Guidance for Manufacturers

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World Health Organization

Guidance: Prevention better than Cure

WHO | Prequalification of

www.who.int/diagnostics_laboratory/evaluations/en/

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In vitro diagnostics and laboratory technology

- In vitro diagnostics and laboratory technology
- Prequalification of IVDs and medical devices
- Procurement of in vitro diagnostics
- Post-market surveillance
- Quality assurance
- Guidance and training
- Country projects

Prequalification of in vitro diagnostics

The World Health Organization (WHO) Prequalification of In Vitro Diagnostics (IVDs) Programme aims to promote and facilitate access to safe, appropriate and affordable in vitro diagnostics of good quality in an equitable manner. Focus is placed on in vitro diagnostics for priority diseases and their suitability for use in resource-limited settings.

LATEST UPDATES

Updated guidance: Reportable changes to a WHO Prequalified IVDs (for public comment no later than 31 March 2016) [pdf 1.14Mb]

A risk based approach for the assessment of in vitro diagnostics (IVDs) [pdf 445kb]

IVDs PREQUALIFICATION PROCESS

Overview of prequalification of in vitro diagnostics pdf, 1.02Mb

Pre-submission Form — The pre-submission form is submitted by the manufacturer to apply for prequalification.

Dossier review — The product dossier is reviewed with the purpose of gaining an understanding of the product, its safety and performance, design and manufacture; and determining if the manufacturer's QMS is of an adequate standard to warrant an inspection.

Site inspection — The manufacturing site inspection is carried out to assess compliance with the quality management standard ISO 13485:2003, with focus on the suitability of the implemented processes and procedures for the reliable supply of products.

EMERGENCY USE ASSESSMENT AND LISTING (EUAL) PROCEDURE

- Zika Virus Disease
- Ebola Virus Disease

Related Topics

- WHO list of prequalified in vitro diagnostic products
- Status of active applications to the prequalification of in vitro diagnostics
- Complaints and Product Alerts
- Streamlining of the Prequalification of Diagnostics
- WHO Prequalification of Male Circumcision Devices
- Procurement of in vitro diagnostics
- HIV incidence assay working group
- Information resources

Recent Highlights

- Change of WHO recommendations on malaria RDT procurement pdf, 662kb
- New alternative performance evaluation mechanism
- New sample product dossier for public comment
- New guidance for manufacturers for public comment
- G6PD Prequalification: Public Announcement to Stakeholders pdf, 426kb
- Newsletter Issue 13, Q1 2016 pdf, 401kb
- Guidance for post-market surveillance pdf, 424kb

OVERVIEW OF THE PREQUALIFICATION OF IN VITRO DIAGNOSTICS ASSESSMENT

WHO Prequalification of In Vitro Diagnostics Programme

INSTRUCTIONS FOR COMPILATION OF A PRODUCT DOSSIER

Prequalification of In Vitro Diagnostics Programme

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Guidance and training

Guidance for Manufacturers

1. Technical Guidance Series

The Prequalification Team – Diagnostics is developing a Technical Guidance Series for manufacturers interested in WHO prequalification of their IVD. The guidance will apply in principle to all IVDs that are eligible for WHO prequalification for use in WHO Member States and will assist manufacturers in meeting prequalification requirements. It has been developed by WHO with input from national regulatory authorities, national reference laboratories and WHO prequalification dossier assessors and inspectors. It should be read in conjunction with relevant international and national standards and guidance.

- TGS 1 Standards applicable to the WHO Prequalification of in vitro diagnostics: TGS 1 identifies standards and guidance that contains valuable information on a range of issues that are encountered in the manufacture, verification, and validation of IVDs.
- TGS 2 Establishing stability of an in vitro diagnostic for WHO Prequalification: TGS-2 provides IVD manufacturers with guidance on possible approaches to determine stability. More specifically it describes the requirements for WHO prequalification in terms of stability testing. (Comments to be submitted to diagnostics@who.int no later than 29 February 2016)
- TGS 3 Principles of performance studies:TGS 3 identifies the key principles that apply when conducting and reporting the study design, results, and conclusion of analytical and clinical performance studies that support performance claims for IVDs undergoing assessment for WHO prequalification. (Comments to be submitted to diagnostics@who.int no later than 31 July 2016)

Related documents

- TGS 1 Standards applicable to the WHO prequalification of in vitro diagnostics pdf, 631kb
- TGS 2 Establishing stability of an in vitro diagnostic for WHO prequalification pdf, 1.04Mb
- TGS 3 Principles of performance studies of an in vitro diagnostic for WHO Prequalification pdf, 613kb
- TGS 2 Comments table for establishing stability of an in vitro diagnostic for WHO prequalification docx, 25kb

