Prequalification of in vitro diagnostics

Updates on 2023 achievements and the way forward

In vitro diagnostics assessment team:
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28 November 2023

Housekeeping rules

- Hybrid meeting
- Presentations followed by Q&A
  - Burning questions: raise your hand
  - Other questions addressed during Q&A
- Colleagues on-line:
  - All microphones are muted
  - Use the Q&A
- Break 11 – 11:30
- WHO Code of conduct

Code of conduc at WHO events

World Health Organization

CODE OF CONDUCT

To Prevent Harassment, including Sexual Harassment, at WHO events

PURPOSE

WHO is committed to enabling events at which everyone can participate in an inclusive, respectful and safe environment. WHO events are guided by the highest ethical and professional standards, and all participants are expected to behave with integrity and respect towards all participants attending or involved with any WHO event.

APPLICABILITY

The Code of Conduct applies to any WHO event, which shall include meetings, conferences and symposia, assemblies, receptions, scientific and technical events, expert meetings, workshops, exhibits, side events and any other forum organized, hosted or sponsored in whole or part by WHO wherever it takes place, and any event or gathering that takes place on WHO premises whether or not WHO is organizing, hosting or sponsoring.

The Code of Conduct applies to all participants at a WHO event, including all persons attending or involved in any capacity in WHO event.

Any other entity responsible for a WHO event commits to implementing the Code of Conduct.

The Code of Conduct is not legal or prescriptive in nature. It supplements, and does not affect, the application of other relevant policies, regulations, rules and laws, including laws regulating the premises in which the WHO event takes place and any applicable host country agreements.

PROHIBITED CONDUCT

Harassment is any behaviour that is directed at another person and has the effect of offending, humiliating or intimidating that person; and the person engaging in the behaviour knows or reasonably ought to know would offend, humiliate or intimidate that other person. Harassment in any form because of gender, gender expression, gender identity, race, religion or belief, nationality, ethnic or social origin, age, sexual orientation, marital status, disability, language or any other reason is prohibited at WHO events.

Sexual harassment is a specific type of prohibited conduct. Sexual harassment is any unwelcome conduct of a sexual nature that might reasonably be expected or be perceived to cause offence or humiliation. Sexual harassment may involve any conduct of a verbal, nonverbal or physical nature, including written and electronic communications, and may occur between persons of the same or different genders.

Examples of sexual harassment include, but are not limited to:

Making derogatory or demeaning comments about someone's sexual orientation or gender identity	Name-calling or using slurs with a gender/sexual connotation	Making sexual comments about appearance, clothing or body parts	Making comments about or rating a person's attractiveness
Asking for sexual favours or repeatedly asking a person for dates	Staring in a sexually suggestive manner	Unwelcome touching, including pinching, patting, rubbing or purposefully brushing up against a person	Making inappropriate sexual gestures, such as pelvic thrusts
Sharing sexual or lewd anecdotes or jokes	Sending sexually suggestive communications in any format	Sharing or displaying sexually inappropriate images or videos in any format	Attempted or actual sexual assault, including rape

COMPLAINT PROCESS

A participant who feels that they have been harassed at a WHO event may report the matter to the organizer of the WHO event or relevant security authority, and a participant who witnesses such harassment should make such a report. The organizer of the WHO event will be expected to take appropriate action in accordance with its applicable policies, regulations and rules.

Examples of appropriate action may include, but are not limited to:

- Requesting the offender to immediately stop the offending behavior
- Suspending or terminating the offender's access to the WHO event or refusing registration at future WHO events, or both
- Conveying the complaint to any investigative or disciplinary authority with jurisdiction over the person accused of harassment
- Conveying a report to the employer or entity with jurisdiction over the person accused of harassment for appropriate follow-up action

The victim of alleged harassment may also seek help from other relevant authorities, such as the police, bearing in mind the applicable legal framework. A participant should never knowingly make a false or misleading claim about prohibited conduct.

PROHIBITION OF RETALIATION

Threats, intimidation or any other form of retaliation against a participant who has made a complaint or provided information in support of a complaint are prohibited. WHO or other entity responsible for a WHO event will take any reasonable appropriate action needed to prevent and respond to retaliation, in accordance with its applicable policy, regulations and rules.

World Health Organization

Session outline

8:45 – 11:00:

Introduction & Welcome

Speaker: Irena Prat

Product dossier

Speaker: Mark Lanigan

Performance evaluations

Speaker: Anne-Laure Page

Labelling review and Public Reports

Speaker: Charles Chiku

ePQS

Speaker: Helena Ardura

Q&A

Moderated by Irena Prat

11:30 – 13:00:

PQ Technical specifications

Speakers: Ute Ströher and Deirdre Healy

Change requests

Speakers: Fatima Gruszka and Helena Ardura

Collaborative registration procedure for IVDs

Speaker: Susie Braniff

Q&A

Moderated by Irena Prat

Wrap Up

Irena Prat, PQT/IVD

About the Team

Team lead:

- Irena Prat

Technical staff:

- Helena Ardura: changes and ePQS
- Susie Braniff: CRP and ERPD transition
- Charles Chiku: labelling and PRs
- Fatima Gruszka: changes and ERPD
- Mark Lanigan: dossiers
- Anne-Laure Page: performance evaluations
- Ute Ströher: TSS, TGS and EUL

Administrative staff:

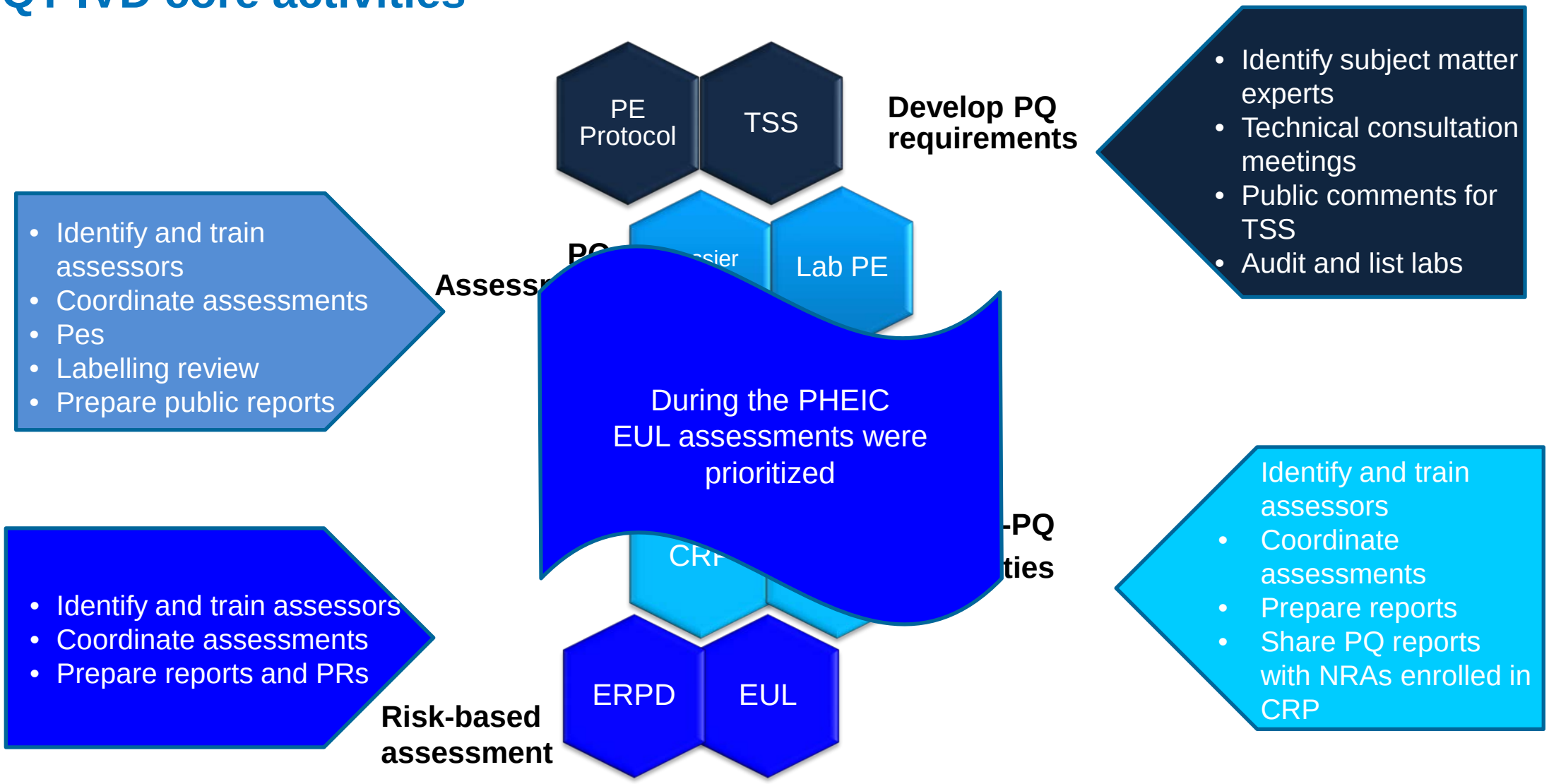
- Delphine Fachard
- Sandrine Hardouin
- Virgie Largado-Ferri

