

37th Board Meeting

Revisions to the Global Fund Quality Assurance Policy for Diagnostic Products

GF/B37/06

03-04 May 2017, Kigali, Rwanda

Board Decision

Purpose of the paper: This document presents, for Board approval, revisions to the existing Global Fund Quality Assurance Policy for Diagnostic Products to reflect new WHO recommendations or guidelines and the Global Fund policy on co-infection and co-morbidities that the Board adopted in 2015. The revised policy also delegates authority to the Strategy Committee to make revisions related to updated guidance.

Part 1: Decision Point

1. Following review and discussion by the Strategy Committee at its Third Meeting on 20-22 March, the following decision point is presented to the Board.

<p><i>Decision Point GF/B37/DP12: Amended and Restated Global Fund Quality Assurance Policy for Diagnostic Products</i></p> <p><i>1. Based on the recommendation of the Strategy Committee, the Board approves the amended and restated Global Fund Quality Assurance Policy for Diagnostic Products, as set forth in Annex 1 to GF/B37/06.</i></p> <p><u>Budgetary implications</u> <i>Not applicable</i></p>

Part 2 - Relevant Past Decisions

Relevant past Decision Point	Summary and Impact
GF/SC03/DP01: Recommendation on Global Fund Quality Assurance Policy for Diagnostic Products	The Strategy Committee (SC) reviewed the proposed revisions to the Quality Assurance Policy for Diagnostic Products ("QA Policy for Diagnostics") which reflect updated WHO recommendations or guidelines and the Global Fund policy on co-infection and co-morbidities that the Board adopted in 2015, as well as additional revisions that delegate to the SC the authority to approve certain updates to the QA Policy for Diagnostic Products based on updated relevant policy or guidance. The Strategy Committee recommended the revised policy for Board approval at its 37 th Meeting.
GF/B22/DP10 – Revision 1.: Quality Assurance Policy for Diagnostic Products (December 2010)¹	The Board approved the Quality Assurance Policy for Diagnostic Products ("QA Policy for Diagnostics"), as set out in Annex 2 to the Report of the Market Dynamics and Commodities Ad-hoc Committee to the Board (GF/B22/11, Revision 1).
GF/SIIC10/DP02: Revision of Quality Assurance Policy for Diagnostic Products (February 2014)	Following the Board's initial approval of the QA Policy for Diagnostics, the Strategy, Investment and Impact Committee (SIIC) reviewed operational updates contemplated at the time of the policy's initial adoption and approved modifications to the policy following review and input by the Market Dynamics Advisory Group (MDAG).
GF/B32/DP08: Market Dynamics Oversight (November 2014)²	Based on the recommendations of the SIIC, the Board agreed with dissolving the MDAG and

¹ <http://www.theglobalfund.org/Knowledge/Decisions/GF/B22/DP10/#>

² <http://www.theglobalfund.org/Knowledge/Decisions/GF/B32/DP08/>

	allocating certain responsibilities with respect to market dynamics oversight, including strategic and operational matters that had previously been under the oversight of the MDAG to the SIIC and the Finance and Operational Performance Committee. This allocation of responsibilities included providing the SIIC with oversight on quality-assurance matters regarding health products to be financed with grant funds.
GF/B33/DPo8- Policy for co-infections and co-morbidities (March 2015)³	Based on the recommendations of the Strategy, Investment and Impact Committee, the Board approved the framework for financing co-infections and co-morbidities of HIV/AIDS, tuberculosis and malaria, as set forth in GF/B33/11, replacing its November 2015 approval of an interim measure for the financing of Hepatitis C virus treatment under GF/B32/DPo7.
GF/B34/EDPo7: Enhanced Governance Structure (January 2016)⁴	The Board approved a new set of standing committees—the Strategy Committee, Audit and Finance Committee and Ethics and Governance Committee. Among the advisory functions delegated to the Strategy Committee, successor committee to the SIIC, was the responsibility to “advise and make recommendations to the Board” on the “adoption of, and modifications to, strategic policies on market dynamic matters such as market-shaping interventions and the sourcing of quality-assured pharmaceuticals, devices and other health products”.

Part 3 - Action Required by the Board

2. The Board is requested to approve the amended and restated Global Fund Quality Assurance Policy for Diagnostic Products, as set forth in Annex 1, based on the Strategy Committee’s recommendation. Annex 1 shows both the clean and track-changes versions of the amended and restated Global Fund Quality Assurance Policy for Diagnostic Products.

Part 4 - Executive Summary

3. This paper relates to/supports achieving impact by:
 - Ensuring that only quality assured diagnostic products in line with WHO guidance and Board policies are procured with grant funds.
4. This paper relates to/supports risk identification, mitigation and prevention and assurance by:
 - Updating the Global Fund Quality Assurance Policy for Diagnostic Products to ensure that only quality diagnostic products are procured with Global Fund resources.
5. At its Third Meeting, the Strategy Committee reviewed the proposed revisions to the Global Fund Quality Assurance Policy for Diagnostic Products (the “QA Policy for Diagnostics”). These revisions

³ <http://www.theglobalfund.org/Knowledge/Decisions/GF/B33/DPo8/>

⁴ <http://www.theglobalfund.org/Knowledge/Decisions/GF/B34/EDPo7/>

are necessary in order to reflect: (i) new WHO recommendations or guidelines and (ii) the Global Fund policy on co-infection and co-morbidities that the Board adopted in 2015.

