Quality Assurance Policy

for the

Procurement of HIV Point of Care technology

under the UNITAID grant

UNICEF Supply Division

Quality Assurance Centre and Health Technology Centre

March 2015

Revisions

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<td>Full review to ensure compliance with latest Global Fund reference document dated Feb 14. Update of Point of Care project requirements to remove inconsistencies while maintaining original QA policy requirements and philosophy.</td>
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1. Introduction

Regulatory systems for HIV Point of Care (PoC) diagnostics are primarily intended to help protect and promote the public health and safety. Public trust and confidence in these systems depends upon the maintenance of safety and performance of HIV PoC technology throughout their life-cycle. This is achieved by a third component, that of built in quality, being quality assured at each part of the design, production and marketing phases of the life cycle of a diagnostic, when used as intended.

Therefore, this Quality Assurance (QA) Policy outlines the principles of QA in relation to the selection and procurement of the HIV PoC technology by UNICEF Supply Division. It harmonises the UNICEF QA policy to the extent possible with the currently accepted Global norms\(^1\), Regulatory Requirements\(^2\) and International Quality Standards\(^3\).

2. Background

UNICEF has engaged in a tri-party agreement with UNITAID and Clinton Health Access Initiative, Inc. (CHAI) to accelerate access to high-quality PoC HIV diagnostic products by addressing market shortcomings and overcoming barriers to entry and uptake for new diagnostics, in order to maximise the impact of these technologies on patient outcomes. CHAI and UNICEF will undertake a set of activities which simultaneously engage both the supply and demand sides of the market in 7 high-volume, early-adopter countries (Ethiopia, Malawi, Mozambique, Kenya, Tanzania, Uganda, and Zimbabwe).

The PoC project has been established to increase access to a new generation of high-quality innovative PoC HIV diagnostic products creating a healthy, dynamic and sustainable market with affordable prices for PoC technologies, particularly for patients living in remote areas.

This will enable earlier initiation of patients onto life-saving antiretroviral therapies (ART) and facilitating timely switching of patients onto more effective second line ART regimens by reducing loss to follow-up and test turn-around time, ultimately reducing mortality and improving patient outcomes.

Within this context, UNICEF has committed to procure all necessary products and items to support the aims of the innovative technologies for CD4 T+ cell enumeration, Early Infant Diagnosis (EID) and HIV Viral Load measurement for the PoC project.

The procurement during the HIV POC project is divided into three phases as follows:

- Products for in-country evaluation
- Products for implementation pilot
- Products for routine clinical use

3. QA Policy

The QA requirements required for UNICEF procurement to support each of project phases are described below.

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\(^1\) Global Harmonization Task Force (GHTF) document GHTF/SG1/N78:2012, Principles of Conformity Assessment for Medical Devices


\(^3\) ISO 13485:2012
3.1 In-country Evaluation

In-country evaluation of new products aims to verify the manufacturer’s claims regarding the technical performance parameters of a product, and to assess whether it produces results in agreement with the existing reference technology used in the country or countries. The products used in this phase are not to be used for patient management or clinical decision-making, and diagnostic results from products used in this phase should not be shared with patients.

An in-country performance evaluation is distinct from proof of principle studies or validation and verification studies that are conducted by product developers before the product is commercially available in order to optimise the performance of the product and establish the technical data required for the product dossier, and from clinical utility studies, feasibility studies, or implementation pilots that are conducted by Ministries of Health for the purpose of measuring the impact of a product on patient outcomes and health system management or developing scale-up strategies or testing policies.

This phase of procurement enables early evaluation of products that have not yet achieved approval from a Regulatory Authority carrying out the scientific assessment of diagnostics products to the equivalent rigour of WHO prequalification, such as Regulatory Authorities of the founding members of the Global Harmonization Task Force (GHTF) and will help to facilitate earlier market entry of new diagnostic products.

Unless a product holds WHO Pre-Qualification or authorised for use by a regulatory authority of a founding member of the Global Harmonization Task Force (GHTF), i.e. USA, Japan, EU, Canada, Australia for HIV immunoassays and HIV Virologocal Technologies the minimum quality requirements for this phase of procurement are:

(a) Products must be manufactured at a site compliant with International Organization for Standardization (ISO) 13485:2003 (or ISO 13485:2012) or an equivalent Quality Management System (QMS) recognised by a Regulatory Authority of the founding members of the GHTF.

(b) In-country evaluations will only be conducted on products that have reached design maturity, and no major design changes are expected as a result of the in country evaluations, as evidenced by data and technical documentation provided by the supplier on the performance of the product in the setting of intended use, to the satisfaction of UNICEF and CHAI.