Consultants:

- Miguel de Mestral: dossier
- Laura Feldcamp: dossier
- Jean-Frédéric Flandin: performance evaluations
- Deirdre Healy: TSS and TGS
- Fabio Pereira Quintino: EUL and changes
- Katerina Zisaki: EUL and changes

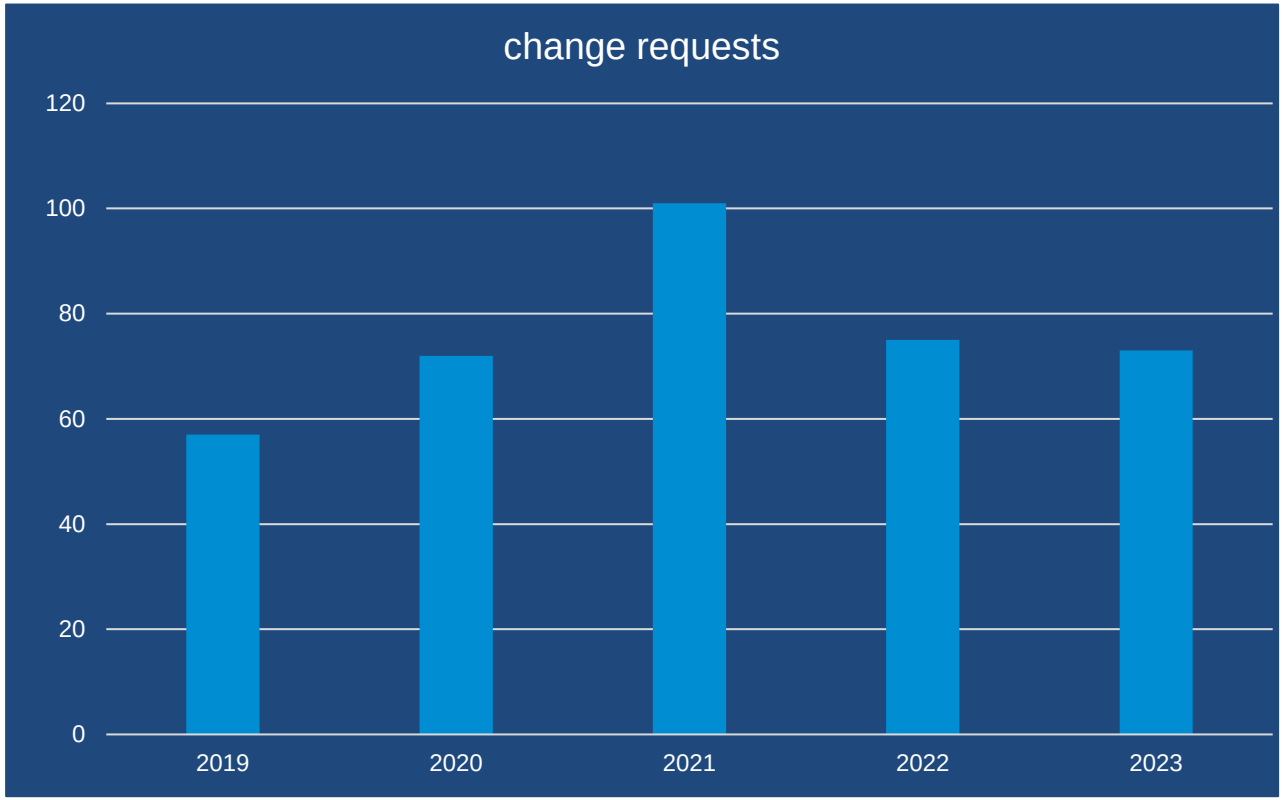



PQT-IVD core activities



→ *PQT-IVD Assessment decisions across PQ and EUL*

- In 2019 PQ assessments were completed for 13 IVDs
- EUL for SARS-CoV-2 opened in 2020
- Since that time the number of assessment completions have doubled or tripled
  - Organogram unchanged
  - Change requests in addition
- EUL for SARS-CoV-2 closed in May 2023
  - Transition of EUL IVDs to PQ
- Still high workload for PQT-IVD
- Focus again on PQ



SARS CoV-2 NAT and Ag RDTs: Transition from EUL → PQ

TSS-20 In vitro diagnostic medical devices used for the qualitative detection of SARS-CoV-2 nucleic acid

TSS-21 SARS-CoV-2 antigen rapid diagnostic tests for professional use and self-testing

End of the PHEIC triggered:

- No new EUL submissions accepted
- Cancellation of ongoing assessments (*unless close to completion)*
- Start of transition phase (EUL → PQ)

EUL listed IVDs will remain eligible for procurement until Jan 31, 2024, provided that the manufacturer adheres to post-listing obligations

- For products transitioning to PQ the EUL listing validity will be maintained until a PQ decision is taken

For products not undergoing PQ assessment, the EUL listing validity will not be extended beyond Jan 31, 2024

- EUL listed IVDs have until Dec 31, 2023, to apply for PQ assessment
- Technical Specifications TSS-20 and TSS-21 have been published

Q & A document available on website

https://extranet.who.int/pqweb/sites/default/files/documents/IVD_Transitioning_FAQ_V2.pdf

Recent achievements

Increase in number of assessments completed

- PQ-ed HPV assays list expanded to 4, additional Syphilis RDT, HCV RDTs and HCV NAT fingerstick also represent major milestones
- In 2023 we have so far listed 11 products (PQ and EUL)

TSS development work

- TSS HBV NAT published
- TSS for SARS-CoV-2 NAT and Ag RDTs published
- NCDs TSS developed: PQ expansion
- Inclusion of 2 labs for TB NAT performance evaluation

PQ scope expansion
TB NAT launched SEP 2022
SARS-CoV-2 launched AUG 2023




Recent achievements

Dossier Assessment

•ToC dossier format fully implemented to optimize manufacturers' submission resources and align with regulators using the ToC standardized format

•Identification and training for new assessors

•Joint assessment sessions

Public Reports content amended based on requests from procurers

CRP roll out continues

•PQ assessment reports are fully adapted to CRP

Coordination of ERPD

- •Effective implementation in collaboration with GF/UNITAID in 2020
- •Expanding scope for other procurers - pilot ERPD launched for NTDs in October

Expanded assessor pool
7 new experts 2022
13 new experts 2023
Strengthened collaboration with NRAs




Challenges

- Submission quality remains challenging, particularly for new applicants
  - very resource intense for PQT
- Extra work during the pandemic slowed down PQ and change review work
  - Backlog close to being fully addressed
- Big demand for scope expansion
  - 2019 expansion plan to be updated based on confirmation from WHO programmes
- Timelines for specific assessment activities remain challenging
  - e.g.: some prospective performance evaluations
- Internal resources are limited while demand is big




Opportunities 1/3

Expanded assessment capacity

- New experts identified and trained to allow for more timely decision-making preserving the current standards
- The team will continue training new assessors and will develop additional targeted guidance
- Collaboration with mature NRAs will be enhanced - participation in PQ assessment sessions and the development of PQ specifications
- Exploring an expanded collaboration with Conformity Assessment Bodies (CABs)

Expanded PQ scope

- Based on feedback received through a formal consultation with stakeholders
- Timelines will be adjusted & plan made publicly available soon