6. Without these revisions, there is a risk that non-quality assured diagnostic products are procured with grant funds and Global Fund policy would be misaligned with current normative guidance and guidelines.
7. The current QA Policy for Diagnostics does not clearly delineate when modifications or amendments to the policy can be approved by the Secretariat, the Strategy Committee or the Board. As such currently all modifications to the policy must be recommended to the Board through the Strategy Committee in line with Section 2.2 (f) of the Charter of the Strategy Committee. Noting the need to be able to update the policy to adapt to changes in normative guidance or incorporate future Board decisions, the Secretariat recommends delegating decision-making powers to the Strategy Committee to review and approve certain modifications to the QA Policy for Diagnostics.

Part 5 - Background

8. The QA Policy for Diagnostics was developed in 2009 based on the recommendations of a group of experts on regulatory, technical, and implementation issues related to diagnostics. It outlines the requirements for the use of Global Fund grant funds for the procurement of diagnostic products⁵ and requires Global Fund Recipients to implement a Quality Assurance System for procurement, supply management and use of such products.
9. At its Twenty-Second Meeting in 2010, the Board approved the QA Policy for Diagnostics based on recommendations made by the Market Dynamics Committee (MDC⁶).
10. On 5 February 2014, the Strategy, Investment and Impact Committee (SIIC) approved amendments to the QA Policy for Diagnostics, in line with the prior MDC recommendation, noting the likely need for future revisions related to the phase in of specific products, such as hepatitis and syphilis tests.
11. The proposed revisions to the QA Policy for Diagnostics presented in this paper takes into consideration: (i) the Board approved policy on co-infections and co-morbidities of HIV/AIDS, tuberculosis and malaria⁷, in particular by including requirements for hepatitis B, hepatitis C and syphilis tests; and (ii) new WHO recommendations or guidelines, in particular criteria to determine procurement eligibility for antigen-detecting malaria rapid diagnostic tests (RDTs), guidelines on Post-Marketing Surveillance of In Vitro Diagnostics (IVDs), guidance on HIV self-testing in-vitro diagnostics (IVDs) and recommendations regarding testing for Glucose-6-phosphate dehydrogenase (G6PD) deficiency⁸. WHO guidance and guidelines for these products were not issued or revised at the time of the last policy revision in February 2014.
12. The Global Fund Secretariat consulted key technical partners⁹ in August 2016 to collect feedback on the proposed changes to the QA Policy for Diagnostics. The suggestions received were considered and integrated in the proposed revised QA Policy for Diagnostics, as appropriate.
13. Annex 1 sets forth the revised policy recommended by the Strategy Committee for Board approval. Annex 2 summarizes the rationale for the proposed changes and Annex 3 summarizes the feedback received from key technical partners.

Part 6 - Discussion

⁵ This includes all durable and non-durable in-vitro diagnostics, imaging equipment and microscopes used for diagnostic, screening, monitoring and surveillance programs

⁶ Board Decision GF/B22/DP10 and GF/B22/11 – Revision 1.

⁷ As set forth in GF/B33/11 and approved by the Board under decision point GF/B33/DP08

⁸ An In Vitro Diagnostic Medical Device used to detect Glucose-6-phosphate dehydrogenase (G6PD) enzyme activity. Current WHO guidelines recommend the evaluation of G6PD status before initiating primaquine therapy (WHO, Testing for G6PD deficiency for safe use of primaquine in radical cure of *P. vivax* and *P. ovale*, Policy Brief October 2016)

⁹ UNITAID, WHO Prequalification Programme, WHO Global Malaria Programme, Stop TB Partnership, USAID, MSF, UNICEF Supply Division, FIND, WHO HIV Department, CHAI.

14. The proposed revisions to the policy extend the requirements of QA Policy for Diagnostics to include: the Global Fund Policy on co-infections and co-morbidities and new and/or updated WHO guidelines for key products; and clearly define which In-Vitro Diagnostics (IVDs), for each disease, are subject to quality standards. Further revisions delegate decision-making power to the Strategy Committee to approve specific modifications to the QA Policy for Diagnostics to more efficiently delineate the manner by which the Board, Strategy Committee and Secretariat engage on quality assurance issues.
15. The QA Policy for Diagnostics ensures that quality diagnostic products are purchased and used within Global Fund supported programs and reduces risks associated with purchase of non-quality assured diagnostic products. It is based on three sets of requirements:
 - i. Clinical standards which require Recipients to ensure that they are selecting diagnostic products that are consistent with WHO guidance or comply with national guidelines;
 - ii. Quality standards which outline minimum standards and criteria that products must meet to be considered quality assured and additional standards for specific products; and
 - iii. Quality of use which guides how diagnostic products procured with grant funds should be employed and the requirements that Recipients should adhere to in order to ensure quality use of procured products.

