificates of Analysis (CoA)

4.3.2.1. The QCA reviews the manufacturer's Certificates of Analysis (CoA) for all products and batches, including those that are not subject to testing or are skipped the testing due to the randomisation scheme and alert GDF when any non-compliance is detected.

4.3.2.2. GDF may request additional testing if deemed necessary[2]. Further procedures, if and when required will be defined by GDF and the QCA during the regular meetings.

4.3.2.3. For all consignments consisting of over 20 batches of the same product/s (rare cases), review of additional CoAs shall be skipped.

4.3.3. Quality Control Testing Data Confidentiality and Archiving

4.3.3.1. Sources, methods, specifications and analysis data are kept strictly confidential and archived for at least 6 years (and made available to GDF on request).

4.3.4. Release and Shipping of Consignments

4.3.4.1. All first line medicines are shipped directly to the recipient country after receipt of the CRF and testing results if applicable.

4.3.4.2. The second line medicines are shipped to the PA's warehouse where they are allocated either to the Strategic Rotating Stockpile (SRS) and to an order only after the verification of the order products, shipping documents and testing results, and as accepted by GDF

4.3.4.3. Dispatch of shipment(s) in parallel with testing to recipient countries is permitted upon recipient and manufacturer concurrence/agreement, and to the PA warehouse as per their standard operating procedure.

[2] GDF may request to the Expert Review Panel advise on any additional testing for products that represent higher potential risk taking into consideration e.g. nature of the product, batch size, nature of excipients, packaging and methods of production (e.g. sterility testing for Injectable medicines)

4.3.5. Reporting

The QCAs submit monthly reports to the GDF QA Officer that include a summary of (but not limited to):

4.3.5.1. Product, Supplier, Batch nos. tested and skipped, Destination, Order no., PSI and QC dates, and Lead times for PSI and QC

4.3.5.2. Report of confirmed OOS cases including Product, Supplier, Batch no., Destination, GDF reference no., Purchase Order no., Parameter tested, Method, Specification, Initial result, First re-test result, Second re-test result, Timeframe per step

4.3.5.1. Consolidated report and copies of the CoAs of all the lots tested

4.3.5.2. Quarterly reports on PSI deviations per suppliers/products

The QCA inspects and conducts physical inventory of the Strategic Rotating Stockpile (SRS), if and when requested by GDF or the PA.

Relationship and responsibilities:

Technical office:

Global Drug Facility
Quality Assurance personnel

Global Health Campus,
Chemin du Pommier 40,
1218 Le Grand-Saconnex, Geneva, Switzerland