Opportunities 2/3

Operational improvements

- Assessment sessions will be held at regular intervals and complemented by between-assessment sessions
- Public assessment reports will be published after PQ listing
- ePQS platform to be implemented early 2024 → enable better transparency on applications status
- The abridged PQ assessment will be further modeled to leverage additional pre-market approvals and avoid duplication of efforts
- The PQ process will be adjusted to allow more activities happening in parallel
- Input from industry will be sought to consider their suggestions to leverage real-world data
- The EUL procedure will be reviewed and revised to reflect the experience gathered during the pandemic

Opportunities 3/3

Inclusivity

- inclusion of LMIC regulators in assessments
- support to QA of IVDs manufactured in Africa

Complementarity PQ/ERPD

- Ongoing ERPD for HIV RDTs manufactured in Africa
- Expansion of ERPD to products beyond those in the scope of GF/Unitaid
- Ongoing ERPD for NTDs
- ERPD for VPDs




Way Forward

Focus again on PQ, changes and TSS development

- New operational model being rolled out with a combination of assessment sessions and between-session assessments
- Operational improvements in the assessment process with specific steps performed earlier and others moved to after PQ-listing
- Assessment capacity expansion: introduction of new assessors, strengthened collaboration with SRAs and collaboration with CABs to be explored
- ePQS to increase transparency on application status
- PQDx expansion to new areas of work, including NCDs: updated expansion plan to be communicated soon




IVD product dossier update

Mark Lanigan
In Vitro Diagnostics Assessment Team
Prequalification Unit
Regulation and Prequalification Department
Access to Medicines and Health Products

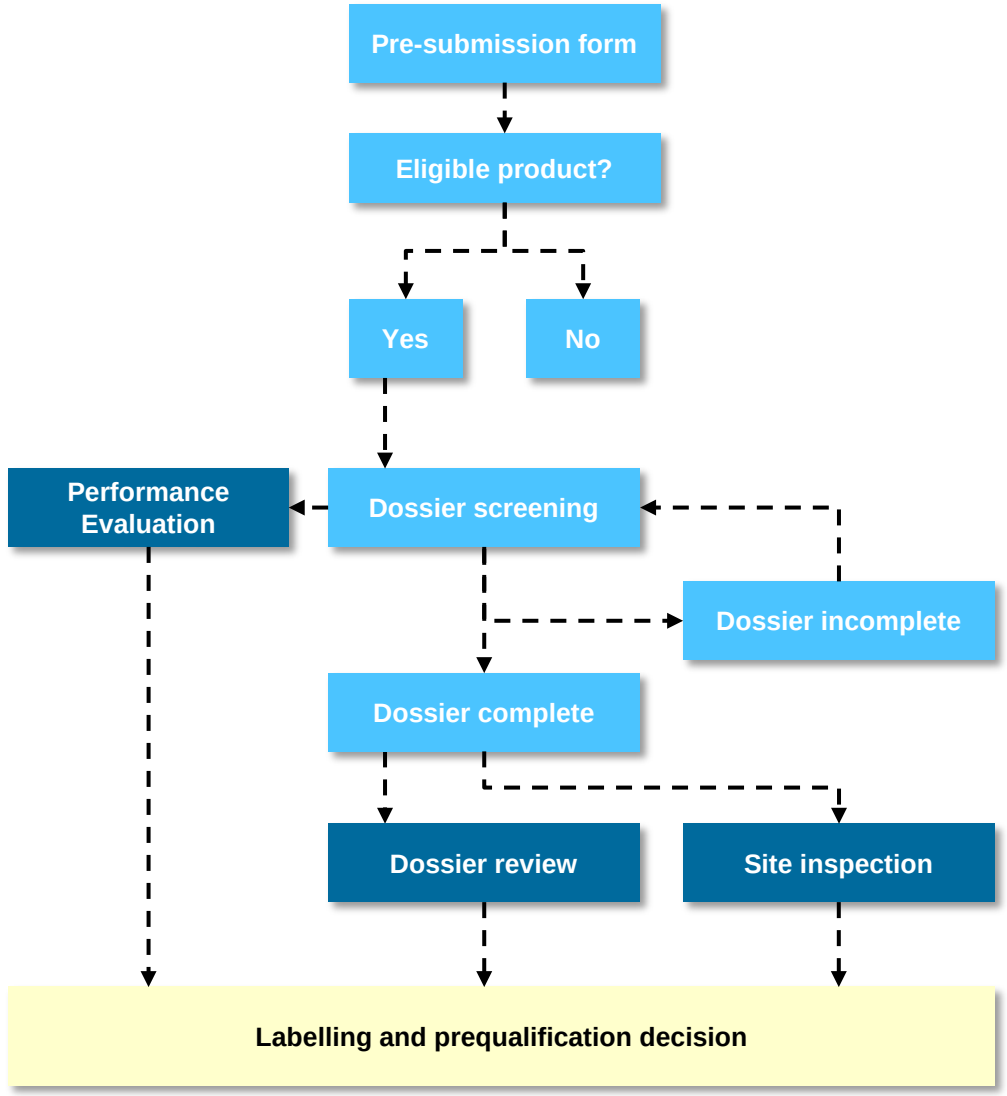
Outline

- 2022/23 update
- Dossier assessment process
- Format and content of a product dossier:
  - *PQDx_018 Instructions for Compilation of a Product Dossier – IMDRF ToC*
  - *TSS[s]*

PQ applications and listings for 2022/23

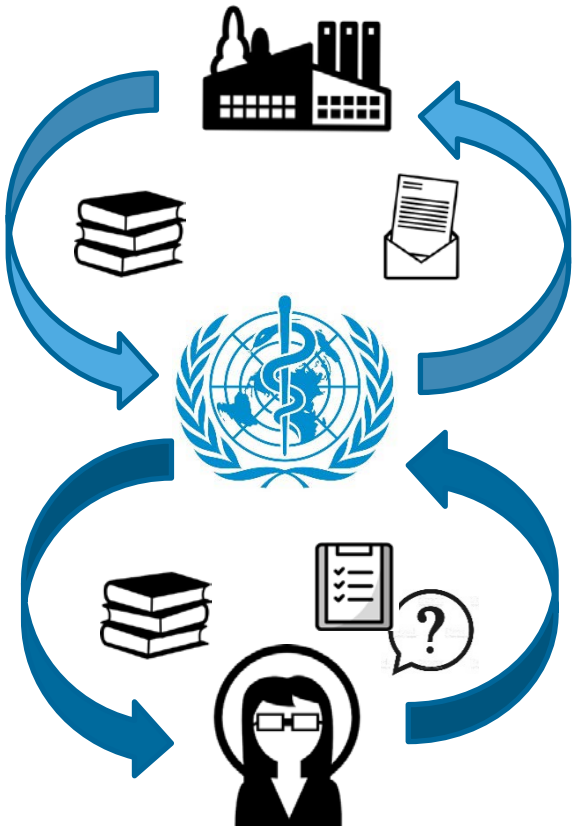
Products	No. applications submitted	No. products listed
HCV RDT	1	2
HCV NAT	1	1
HIV RDT	4	1
HIV NAT	-	2
HPV	2	1
M.TBc	14	-
Syphilis	1	1
Malaria	-	1
Total	23	9

Dossier assessment



Dossier assessment

- Manufacturer submits dossier to WHO
- Dossier screened for completeness
- Dossier sent to subject matter expert for technical review
- Expert provides completed dossier review report & notes any deficiencies
- Drafts requests for further information
- WHO prepares dossier review letter for manufacturer requesting additional information or clarifications
- Process repeated with manufacturer's Corrective Action Plan (CAP)



What does the product dossier contain?