Revisions due to changes or updates of normative guidelines

16. As the Global Fund only procures diagnostic products that are consistent with WHO guidance or that comply with applicable national guidance, the Secretariat regularly assesses the impact of new, revised or updated normative guidance or guidelines on the QA Policy for Diagnostics. Since the last revision of the QA Policy for Diagnostics in February 2014, WHO has issued or revised existing guidelines in a number of areas that should be reflected in the policy in order to align with these guidelines.
17. These areas include: HIV self-testing (HIVST) and G6PD testing; new WHO criteria to determine product eligibility for antigen-detecting malaria rapid diagnostic tests (RDTs), and Post-Marketing Surveillance of In Vitro Diagnostics (IVDs).

HIV Self-Testing (HIVST)

18. Current WHO guidelines encourages countries to pilot and explore the use of HIV self-testing (HIVST) to scale up HIV testing, especially among people not reached by existing HIV testing services.¹⁰ Accordingly, the Global Fund is supportive of countries including operational research on HIVST as part of their HIV funding or reprogramming requests as a means to increase access to and uptake of HIV testing among high-risk populations who may not be otherwise tested¹¹. The Secretariat proposes to amend the QA Policy for Diagnostics revision by including quality requirements for HIV self-testing rapid diagnostic tests (RDTs) in line with the WHO Technical Specification on Human Immunodeficiency Virus (HIV) rapid diagnostic tests for professional and/or self-testing.¹²

Procurement eligibility for antigen-detecting malaria rapid diagnostic tests (RDTs)

19. In May 2016, WHO announced changes to the WHO criteria used to determine procurement eligibility for antigen-detecting malaria rapid diagnostic tests (RDTs). Since 2009, WHO

¹⁰ WHO guidelines on HIV self-testing and partner notification: supplement to consolidated guidelines on HIV testing services see: <http://www.who.int/hiv/topics/vct/en/>

¹¹ Global Fund Briefing Note: operational research to improve implementation and uptake of HIV self-testing: http://www.theglobalfund.org/documents/core/infonotes/Core_OpResearchImplementationHIVSelfTesting_BriefingNote_en/

¹² WHO Technical Specification TSS-1: Human Immunodeficiency Virus (HIV) rapid diagnostic tests for professional and/or self-testing: http://www.who.int/diagnostics_laboratory/guidance/technical_specification_series/en/

recommendations on malaria RDT procurement have been based on product performance in the WHO Malaria RDT Product Testing Programme, in collaboration with FIND and the US Centers for Disease Control and Prevention and/or WHO prequalification Programme for Diagnostic products. As of 31 December 2017, WHO Prequalification Programme will determine the procurement eligibility of malaria RDTs as such only those products that meet these requirements will be eligible for procurement. The proposed revisions to the policy reflect alignment with these recommendations.

Post-Marketing Surveillance of In Vitro Diagnostics (IVDs)

20. In 2015, WHO published guidance on Post-Marketing Surveillance of In Vitro Diagnostics (IVDs). These guidance describe the initial measures that should be taken to ensure the ongoing compliance of WHO-prequalified IVDs with WHO prequalification requirements for safety, quality and performance after they are placed on the market. However, in light of the current lack of adequate post-market surveillance in many settings, the principles of this guidance may also be applied to non WHO prequalified IVDs.¹³ The Secretariat recommends that the QA Policy for Diagnostics be revised to align with the 2015 WHO guidance which will help ensure the continued quality, safety and performance of diagnostics products procured with grant funds.

WHO Recommendations on G6PD deficiency testing

21. To support safe use of primaquine for the prevention of relapse of Plasmodium vivax and ovale infections, the WHO Malaria Policy Advisory Committee recommends G6PD testing in regions with high prevalence of G6PD deficiency prior to initiating primaquine treatment.¹⁴ The recommended revisions to the policy incorporates the inclusion of quality requirements for G6PD tests to guide Global Fund implementers.

Revisions related to Co-infections and co-morbidities (COIMs) Policy

22. With the adoption of the Board policy on co-infections and co-morbidities of HIV/AIDS, tuberculosis and malaria (GF/B33/DPo8), the current QA Policy for Diagnostics should be revised to include those products that are linked to this policy. The proposed revisions recommend the inclusion of quality requirements for hepatitis B, hepatitis C and syphilis tests in order to guide Global Fund implementers regarding the procurement of such tests to diagnose co-infections in line with the Board policy.
23. These changes are included in Section 8 of the revised QA Policy for Diagnostics.