In the event that the manufacturer does not have a certified ISO 13485 system in place, or an equivalent QMS recognised by a Regulatory Authority of the founding members of the GHTF, and has a product that is ready for in country evaluation, the manufacturer must demonstrate they have a plan, have already engaged with, and are progressing towards certification by, a notified body to ISO 13485:2012. Further, UNICEF reserve the right to undertake a physical review of the manufacturing and QMS status on site to confirm the declared position.
3.2 Implementation Pilot

Once a product has completed an in-country evaluation it will be eligible for consideration for the implementation pilot. In some cases, countries may require a product to be evaluated in the country itself before it can be procured for implementation pilot, but this will not be a requirement of the project. Repetitions of product evaluation will be avoided where possible and the project will promote the acceptance of one successful evaluation per product in the 7 focus countries.

During an implementation pilot, a new diagnostic product will be used to provide test results to patients in the context of routine care and treatment programs, in order to evaluate clinical utility and feasibility of the product and to measure its impact on patient outcomes and health system management.

However, during an implementation pilot, use of the product will be limited to a relatively small number of testing sites to measure the impact that the product has on patient outcomes and health system management, and to develop deployment models for how best to implement the product at scale.

The minimum quality requirements for this phase of implementation pilot shall follow the principles of the Global Fund (GF) Quality Assurance Policy⁴ for procurement of HIV, TB and Malaria diagnostic products, amended as required for UNICEF use, which are as follows:

(a) UNICEF Supply Division will only procure diagnostic products for an implementation pilot that are included in the following list of approved products:


The devices listed above have been recommended by WHO after technical review of product quality and performance:

OR

Authorised for use by a regulatory authority of a founding member of the Global Harmonization Task Force (GHTF), i.e. USA, Japan, EU, Canada, Australia for HIV immunoassays and HIV Virological Technologies

OR

Acceptable for Procurement, based on the advice of an Expert Review Panel convened by the Global Fund, (see Part 4).

3.3 Routine Clinical Use

The minimum quality requirements for routine clinical use are:

(a) UNICEF Supply Division will only procure diagnostic products for an implementation pilot that are included in the following list of approved products:


The devices listed above have been recommended by WHO after technical review of product quality and performance:

OR

Authorised for use by a regulatory authority of a founding member of the Global Harmonization Task Force (GHTF), i.e. USA, Japan, EU, Canada, Australia for HIV immunoassays and HIV Virologocal Technologies

OR

Acceptable for Procurement, based on the advice of an Expert Review Panel convened by the Global Fund, (see Part 4).

3.4 Post Market Surveillance

Post Market Surveillance (PMS) of the HIV PoC diagnostics will follow the applicable sections of the latest version of the WHO Guidance for post-market surveillance of in vitro diagnostics\(^5\)

UNICEF reserves the right to conduct inspections of products and processes when procuring any HIV PoC diagnostics. These inspections may be conducted at any time during the manufacturing cycle or the supply chain. The inspections may be conducted by UNICEF staff or a UNICEF nominated third party inspection agency.

Any product failure or adverse event identified during any of the above three phases of use shall be reported by the end user immediately to UNICEF Supply Division (SD). UNICEF will advise the suppliers of any recorded adverse events and will subsequently manage the complaint through the UNICEF complaint procedures.

The link to UNICEF complaint form is: [http://www.unicef.org/supply/index_66223.html](http://www.unicef.org/supply/index_66223.html)


The ERPD is a mechanism to assess the risks associated with procurement of diagnostic products that may have a high public health impact, but have not yet undertaken a stringent assessment, either by the World Health Organization (WHO) Prequalification or by one of the Regulatory Authorities of the Founding Members of the GHTF.

The Global Fund, in partnership with UNITAID, is running several ERPDs. These review panels will allow manufacturers to voluntarily submit their product for expert review prior to or during any review by WHO Prequalification or assessment by one of the Regulatory Authorities of the Founding Members of the GHTF. Please refer to the GF web pages for up to date information on the calendar for reviews and outcome of previous reviews\(^6\).

If required, UNICEF shall request an ad-hoc product specific ERPD to be conducted by The Global Fund and WHO.

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5. Abbreviations

CHAI  Clinton Health Access Initiative, Inc
EID  Early infant diagnosis
ERPD  Expert review panel for diagnostics
GF  Global Fund
GHTF  Global harmonization task force
ISO  International Organization for Standardization
IVD  In-vitro diagnostics
PDI  Pre-delivery inspection
PMS  Post market surveillance
PoC  Point of care
QA  Quality assurance
QMS  Quality management system
SD  Supply Division
WHO  World Health Organization

6. Definitions

Diagnostic Products: all In-Vitro Diagnostics (IVDs) used for diagnosis, screening, surveillance or monitoring purposes.

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).

Manufacturer:

a) the ‘person with responsibility for the design, manufacture, packaging and labelling of a device before it is placed on the market under his own name, regardless of whether these operations are carried out by that person himself or on his behalf by a third party;’ or
b) a person who ‘assembles, packages, processes, fully refurbishes and/or labels one or more ready made products and/or assigns to them their intended purpose as devices with a view to their being placed on the market under his own name.’ This does not apply to a person who assembles or adapts devices already on the market to their intended purpose for an individual patient.

Quality Assurance (QA): a set of activities intended to establish confidence that quality requirements will be met. QA is one part of quality management.

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