IMDRF - ToC

WHO – PQDx_18 ToC
Instructions for compilation of a product dossier

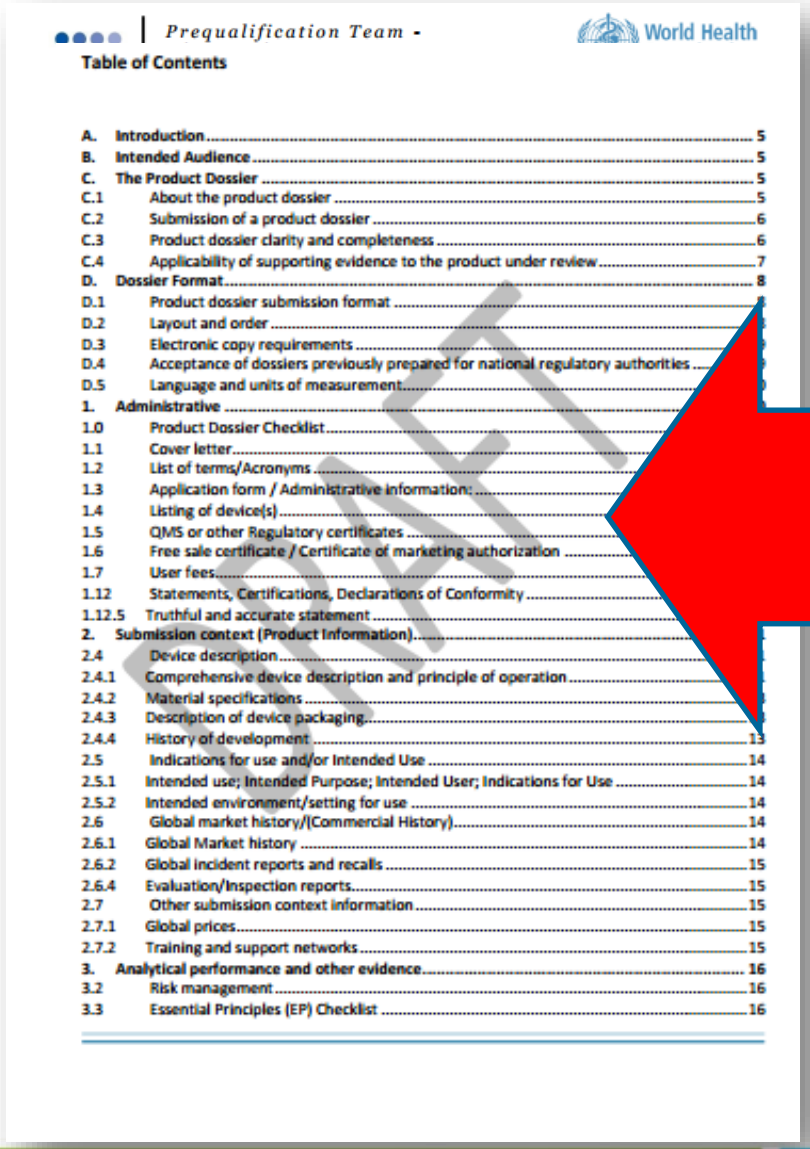
WHO – Technical Guidance Series (TGS)

WHO – Technical Specifications Series (TSS)

Format & layout of content

Quality & suitability of content

Product Dossier: content and format



Prequalification Team - World Health

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ToC format
C. The product dossier
D. Dossier format
1. Administrative
2. Submission context
3. Non-clinical evidence
4. Clinical evidence
5. Labelling and promotional evidence
6. Quality management system

“C. The product dossier”

- “The manufacturer shall carry out relevant investigations to support the intended use…”
- Refer to the edition of the TSS relevant to your product
- For each performance study submitted in a product dossier, the following shall be provided:
  - Study Description
  - Study summary
  - Full study protocol and report
    - Objectives; design; method, etc
    - Both summary and detailed results
    - Details of analyses
    - Conclusions




“D. Dossier format”

- Information divided into sections, with page format “1 of 2, 2 of 2, etc”
- Optical character recognition (OCR) for scanned documents
- Documents in English; certified translations
- Measurements expressed using International System of Units (SI)

“2 Submission context”

2.4 Device description

- Describe the product as a whole, its design, formulation and design changes

2.5 Indications for use and/or Intended Use

- Describe the function of the product; what it’s intended to detect

2.6 Global market history/(Commercial History)

- What regulatory versions of the product exist
- In which countries is the product supplied, and when did this begin
- Have adverse events, etc, been reported?

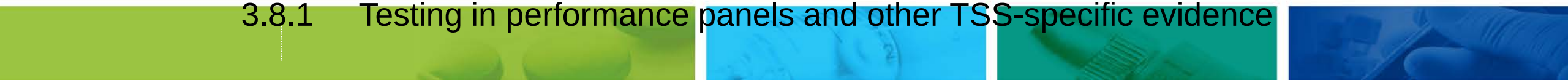
2.7 Other submission context information

- Provide indicative pricing for the product
- Describe the training and support networks that exist in each country of supply




“3. Analytical performance and other evidence

3.2	Risk management
3.3	Essential Principles (EP) Checklist
3.5	Analytical performance
3.5.1	Stability of specimen(s)
3.5.2	Validation of Specimens
3.5.3	Metrological traceability of calibrator and control material values
3.5.4	Accuracy of measurement [trueness, precision]
3.5.5	Analytical sensitivity
3.5.6	Analytical specificity
3.5.7	High dose hook effect
3.5.8	Measuring range of the assay
3.5.9	Validation of assay cut-off
3.5.10	Validation of the assay procedure
3.6	Other studies
3.6.4	Usability/Human factors
3.6.5	Stability of the IVD
3.6.5.1	Claimed shelf life
3.6.5.2	In-use stability
3.6.5.3	Shipping stability
3.8	Other evidence
3.8.1	Testing in performance panels and other TSS-specific evidence



“4. Clinical evidence”

4.2.3 IVD medical device specific clinical studies
4.5 Other clinical evidence
4.5.1 Qualification of Usability




“5. Labelling and promotional material

5.2 Product/package labels

5.3 Package insert/Instructions for use

5.6 Technical/operators manual

5.8 Other labelling and promotional materials

What does the product dossier contain?

IMDRF - ToC

WHO – PQDx_18 ToC
Instructions for compilation of a product dossier

Format & layout of content

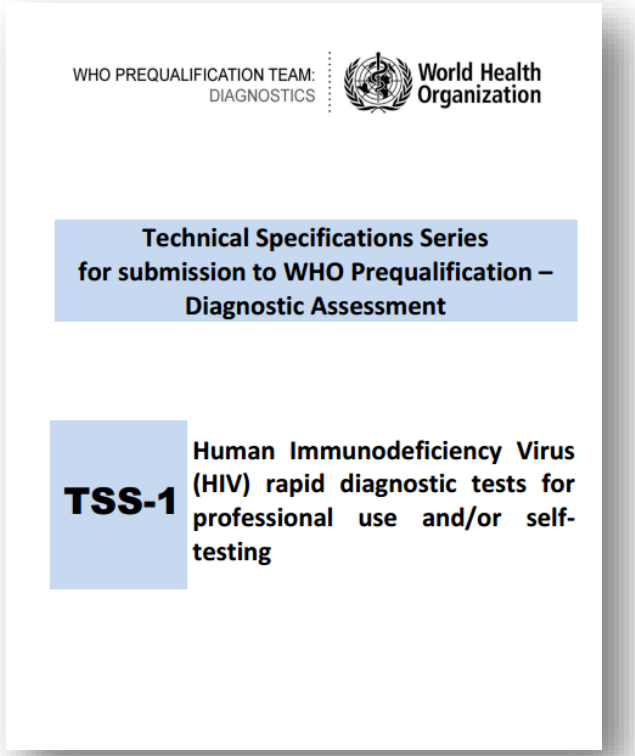
WHO – Technical Guidance Series (TGS)

WHO – Technical Specifications Series (TSS)

Quality & suitability of content

Example: HIV RDT

- TSS-1:
- Part 1 Establishing Analytical Performance
- Part 2 Establishing Clinical Performance
- Part 3 Qualification of Usability (self-testing)



Part 1 Establishing Analytical Performance

1.3 Precision of measurement			
Aspect	Testing requirements	Comments	References
	The effect of operator-to-operator variation on IVD performance is to be included as part of the precision studies (see also Comment 8). Testing should be done: • by personnel representative of intended users; • unassisted; and • using *only* those materials provided with the IVD (e.g. instructions for use, labels and other instructional materials).	5. Where possible, the testing panel should be the same for all operators, lots and sites. 6. Lots should be composed of different batches of critical components. 7. Results must be statistically analyzed by ANOVA to identify and isolate the sources and extent of any variance. In addition, the percentage of correctly-identified, incorrectly-identified and invalid results should be tabulated for each	
1.4 Performance panels			
1.4.1 Genotype panels	Testing of WHO International Reference Preparations and/or commercial HIV genotype panels including: • all HIV-1 subtypes (e.g. A,B,C,D,G, etc.) HIV-2, HIV-1 group O, and common circulating recombinant forms (CRFs); • at least 10 each of the most common subtypes (Subtype C, Subtype A, Subtype B, CRF02_AG, CRF01_AE and Subtype G); and • at least 3 less common subtypes (other CRFs and unique recombinant forms (URFs). • panel of specimens with a range of analyte	1. Testing should be performed using more than 1 final (locked-down) design lot. 2. All confirmed subtype-positive specimens should be detected by the IVD. 3. All reasonable attempts should be made to test rare subtypes. 4. For IVDs including a claim for detection of HIV Ag, appropriate specimens for the same subtypes must also be included in the testing panel. Use of panels of viral-like-particles (VLPs) or viral cultures may be considered acceptable however their use in place of characterized	Health Canada (7)