Rationale for Revisions

24. As required by Section 19 of the QA Policy for Diagnostics, the proposed revisions were shared for comments to partners⁹. A limited number of comments were received, noting the limited scope of recommended changes. The comments received were taken into account, as appropriate, and are included in the revised QA Policy for Diagnostics, and are detailed in Annex 3.
25. The recommended revisions to the QA Policy for Diagnostics reflect the phase in of additional requirements for specific products required for the diagnosis of HIV, malaria and tuberculosis and co-infections including hepatitis B, hepatitis C and syphilis, as well as IVDs providing information that is critical for patient treatment of these diseases, such as testing for G6PD deficiencies for malaria. The scope of the changes are the following:
 - Inclusion of stringent evaluation requirements for IVDs for HIV self-testing, G6PD testing, hepatitis B, hepatitis C, syphilis and malaria, and

¹³ http://www.who.int/diagnostics_laboratory/postmarket/en/

¹⁴ <http://www.who.int/malaria/mpac/mpac-march2015-erg-g6pd.pdf>

- Non-material editorial changes necessary to adapt the QA Policy for Diagnostics in light of the inclusion of the above-mentioned new requirements, and
 - Adaptation of the previous Transitional Provisions (Sections 17 to 19) in order to reflect the new requirements.
26. The Secretariat will continue to, as part of the operationalization of the changes, provide clear guidance to implementers on which IVD products, by disease component and by category, that are eligible for procurement with grant funds.
 27. Noting the need to be able to reflect new, revised or updated recommendations or guidelines in a timely manner, the Secretariat is proposing additional revisions to the QA Policy for Diagnostics, that delegate decision-making powers to the Strategy Committee so that the Strategy Committee can approve future updates due to changes in Global Fund policy or WHO guidelines, which may require the inclusion of additional diagnostic products, as well as updates to clinical standards. These additions are included in sections 19 and 20 of the revised QA Policy for Diagnostics.
 28. The Board would continue to review and approve, based on the Strategy Committee's recommendation, changes related to the overall approach of the quality assurance for diagnostics.
 29. The revised QA Policy for Diagnostics is presented in Annex 1.

Part 7 – Risk Assessment Process Summary/Outcomes

30. This proposed changes to the QA for Diagnostics policy do not increase the overall levels of risk related to the selection, procurement and use of Diagnostic Products. The proposed revisions have been made in order to reduce the risk of procuring and using substandard Diagnostics Products for the following products: HIV Self-testing RDTs, G6PD tests and hepatitis B, hepatitis C and syphilis tests.
31. From a sourcing perspective, at least one product for each of the above-mentioned diagnostic products is available on the market and currently meets quality standards and therefore is eligible for procurement with grant funds.

Part 8 - Recommendation

32. The Strategy Committee has reviewed and discussed the revisions and recommends for Board approval the amended Global Fund Quality Assurance Policy for Diagnostic Products set forth in Annex 1.

Annex 1: Revised Global Fund Quality Assurance Policy for Diagnostic Products

GLOBAL FUND QUALITY ASSURANCE POLICY FOR DIAGNOSTICS PRODUCTS

(Issued on 14 December 2010, most recently amended on 4 May 2017¹)

BASIC PRINCIPLES

1. Diagnostic Products procured with Global Fund financing/resources may only be procured in accordance with this Policy.
2. Global Fund Recipients shall implement a Quality Assurance System for the procurement, supply management and intended use of all Diagnostic Products procured with Grant Funds in accordance with the guidelines specified in this Policy and on its website², so as to ensure the quality of diagnostic results.

DEFINITIONS

3. Capitalized terms and acronyms used in this Policy shall have the meaning given to them below, unless the context requires otherwise.

Diagnostic Products: all durable and non-durable in vitro diagnostics (IVDs), imaging equipment and microscopes used in Global Fund-financed programs for diagnosis, screening, surveillance or monitoring purposes.

External Quality Assessment (EQA): a program that assesses the performance of laboratories and/or testing sites by demonstrating the reliability and accuracy of testing results. EQA may include proficiency testing (otherwise known as an EQA scheme), or on-site visits to assess the laboratory practices and procedures, or a combination of the above³.

Expert Review Panel (ERP): a panel of technical experts independent of the Global Fund which, in accordance with its terms of reference and under the oversight of WHO, analyzes the potential risks and benefits of Diagnostic Products and advises the Global Fund on use of Grant Funds for procurement of Diagnostic Products for a time-limited period.

Glucose-6-phosphate dehydrogenase (G6PD) Test: an In Vitro Diagnostic Medical Device intended by the manufacturer for the detection of Glucose-6-phosphate dehydrogenase (G6PD) enzyme activity.

¹ As approved by the Board under decision point GF/B37/DP12 and set forth in Annex 1 to GF/B37/06.

² <http://www.theglobalfund.org/en/sourcing/qa/diagnostics/>

³ Adapted from: ISO 17043. Conformity assessment – General requirements for proficiency testing.

Grant Funds: grant financing or any other financing provided by the Global Fund.