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Technical Guidance Series

- TGS1 Standards applicable to the WHO Prequalification of in vitro diagnostics
- TGS2 Establishing stability of an in vitro diagnostic for WHO Prequalification (draft)
- TGS3 Principles of performance studies(draft)

4.2 Assay design

Source	Document number	Document name	Date published
CLSI	MM03-Ed3	Molecular Diagnostic Methods for Infectious Diseases, 3rd Edition	27-Feb-2015
CLSI	MM06-A2	Quantitative Molecular Methods for Infectious Diseases; Approved Guideline - Second Edition	30-Nov-2010
CLSI	MM09-A2	Nucleic Acid Sequencing Methods in Diagnostic Laboratory Medicine; Approved Guideline—Second Edition	28-Feb-2014
CLSI	MM12-A	Diagnostic Nucleic Acid Microarrays; Approved Guideline	30-May-2006
CLSI	MM16-A	Use of External RNA Controls in Gene Expression Assays; Approved Guideline	29-Aug-2006
CLSI	MM17-A	Verification and Validation of Multiplex Nucleic Acid Assays; Approved Guideline	21-Mar-2008
CLSI	MM22-A	Microarrays for Diagnosis and Monitoring of Infectious Diseases; Approved Guideline	27-Feb-2014
CLSI	M53-A	Criteria for Laboratory Testing and Diagnosis of Human Immunodeficiency Virus Infection; Approved Guideline	30-Jun-2011
CLSI	I/LA18-A2	Specifications for Immunological Testing for Infectious Diseases; Approved Guideline	Sept-2001
CLSI	POCT04-A2	Point-of-Care In Vitro Diagnostic (IVD) Testing; Approved Guideline—Second Edition	Aug-2006
CLSI	POCT09-A	Selection Criteria for Point-of-Care Testing Devices; Approved Guideline	30-Apr-2010
EU	EN 13641:2002	Elimination or reduction of risk of infection related to in vitro diagnostic reagents	17-Dec-2002
FDA	1546	Class II Special Controls Guidance Document: Instrumentation for Clinical Multiplex Test Systems - Guidance for Industry and FDA Staff	10-Mar-2005
FDA	1620	Statistical Guidance on Reporting Results from Studies Evaluating Diagnostic Tests	13-Mar-2007
FDA	2231	Guidance for Industry and FDA Staff - Assayed and Unassayed Quality Control Material	07-Jun-2007
FDA	1646	Class II Special Controls Guidance Document: Plasmodium Species Antigen Detection Assays	20-May-2008
FDA	1737	In Vitro Companion Diagnostic Devices	06-Aug-2014

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Others in the **Technical Guidance Series**

- Test method validation
- Instructions for use
- Specimen stability
- Use of reference materials for manufacturing of PQ products
- Flex studies
- Interfering substances
- Specimen equivalence
- Reporting
- Component stability
- QC panels
- Outsourcing and Supplier management
- Risk Management

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Sample Dossiers

- POC CD4 IVD 2014
- HIV RDT for Self Testing 2015
- HIV NAT (Qualitative) 2016
- HIV NAT (Quantitative) Q2 2016
- Malaria RDT (not yet started)

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WHO Technical Specification Series

- Guidance specific to each type of IVD accepted to PQ to address the question “how much do you consider to be ‘sufficient’ for prequalification?”
- Will not only inform manufacturers but will provide clarity to reviewers as to WHO expectations for PQ
- Once each TS is developed, the requirements will be incorporated into a specific dossier assessors reporting template and be used in the grading tool.

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WHO Technical Specification Series

- HIV RDTs*
- HIV NAT
- HBV RDTs and EIAs
- HCV RDTs and EIAs
- CD4
- Malaria RDTs and G6PD RDTs
- POC HPV NATs
- HIV/Syph RDTs

Further Guidance

WHO PQ Requirements Guidance

- Post market surveillance for IVDs (2015)
- EQA (2016)
- Reportable changes to a WHO Prequalified IVD (2016)
- Reportable changes to a WHO Prequalified Medical Device (to be developed)
- What is REALLY needed is guidance on how to deal with changes DURING PQ

Other PQ Dossier Associated Activities

ISO

ISO/NP 20916

Clinical performance studies for in vitro diagnostic devices (IVDs) using specimens from human subjects -- Good study practice

Other PQ Dossier Associated Activities

International Medical Device Regulators Forum (IMDRF)

- IVD Table of Contents
  - Classification matricies
- Common data elements for medical device identification
- Competency, training and conduct requirements for regulatory reviewers

Any questions?