Part 2 Establishing clinical performance

2.1 Diagnostic sensitivity and specificity			
2.1.1 Diagnostic sensitivity and specificity	Diagnostic sensitivity and specificity should be determined for each claimed specimen type. Testing should be conducted: • at different geographical settings (minimum of 2 regions); • by a variety of intended users; and • using more than one master lot.	1. Prequalified HIV RDTs are generally used by lay providers and health care workers. For prequalification purposes, these should be considered as the intended user, rather than a trained laboratory professional. 2. Where an IVD is intended to detect multiple analytes without differentiating which analyte is detected, specimens chosen for the testing panel must comprise those that are reactive only for each individual analyte (i.e. not dual HIV-1/HIV-2 positive, etc). 3. A separate specimen should be collected prior to testing to establish the reference result. The testing algorithm used to determine the reference results should include a state of the art 4th generation immunoassay (EIA), with all initially reactive specimens reflexed for full characterization of the HIV status. 4. Problematic specimens, those with unexpected results but which otherwise meet selection criteria for a study, should not be systematically excluded from analysis. 5. Consideration should be given to the influence of antiretroviral medications present in a specimen on the serostatus of such specimens, and how this might affect specimen selection. 5. Lots (locked-down design) should be comprised of different batches of critical components. 6. Where possible, all discrepant results (between assay under	EC CTS (2) Health Canada (7)
2.1.2 Diagnostic sensitivity	Testing of: • At least 400 specimens confirmed HIV-1 antibody positive. • At least 100 specimens confirmed HIV-2 antibody positive (where HIV-2 detection is claimed; see Comment 2). • At least 50 specimens confirmed HIV p24 Ag positive (where Ag detection is claimed; see Comment 2).		
2.1.3 Diagnostic specificity	Testing of: • At least 1000 HIV antibody/antigen negative specimens.		




Part 3 Qualification of usability (self-testing)

3.1 Qualification of usability (self-testing)			
3.1.1 Label comprehension study	Questionnaire-based testing of subjects, representative of end users, to assess ability of intended users to correctly comprehend key messages from packaging and labelling: • Proper self-selection (whether or not users understand if it is appropriate for them to	1. Instructions for use and labelling should be clear and easy to understand; use of pictorial instructional material is encouraged.	ISO 18113:2011 (16) ISO 15197:2013(en) (17) IEC 62366-1:2015 (18) MHRA (19)
3.1.2 Results interpretation study	A minimum of 400 subjects to interpret the results of contrived IVDs (e.g. static/pre-made tests) to assess their ability to correctly interpret pre-determined test results. Contrived tests should be made to	1. The study group may include subject recruited as part of the label comprehension study.	FDA CLIA Waiver Requirements (23) WHO HIV testing
3.1.3 Observed untrained user study	Testing by at least 900 self-testing subjects comprising: at least 200 self-testers in each of two high-prevalence (>5%), geographically diverse population and at least 500 self-testers from a low-prevalence (<5%) population. • Each subject to self-collect test specimen and perform test according to only those materials provided with the IVD (e.g. instructions for use,	1. A separate venous whole blood specimen should be collected prior to testing to establish the reference results for HIV-1 status (and HIV-2 where detection is claimed). The testing algorithm used to determine the reference results should include use of a state of the art 4th generation immunoassay (EIA), with all initially reactive specimens reflexed for confirmation of the HIV status. 2. For WHO purposes the term 'professional use' encompasses a diversity of skills, training and experience and does not necessarily	

Compiling a product dossier

- **Use the format, and provide the content, defined in PQDx_018 v5 - Instructions for Compilation of a Product Dossier – IMDRF ToC :**

https://extranet.who.int/prequal/sites/default/files/document_files/PQDx_18_TOC_Instructions_March2023.pdf

- **Also refer to the TSS[s] relevant to your product**

- **If you have any questions, please contact us at:** diagnostics@who.int

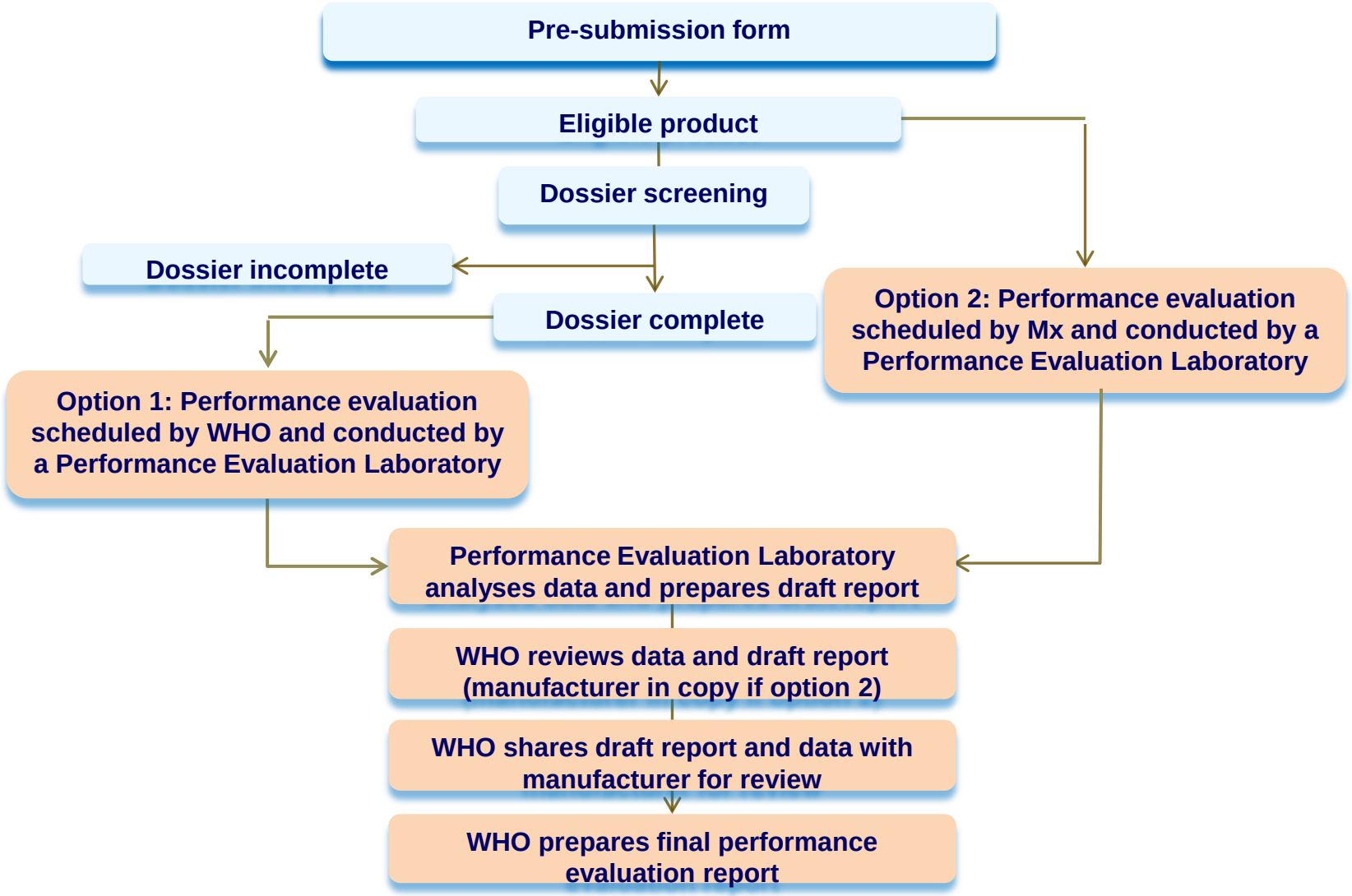



Performance evaluations

Anne-Laure Page

PQ performance evaluation

- One of the three components of prequalification assessment
- Applicable to all IVDs in current PQ scope (full or abridged assessment)
- Complements (does not replace) manufacturer's studies
- Aims at independently verifying some of manufacturer's claims
- Acceptance criteria (e.g. UN procurement criteria, TPP) where available
- If no acceptance criteria, consistency with performance in IFU