HIV Immunoassays: a serological technique that relies on the interaction between antigen and antibody for detection of HIV-1/2 antibodies and/or HIV-1 p24 antigen, i.e. rapid diagnostic tests (RDTs), agglutination assays, enzyme immunoassays (EIA) (including microtiter plate EIA, comb format EIA,), line immunoassays, and Western blotting.

HIV Self-Testing: the process in which an individual who wants to know his or her HIV status collects a specimen, performs a test and interprets the result themselves often in a private setting.⁴

HIV Virological Technology: a testing method that directly detects the presence of HIV nucleic acids, HIV particle components and/or the activity of the virus' components. These assays include quantitative (required for viral load measurements) and qualitative methods (for EID).

International Organization for Standardization (ISO): the non-governmental organization, including national standards institutes of 163 countries, which sets standards, including generic standards (e.g. ISO 9000 series) or product-specific requirements for implementing a quality management system (e.g. ISO 13485 for medical devices).

In Vitro Diagnostic Product (IVD) medical device: a medical device, whether used alone or in combination with other devices, 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 including, reagents, calibrators, control materials, specimen receptacles, software, and related instruments, apparatus and other articles⁵.

Lot: a defined quantity of products, manufactured in a single process or series of processes and therefore expected to be homogeneous.

Lot Testing: quality control testing of a lot or batch of a Diagnostic Product after manufacture and release from the manufacturing site.

Malaria Rapid Diagnostic Test: immunochromatographic lateral flow devices for the detection of malaria parasite antigen, and designed to provides a result timely enough to inform immediate treatment (e.g. within 60 minutes).

Manufacturer: any natural or legal person with responsibility for design and/or manufacture of Diagnostic Products with the intention of making it available for use, under the Manufacturer's name;

⁴ <http://who.int/hiv/pub/guidelines/hiv-testing-services/en/>

⁵ Global Harmonization Task Force Document SG1/N045:2008.

whether or not such a Diagnostic Product is designed and/or manufactured by the Manufacturer itself or on its behalf by another person(s).

Recipient: any legal entity that receives Grant Funds.

Regulatory Authorities of the Founding Members of the Global Harmonization Task Force (GHTF): the regulatory authorities of the United States, the European Union, Japan, Canada and Australia.

Quality Assurance: refers to all measures taken from manufacturing processes, to selection and the use of a Diagnostic Product, including Quality Monitoring, to ensure that the Diagnostic Products are of the quality required for the Manufacturer's intended use.

Quality Management System: a management system to direct and control an organization with regard to quality⁶ (for quality system essentials for: facilities and safety, organization, personnel, equipment, purchasing and inventory, process control (QC), information management, document and records, customer service, external quality assessment).

Quality Monitoring: all activities undertaken to ensure that the Diagnostic Products continue to conform with the Manufacturer's established quality specifications during the storage, distribution and use of such product, including but not limited to Lot Testing, reporting of deficient Diagnostic Product and surveillance, as part of a Quality Assurance system.

Total Cost of Ownership (TCO): the total amount of all direct and indirect monetary costs related to the procurement, storage and distribution of a Diagnostic Product by a Recipient, including the price of the product itself, any reagents and other consumables, transportation, customs clearance, insurance, in-country distribution and storage, Quality Assurance and Quality Monitoring, training, and validation of new diagnostic algorithms, and, as applicable, operating costs including cost of installing, servicing, commissioning and maintaining equipment.

WHO: the World Health Organization.

INTERPRETATION

4. In this Policy, unless the context otherwise requires:
 - (i.) headings do not affect the interpretation of this Policy;
 - (ii.) the singular shall include the plural and vice versa;

⁶ Adapted from: ISO 9001 Quality management systems – requirements.

- (iii.) any phrase introduced by the terms “including”, “include”, “in particular”, “such as”, or any other similar expression shall be illustrative only and shall not limit the sense of the words preceding those terms; and
- (iv.) reference to an undated ISO standard designates the latest version of that standard.

APPLICABLE LAWS AND REGULATIONS

- 5. Each Recipient shall ensure that the procurement of Diagnostic Products with Grant Funds is undertaken in compliance with all applicable laws and regulations.

CLINICAL STANDARDS

- 6. Grant Funds may only be used to procure Diagnostic Products that are consistent with WHO guidance or comply with applicable national guidelines, and provided that funding requests submitted by Recipients include the following:
 - (i.) A description of the Diagnostic Products to be procured with Grant Funds. Upon request by the Global Fund, applicants shall provide a copy of, or refer to, the relevant WHO guidance or national guidelines supporting the use of the Diagnostic Products to be procured; and
 - (ii.) A technical justification, satisfactory to the Global Fund, for the procurement of Diagnostic Products that are consistent with WHO guidance but may not be consistent with national guidelines and vice versa. The Global Fund may, in its sole discretion, refer the technical justification provided, to the relevant WHO disease program for review and advice.