Pre-submission form
Eligible product
Dossier screening
Dossier incomplete
Dossier complete
Option 1: Performance evaluation scheduled by WHO and conducted by a Performance Evaluation Laboratory
Option 2: Performance evaluation scheduled by Mx and conducted by a Performance Evaluation Laboratory
Performance Evaluation Laboratory analyses data and prepares draft report
WHO reviews data and draft report (manufacturer in copy if option 2)
WHO shares draft report and data with manufacturer for review
WHO prepares final performance evaluation report

Summary of activities

- Since last December 2022
  - 12 performance evaluations completed
    - 5 HIV NAT
    - 4 malaria RDTs
    - 1 G6PD test, 1 CD4 rapid test, 1 HCV RDT
  - 2 listed performance evaluations laboratories (TB NAT)
  - Specimen collection for new panel for HIV serology

Specimen panel for the evaluation of HIV / HIV-syphilis tests

- Panel used for evaluation of HIV serology tests at ITM for > 20 years
  - Need to be renewed (age, change in epidemiology)
  - Same panel for all laboratories
- 6 performance evaluation laboratories collected HIV positive and negative specimens (10 to 15 mL plasma)
- Sent to ITM for characterization (HIV serology and syphilis)
- Aliquots prepared for sharing with all PELs listed for HIV serology

- Current status: HIV reference testing on-going (syphilis completed)
- Panel expected to be available in Q1 2024

HIV serology

- Development of protocol for HIV urine tests and parallel revision of protocol for HIV oral fluid tests
  - Require testing on HIV-positive individuals not on ART
  - Identification and audit of lab that can conduct the evaluation
  - Increase analytical panels (e.g. HIV-2 specimens)
  - Preparing submission to WHO ERC

- Revision of other HIV serology protocols (serum/plasma and capillary blood)
  - New panel for « main » protocol for HIV tests on serum and plasma and HIV-syphilis dual tests
  - Align analytical panels with above
  - Protocol revision planned for Q1 2024, once panel fully characterized

HPV nucleic acid tests

- New protocol developed for HPV mRNA tests
  - Analytical performance (LoD, reproducibility, genotype detection, cross-contamination)
  - Applicable for tests that meet Meijer 2009 criteria and can be considered as possible comparators for virologic evaluation

- Method for virologic evaluation of HPV DNA and mRNA tests under review

Malaria

- Collection of new specimens with *P. falciparum* hrp2/3 deletion in Africa planned for 2024

- Revision of protocol in parallel with revision of TSS requirements scheduled for 2024
  - Hrp2/3 deletion panels
  - Addition of P. vivax international standard

TB NAT

- Protocol for the evaluation of tests for the detection of TB
  - Initial version developed and approved by WHO ERC in Feb 2023
  - Further review due to
    - Implementation considerations from two listed laboratories
    - Parallel development of protocol for reflex tests for drug resistance detection
  - Amendment submitted to WHO ERC
  - First evaluation scheduled Q1 2024
- Protocol for the evaluation of reflex tests for drug resistance detection
  - Submitted to external reviewers
  - Next step: submission to WHO ERC
- 2 listed laboratories (South Africa, India)
  - Only option 1 (under discussion)
  - One additional candidate laboratory under assessment

SARS-CoV-2

- Protocol for the evaluation of SARS-CoV-2 NAT - draft
  - Analytical performance: LoD, reproducibility, variant detection, cross-contamination
  - Clinical performance: panel of stored specimens
  - Ease of use and operational characteristics

- Protocol for the evaluation of SARS-CoV-2 Antigen RDT – in development
  - Analytical performance (analytical sensitivity, variant detection, others TBD)
  - Clinical performance: TBD
  - Ease of use and operational characteristics

- PEL: considering expansion of scope for listed PELs

HbA1c point of care tests and blood glucose meters

- Protocols are being finalized
- PELs to be identified and assessed

Performance evaluation laboratories – list

- 15 listed laboratories

  https://extranet.who.int/prequal/vitro-diagnostics/prequalified/performance-evaluation-laboratories

Performance Evaluation Laboratories

Analyte | Laboratory | Apply

Download list as CSV file

Laboratory	Country	Date of Listing	Laboratory Option List	Analyte (s)
Biotechnology and Genetica Laboratory,Instituto Nacional de Saude (INS)	Mozambique	9 Jun, 2022	Option 1	HIV NAT (quantitative) HIV NAT (qualitative - EID)
CDC Division of Global HIV/TB International Laboratory Branch Viral Load and Early Infant Diagnosis Team	United States	10 Sep, 2018	Option 1 Option 2	HIV NAT (quantitative) HIV NAT (qualitative - EID)
Central Public Health Laboratories Kampala	Uganda	8 Apr	Option 1	HIV NAT

Performance evaluation laboratories

- Started re-auditing of listed laboratories
- Aim to provide closer support for first PQ evaluation (e.g. TB)
- In person PEL meeting planned Q2 2024
  - Share experience
  - Identify areas where more support needed
  - Standardization across PELs
- Revision of audit process of candidate laboratories scheduled for 2024
  - Align with ISO 15189:2022

Priorities for 2024

- Finalize protocols for new types of tests and clear backlog
  - HIV tests on urine and oral fluid
  - HPV mRNA test
- Use of new panel for evaluation of HIV and HIV-syphilis tests
- Panel of *P. falciparum* hrp2/3 deletion
- Evaluation of TB and SARS-CoV-2 products
- Prepare for evaluation of diabetes tests (HbA1c and blood glucose meters)
  - Finalise protocols
  - Identify PELs
- Enhance support to PELs

Labelling review and public reports updates

Charles Chiku

Objective

Provide an overview of labelling review approach and updates.

Labelling Principles

requirements to promote reduction in regulatory burden and allows patients to have access to IVDs of acceptable safety, quality and performance.

PQ conducts labelling review ensures that the labelling communicates safety and performance related information to users of IVD.

General Principles:

- The information needed to identify and use the device safely (in vitro diagnostic use, name, product code, UDI)
- Instructions for Use (intended use statement, principle of the test, materials provided/required not provided, performance characteristics)
- Appropriateness of the labelling format, medium, content, readability and location.
- Full or abbreviated instructions based on the risk classification of the IVD
- Provision of labelling in the appropriate medium to the intended use population
- Residual risks to be included as warnings or precautions
- Use of symbols that is proportional to the qualification, education and skills of the intended users.

Labelling review

- Labelling review is conducted at all stages of the assessment.
- clarity, correctness, consistency with the information submitted in the product dossier, international guidance and requirements, and suitability for the target user group in resource-limited settings.
- Review of records that supports safety and performance claims.
- Follow up through an onsite inspection for issues identified during the dossier review.
- Font size for both labelling.
- Suitability of labelling to hot and humid conditions.
- Universal symbols and warning legibility and comprehensiveness;
- Clarity of diagrams if applicable;
- Document control of IFU and labels of accessories supplied within the kit; and
- Confirmation that IFU procedure is followed during QC testing and final release testing.

Labelling review assessment

- Compilation of labelling associated nonconformities identified at all the assessment stages.
- Labelling parts of the test kit –IFU, job aides, outer test kit box, inner test kit pouches, specimen transfer devices, buffer bottle, etc.
- Review of final labelling to verify if the claims are supported by evidence submitted in the technical documentation.
- Non-critical changes may be accepted as commitments e.g some cases may require approval by the Notified Bodies.
- Application may be cancelled if there are critical deficiencies and the manufacturer not willing to address them.