If, a Recipient proposes to use Grant Funds to procure Diagnostic Products other than the ones already approved by the Global Fund, it shall provide the Global Fund with a brief description of the Diagnostic Products and, if applicable, the technical justification described in paragraph 6 (ii) above, for approval by the Global Fund.

QUALITY STANDARDS

- 7. Grant Funds may only be used to procure Diagnostic Products that meet, at minimum, the following standards:⁷
 - (i.) IVDs and imaging equipment shall be manufactured at a site compliant with the requirements of ISO 13485 or an equivalent Quality Management System recognized by one of the Regulatory Authorities of the Founding Members of GHTF; and

⁷ Recipients may request the inclusion of higher standards or requirements for the purchase of IVDs. However, any request must be accompanied by a justification/rationale as to why these should be included and is subject to the approval of the Global Fund.

- (ii.) any Diagnostic Product for which Section 7 (i) above does not apply, such as microscopes, shall be manufactured at a site compliant with all applicable requirements of the ISO 9000 series or an equivalent Quality Management System recognized by one of the Regulatory Authorities of the Founding Members of GHTF.
8. In addition to the requirements outlined in Section 7 above, In-Vitro Diagnostic Products with respect to HIV, tuberculosis and malaria and to hepatitis B, hepatitis C and syphilis co-infections, as well as IVDs providing information that is critical for patient treatment of these diseases, such as testing for G6PD deficiency, must meet any one of the following standards:
- (i.) prequalification by the WHO Prequalification of In Vitro Diagnostics Programme; or
 - (ii.) for tuberculosis: recommendation by relevant WHO programme; or
 - (iii.) authorization for use by one of the Regulatory Authorities of the Founding Members of GHTF when stringently assessed (high risk classification)⁸ ; or
 - (iv.) acceptability for procurement using Grant Funds, as determined by the Global Fund⁹, based on the advice of the WHO Expert Review Panel.

At its discretion, for Diagnostic Products for which there is a public health need and which are not yet compliant with Section 8(i), (ii) and (iii), the Global Fund may request advice from the WHO Expert Review Panel to determine the acceptability for procurement of such Diagnostic Products for use by Recipients, for a time-limited period as recommended by the ERP, pending full assessment by one of the processes listed in Section 8(i), (ii) and (iii).

Manufacturers of Diagnostic Products referred to in this Section 8 are encouraged to submit their applications for full product review to the WHO Prequalification of In Vitro Diagnostics Programme or for stringently regulated products types (those to which the option described under Section 8(iii) is applicable) to one of the Regulatory Authorities of the Founding Members of GHTF.

9. Upon the request of the Global Fund, the WHO Expert Review Panel will advise the Global Fund on the potential risks and benefits associated with the use of a Diagnostic Product not meeting the criteria as per Section 8. Such determination of the Global Fund may not be disputed, challenged or appealed.

⁸ This option is not applicable to RDTs for HIV-Self-Testing

⁹ Notwithstanding a determination made by the Global Fund that a relevant product is acceptable or not-acceptable for procurement by a Recipient using Grant Funds, the Global Fund shall not be responsible or liable for any loss or damage arising out of or in connection with the manufacture, distribution, use or non-use of such product. The Global Fund may revoke or amend such determination in its sole discretion at any time.

QUALITY OF USE

10. A quality system defines a systematic approach to ensuring quality testing through use of standard operating procedures, management of documents and records, implementation of quality control and external quality assessment, including proficiency testing and on-site supervisory visits. The quality system extends to appropriate physical infrastructure, procedures for purchasing and inventory, equipment maintenance, customer service, human resource management and review, and continual process improvement¹⁰.
11. Each Recipient shall comply with WHO guidance for good purchasing, storage, inventory management and distribution practices applicable to Diagnostic Products, as indicated by the Global Fund on its website from time to time.
12. Each Recipient shall ensure that Diagnostic Products are only used by appropriately trained and suitably qualified persons in settings for which the Diagnostic Products are intended. Recipients shall also implement appropriate information management and record-keeping, use best efforts to support and participate in External Quality Assessment (EQA) programs, and ensure good facility management, safe and efficient operations with appropriate process controls, and calibration and maintenance of relevant equipment, as specified in relevant WHO guidance.
13. Recipients shall arrange for the monitoring of the quality of Diagnostic Products procured with grant funds in line with relevant WHO guidelines on Post-Market Surveillance of In Vitro Diagnostics. The cost of conducting quality control activities may be budgeted for in Global Fund grants. Recipients must submit the results of quality control testing to the Global Fund.
14. Recipients shall use best efforts to develop and maintain a mechanism to report defects relating to Diagnostic Products to the appropriate regulatory authorities and to the Global Fund and facilitate appropriate communications with Manufacturers, procurement agents, distributors and end users.
15. The costs to the Recipient of conducting any relevant quality assurance and capacity building measures related to the procurement, supply management and use of Diagnostic Products with Grant Funds, as far as they are not covered from other funding sources, may be included in the relevant Global Fund grant budget, which is subject to approval by the Global Fund.

GENERAL PROVISIONS

16. In addition to the requirements set out in this Policy, each Recipient must also comply with the following:

¹⁰ Adapted from: ISO 15189 Medical laboratories – Particular requirements for quality and competence. CLSI GP26-A4 Application of a Quality Management System Model for Laboratory Services; Approved Guideline-Third Edition

- i. All other Global Fund procurement policies and principles that may be applicable to Diagnostic Products, as published on the Global Fund website; and
- ii. The standard terms and conditions of Global Fund Grant Agreements, including the requirement for a competitive process to be undertaken to obtain the lowest possible price for relevant Diagnostic Products, taking into account Total Cost of Ownership (TCO), and ensuring that the Manufacturer and manufacturing site of the Diagnostic Product are disclosed in all applicable tender and procurement-related documentation.

IMPLEMENTATION

17. The QA Policy shall apply with effect for all Diagnostic Products as defined in section 7 and 8 on 4 May 2017, except for the requirements defined in section 8 for Malaria RDTs, which shall commence and apply in full force and effect on 31 December 2017.
18. If a Recipient has directly or indirectly through a procurement agent entered into a legally binding contract with a Manufacturer to procure Diagnostic Products with Grant Funds which do not comply with this Policy on or before the effective date of this Policy as per Section 17 above, the Recipient must promptly notify the Global Fund and provide reasonable details about the terms of that contract and procurement. The Global Fund may, after consultation with the Recipient, decide not to authorize the use of Grant Funds for the procurement of the Diagnostic Products that are non-compliant with this Policy. The Recipient shall manage its relevant contractual relationship with suppliers as it deems suitable.
19. The Global Fund's Standing Committee responsible for overseeing quality assurance of health products (the "Committee") will oversee implementation of this Policy. In order to align with any new, or modifications to existing, (i) recommendations or guidance issued by the WHO or other collaborating agencies, and/or (ii) relevant Global Fund policies, the Committee may approve the extension of requirements described in Sections 7 and 8 of this Policy to Diagnostic Products not otherwise referred to in Sections 7 and 8, respectively.
20. Upon approval of the extension of requirements referenced in Section 19 of this Policy or other modification to this Policy, Recipients shall be notified accordingly of the effective date of such change.

Annex 2. Rationale for Secretariat Proposed Revisions to the Global Fund QA Policy for Diagnostic Products¹

Alignment with new and/or updated WHO recommendations, guidance or process	Secretariat Proposed Change to the Policy
<p>WHO is developing new guidance on HIV self-testing as part of the updated Consolidated guidelines on HIV testing services, for release in December 2016. While a formal recommendation on HIV self-testing has not yet been issued, WHO has already provided programmatic guidance and encouraged countries to start piloting and conducting demonstration projects to evaluate self-testing in their particular contexts.</p> <p>The Global Fund has provided guidance for implementers considering HIV Self-testing in their HIV Response through a Briefing note: operational research to improve implementation and uptake of HIV self-testing</p>	<p><i>Include HIV self testing in section 8 of the QA Policy for Diagnostic Products</i></p>
<p>To support safe use of primaquine for the prevention of relapse of P. vivax and ovale infections, WHO MPAC recommend G6PD testing in regions with high prevalence of G6PD deficiency prior to primaquine treatment</p> <p>http://www.who.int/malaria/mpac/mpac-march2015-erg-g6pd.pdf</p>	<p><i>Include G6PD tests in section 8 of the QA Policy for Diagnostic Products</i></p>
<p>In May 2016, WHO Prequalification and WHO Global Malaria Programme, announced jointly changes to the WHO criteria used to determine procurement eligibility for malaria RDTs.</p> <p>As of December 2017, WHO Prequalification will also become the determinant of procurement eligibility of malaria RDTs. The results of the WHO Product Testing scheme will continue to be used as the independent performance laboratory evaluation component of the prequalification process. Only those products that meet WHO PQ requirements by December 2017 will be eligible for WHO procurement. WHO though this Public announcement is encouraging, RDT procurers and National Malaria Control to review their procurement policies for malaria RDTs and seriously consider bringing them in line with these revised WHO recommendations.</p>	<p><i>Update the standards in section 8 of the QA Policy for Diagnostic Products</i></p>
<p>In 2015, WHO published guidelines on Post-Marketing Surveillance of In Vitro Diagnostics (IVDs).² These guidelines describe the initial the measures that should be taken to ensure the ongoing compliance of WHO-prequalified IVDs with WHO prequalification requirements for safety, quality and performance after they are placed on the market. However, in light of the current lack of</p>	<p><i>Update the guidance in the section 13 of the QA Policy for Diagnostic Products</i></p>

¹ This Annex describes the substantial changes proposed to be made to the QA Policy for Diagnostic Products. Other non-material, editorial changes appear in the compared version of the Policy, showing all proposed changes, in Annex 1.