Prequalification Decision

- DOSSIER ASSESSMENT
- MANUFACTURING SITE INSPECTION
- PRODUCT PERFORMANCE EVALUATION
- LABELLING ASSESSMENT




Public Report Content

- When a product meets the WHO prequalification, a public report is generated that will be made publicly available.
- WHO Public Reports include the following details:
    - o Name of the product
    - o PQ application number
    - o Product code(s)
    - o Name of the legal manufacturer
    - o Regulatory version

Public Report con’d

- o PQ decision and assessment dates
- o Summary of amendments for amended PR
- o Intended use, principle of the assay, materials provided, materials required but not provide
- o Summary of findings (dossier, manufacturing site inspection, performance evaluation)
- o Labelling

  https://extranet.who.int/pqweb/vitro-diagnostics/prequalification-reports/whopr

WHO Prequalification of In Vitro Diagnostics Programme
PUBLIC REPORT

Product: Bioline HIV/Syphilis Duo[1]
Number: PQDx 0179-012-00

Bioline HIV/Syphilis Duo with product codes 06FK30, 06FK35 and 06FK37, manufactured by Abbott Diagnostics Korea Inc[2]., Rest-of-World regulatory version, was accepted for the WHO list of prequalified in vitro diagnostics and was listed on 28 October 2015.

Summary of prequalification status for Bioline HIV/Syphilis Duo

	Date	Outcome
Status on PQ list	28 October 2015	listed
Dossier assessment	14 July2015	MR
Site inspection(s) of quality management system	24 July 2015	MR
Product performance evaluation	Quarter (Q) 3 2014-Q1 2015	MR

MR: Meets Requirements

Report amendments and/or product changes

This public report has since been amended. Amendments may have arisen because of changes to the prequalified product for which WHO has been notified and has undertaken a review. Amendments to the report are summarized in the following table, and details of each amendment are provided below.

Version	Summary of amendment	Date of report amendment
4.0	Updated labelling (IFU and labels). the product was rebranded from SD BIOLINE HIV/Syphilis Duo to Alere HIV/Syphilis Duo. Corrections/clarifications on IFU. Alere logo on IFU and boxes.	15 June 2017
5.0	Rebranding of Alere HIV/Syphilis Duo to SD BIOLINE	07 December 2018.




List of Prequalified IVDs

World Health Organization

WHO list of prequalified in vitro diagnostic products

RoW: Rest of the world. Regulatory version applied to products not approved by stringent/mature NRAs or not regulated

Last update: 20 November 2023

Year prequalified	Type of assay	Product name	Product code(s)	Regulatory version	Manufacturer
2023	HCV RDT	First Response HCV Card Test	PI03FRC25, PI03FRC50, and PI03FRC100	RoW	Premier Medical Corporation Private Limited
2023	HIV NAT	cobas HIV-1/HIV-2 Qualitative nucleic acid test for use on the cobas 6800/8800 and cobas HIV-1/HIV-2 Qualitative Nucleic acid test for use on the cobas 5800/6800/8800 Systems	07862113190, and 09040528190	CE-marked	Roche Molecular Systems, Inc.,
2023	HCV RDT	HCV Hepatitis C Virus Rapid Test Device (Whole blood/Serum/Plasma)	IHC-402WA, IHC-402WB, IHC-402WC, and IHC-402WD	RoW	ABON Biopharm (Hangzhou) CO., LTD
2023	HIV NAT	SAMBA II HIV-1 Qual Whole Blood Test	4500-12	CE-marked	Diagnostics for the Real World Ltd
2023	HPV Virological Technologies	cobas HPV	07460155190, 07460171190, 07002238190, 06997546190, 06997511190, 06997538190, 06997503190	CE-marked	Roche Molecular Systems, Inc.

Post-PQ stage

- aim of ensuring that safety and clinical performance of the IVD for its intended use are not affected by the introduction of labelling changes.
- a change may introduce new hazards that may not have been previously identified.
- adversely affect risks associated with existing hazards.
- alter the presentation of existing or new risks to the user (this can involve labelling changes or new indications for use).
- changes to labelling should be reported to WHO, including those related to actions including field safety corrective actions taken related to concerns arising from post-market surveillance , adverse events and user feedback.
- changes to labelling are reviewed in the context of validation and verification or any other relevant evidence.

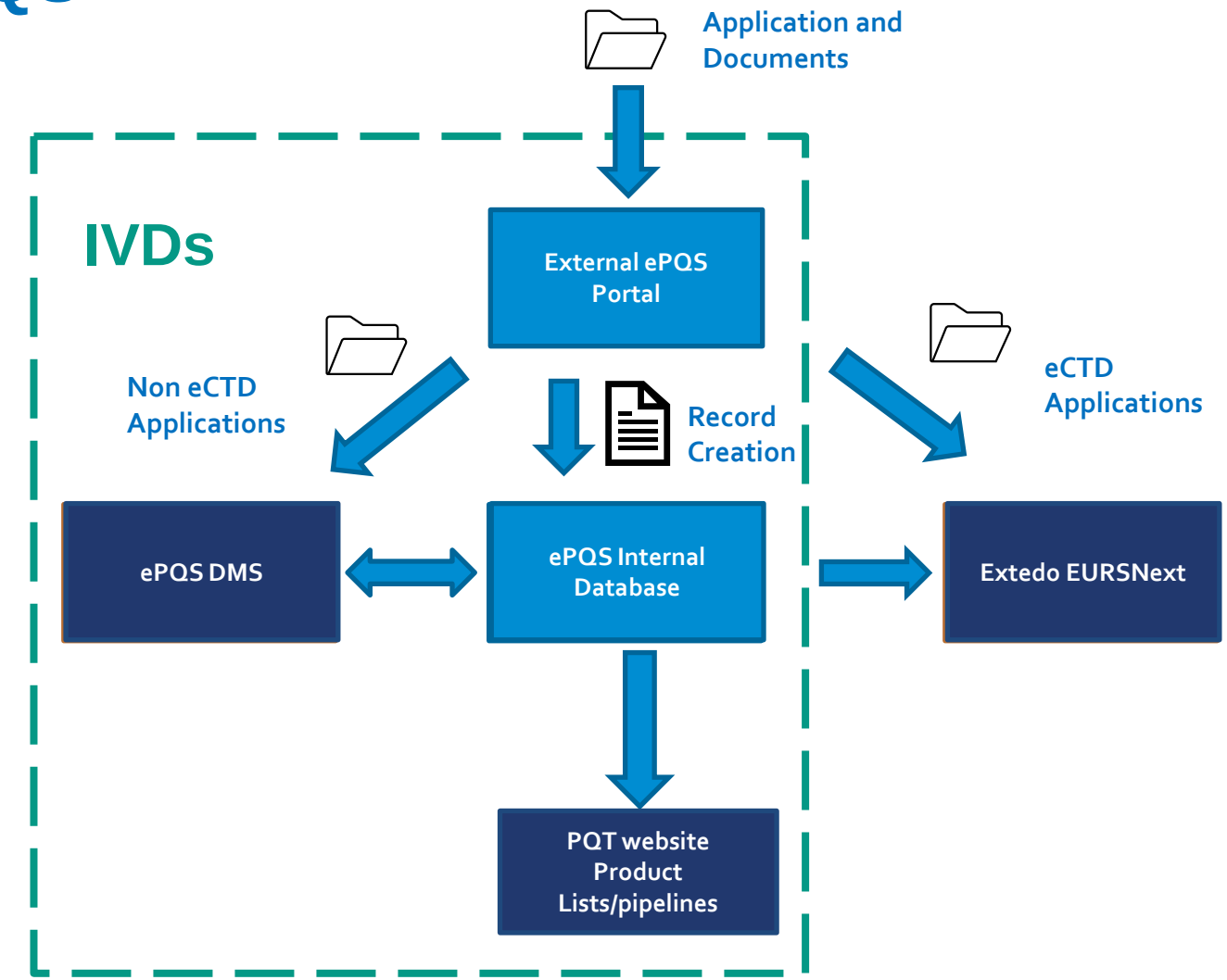
Updates

- 5 PQ’d products (2 HIV NAT, 1 HCV NAT and 2 HCV NAT).
- 29 Public reports were amended due to approved post PQ changes.
- Update: Labelling review to occur at the same time with dossier review to shorten the time lines.

ePQS

Helena Ardura

ePQS


Application and Documents
IVDs
External ePQS Portal
Non eCTD Applications
Record Creation
eCTD Applications
ePQS DMS
ePQS Internal Database
Extedo EURSNext
PQT website Product Lists/pipelines

Current implementation status

- ✓ All PQ streams are now using ePQS.
- ✓ Web Publishing: WPEL, PQ, EUL lists and pipelines are now coming from ePQS.
- ✓ The DMS is being finalized and document migration will follow
- ✓ Document migration last milestone after which all teams will be working exclusively in ePQS.
- ✓ Portal opening to follow.