² WHO guidelines on Post-market Surveillance, Geneva, 2015

adequate post-market surveillance in many settings, the principles of this guidance may also be applied to other IVDs	
Alignment with Global Fund Board Policy on COIMs	Proposed Change
In follow-up to the interim decision taken at the 32 nd Board Meeting on Global Fund support to Hepatitis C (GF/B32/DP07), and based on the recommendations of the SII Committee, the Board has approved the framework for financing co-infections and co-morbidities of HIV/AIDS, tuberculosis and malaria, as set forth in GF/B33/11.	<i>Include hepatitis B and C and syphilis tests in section 8 of the QA Policy for Diagnostic Products</i>
Operational clarifications	Proposed Change
ISO 13485:2003 has been superseded by ISO 13485:2016 with a transition period for the superseded standard. We recommend to remove references to a publication date of an ISO standard in line with paragraph 4 section (d) of the QA Policy regarding undated ISO standards.	<i>Refer to ISO 13485 in section 7 (i) of the QA Policy for Diagnostic Products</i>
The QA Policy shall apply with effect for all Diagnostic Products as defined in section 7 and 8 on the 1 st January 2017, except for the requirements defined in section 8 for Malaria RDTs, which shall commence and apply in full force and effect on 31 December 2017. http://www.who.int/malaria/news/2016/rdt-procurement-criteria/en/	<i>Amendment to the Transitional Provisions of the QA Policy for Diagnostic Products</i>

Annex 3. Partner Feedback to Proposed Changes in the Global Fund QA Policy for Diagnostic Products

WHO Prequalification Diagnostics Team (PQ Dx):	Response
WHO PQ Dx raised concerns that syphilis IVDs are not stringently reviewed by any of the GHTF founding member regulatory authorities. The level of scrutiny of syphilis IVDs applied by GHTF regulators would be lower than for HIV, HBV and HCV.	As per the revised policy, syphilis test should be only prequalified, and/or ERP authorized to provide enough assurance.
WHO PQ Dx asked for clarification with reference to hepatitis B markers.	The revised policy specifies the various markers (virological and serological).
WHO PQ Dx asked for clarification with regard to the inclusion of IVDs for hepatitis B, hepatitis C and syphilis and in particular if the change relates to RDTs or to other assay formats as well.	The inclusions focus on the intended use and not on the method/technology/platform.
WHO PQ Dx suggested to add reference to requirements for manufacturers to conduct post-market surveillance including notification of all field safety corrective actions (FSCA) to Global Fund, irrespective if the Global Fund is impacted or not. This would ensure that GF is aware of FSCA such as product recalls, changes to the IFU etc	These requirements are to be implemented by manufacturers and will be communicated directly to them.
WHO PQ Dx suggested to revise lot testing to preclude pre-shipment lot testing ; with the expanded evaluation of malaria RDTs there will be a thorough assessment of the manufacturers capacity to conduct final QC lot release. WHO PQDx advised to focus on post-shipment lot testing, either pre- or post- distribution to the end-user sites to ensure that quality is preserved after product delivery in line with WHO Guidelines on post-market surveillance	Post shipment can be performed in case of doubt. The revised policy suggests to the Implementers to conduct post-marketing surveillance at all steps of the supply chain according to WHO Guidelines as specified in section 13 of the revised QA Policy.
WHO PQDx recalled that TB Diagnostics Products are currently not within the PQ scope.	Quality requirements detailed in the section 8 of the QA Policy have been updated accordingly.
Due consideration should be given to the fact that products that have undergone stringent review in a GHTF jurisdiction may fail to meet PQ requirements. WHO PQDx has had 2 PQ Notices of Concern (NoC) for high-risk CE-marked products.	The point is noted. In principles, the latest information should be used for decision making. The possibility for the Global Fund to take action on the basis of NoCs issued by WHO PQDx or by regulatory agencies of the founding members of the GHTF is reserved.
USAID comments	Response
USAID raised concerns that there will be insufficient numbers of pre-qualified non-HRP-2 RDTs by the end of FY 2017 to ensure full open competition for countries that require Pf/Pv or Pf/Pan combo tests. A growing number of countries in Africa reporting possible	One option available for addressing these challenges, as per the existing QA Policy, is the use of the ERP for Diagnostics mechanism to do a

<p>HRP-2 deletions in some areas of their country, will lead to an increasing demand for non-HRP-2 falciparum tests</p> <p>Lastly, and particularly in light of the challenges USAID mentioned, that there is a need for new RDTs addressing the existing and potentially new gaps in market, including RDTs that detect different antigens and more sensitive tests for non-falciparum species. USAID is concerned that the Global Fund is increasing barriers to introduction of new products.</p>	<p>risk benefit analysis of product dossiers that have not yet been prequalified, in particular when insufficient number of tests, such as non-HRP-2 RDTs, are available for procurement with grant funds.</p> <p>The use of the ERP for Diagnostics mechanism may also facilitate uptake of new RDTs or new technologies on the market.</p>
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