Opening of the ePQS Portal

Registration for Portal access will open early 2024.

Please continue to check the new ePQS Portal page on the PQT website:
ePQS Portal | WHO - Prequalification of Medical Products (IVDs, Medicines, Vaccines and Immunization Devices, Vector Control)

Guidance information will continue to be added to this page.

Webinars and clinics for users are planned as the portal opens to assist applicants.

World Health Organization | Prequalification of Medical Products
IVDs, Medicines, Vaccines and Immunization Devices, Vector Control

https://extranet.who.int/prequal/epqs-portal

World Health Organization

Contact us | Glossary and Acronyms | FAQ | Complain

Product Streams | Events | News | ePQS | About

ePQS Portal

The **ePQS Portal** is the externally-facing Salesforce Community site of the WHO Prequalification Unit's new ePQS system. ePQS is a platform for the processing of Prequalification Information for medicines, diagnostics, vector control products, vaccines, immunization devices, quality control laboratories and inspections.

Within the portal, users will have the ability to:

- View Salesforce records relevant to the user
- Submit applications
- Upload and download documents securely
- View and monitor notifications for pending activities

Registered users will be able to access the Portal at this link: https://who.my.site.com/ePQS/s/login/

Guidance notes related to the features of the portal, processes around applications, document submissions, and many other topics will be progressively posted to this

Contacts & Accounts

- In the portal, access to records will be based upon the user's relationship to an Organization (Account).
  - *e.g., users belonging to 'Alpha Biotech Co.', will only be able to see 'Alpha Biotech Co.' records.*
- Contact to Account relationship will determine record access.
- As part of the registration process, the manufacturer will have to select 2 official contacts for the account they belong to.
- Please check portal webpage for more information.
  https://extranet.who.int/prequal/epqs-portal

Q&A

11:30 – 13:00

PQ-IVD Technical specifications series: UPDATE

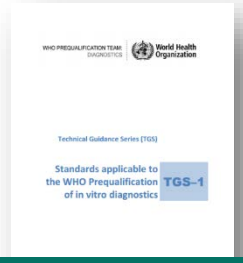
Deirdre Healy & Dr Ute Ströher
28 November 2023

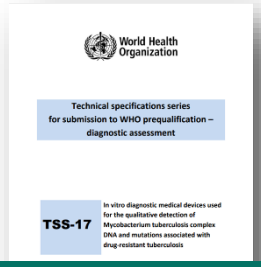
Outline

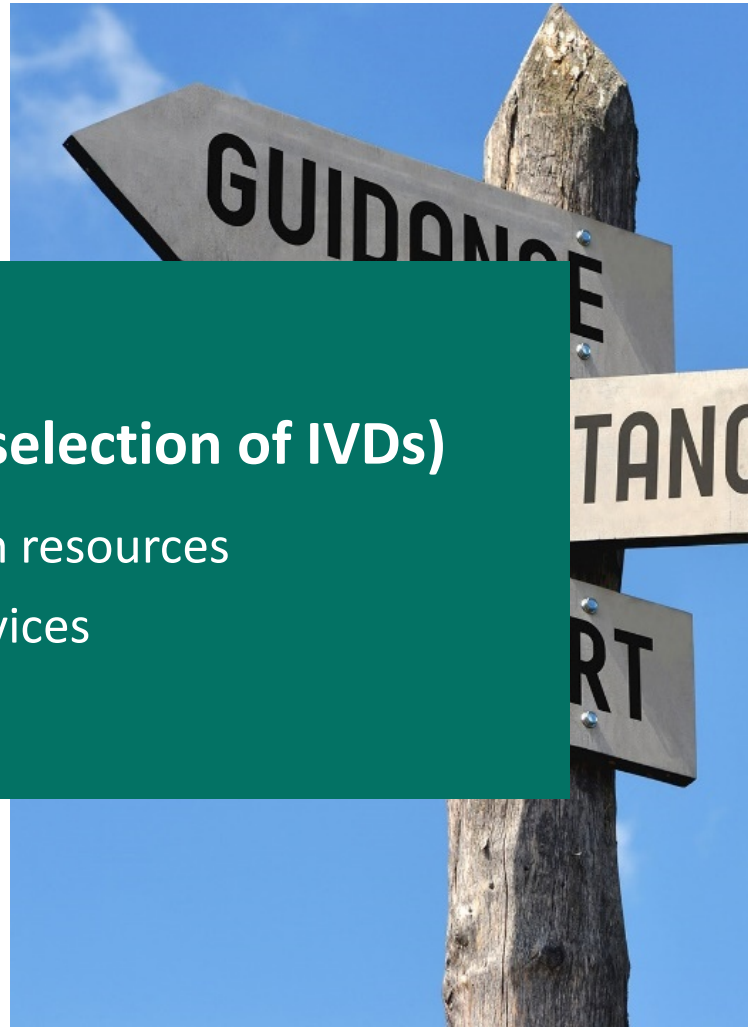
- Overview of PQ-IVD technical specifications series (TSS) documents published in 2023
- PQ-IVD TSS in development
- PQ-IVD TSS under revision
- PQ-IVD TSS planned for 2024/2025

PQ IVD Guidance documents

https://extranet.who.int/prequal/vitro-diagnostics/guidance-documents







Techr

- App
- Foc
  Me
- Each TGS provides detailed guidance on a specific aspect related to IVD performance

↔ WHO Procurement and technical specifications (for selection of IVDs)

- facilitate the management of financial, infrastructural and human resources
- provide guidelines in procurement and acquisition of medical devices

of infections, conditions, etc.

- Requirements that address needs of Member States incl resource limited settings

PQ-IVD TSS published in 2023

PQ-IVD Technical specifications published in 2023

***TSS-18**

HbA1c point of care analysers for professional use

TSS-19

IVD medical devices for monitoring of blood glucose in capillary blood

TSS-20

IVD medical devices used for the qualitative detection of SARS-CoV-2 nucleic acid

TSS-21

SARS-CoV-2 antigen rapid diagnostic tests for professional use and self-testing

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*** December 2023**

https://extranet.who.int/prequal/vitro-diagnostics/technical-specifications-serieshttps://extranet.who.int/prequal/vitro-diagnostics/technical-specifications-series

TSS-18 HbA1c POC analysers & TSS-19 BGMS

- Expansion of PQ: non-communicable diseases (NCD), risk class C
- TSS-18 & 19 public comment period (Feb-Apr):
  62 comments received for TSS-18, 21 comments for TSS-19 (regulators, industry, labs, ISO)

TSS-18	TSS-19
professional use	self-testing, lay user, professional use
	aligned with ISO 15197
	& PQ requirements critical for LMIC
monitoring patients with DM, as an aid to diagnosis of type 2 DM	monitoring diabetes, aid in monitoring BG levels in people with diabetes, monitoring people with conditions that may result in hypo- or hyperglycaemia
capillary blood, venous blood	finger stick capillary blood

TSS-20 & 21: SARS-CoV-2 IVDs

- Published as part of transition from EUL to PQ
- Emergency Use Listing (EUL) is an extraordinary process intended to provide guidance to interested UN procurement agencies and NRAs of WHO Member States on IVD **quality, safety and performance**
- End of the PHEIC (May 5, 2023) triggered:
  - No new EUL submissions accepted
  - Cancellation of ongoing assessments (unless close to completion)
  - Start of transition phase (EUL → PQ)

- Q&A document available:

  https://extranet.who.int/pqweb/sites/default/files/documents/IVD_Transitioning_FAQ_V2.pdf

Transition from EUL → PQ

- EUL listed IVDs will remain eligible for procurement until **31 Jan 2024**, provided that the manufacturer adheres to post-listing obligations
  - commitments, change notifications, PMS
  - for products transitioning to PQ the EUL listing validity will be maintained until a PQ decision is taken
- For products **not** undergoing PQ assessment, the EUL listing validity will not be extended beyond Jan 31, 2024
- To remain eligible for procurement manufacturers of EUL listed IVDs will have until **31 Dec 2023** to apply for PQ assessment (PQ pre-submission form)
- Technical Specifications TSS-20 & TSS-21 have been published
  - SARS-CoV-2 IVDs (NAT & Ag RDTs) are now eligible for WHO PQ

Scope of TSS-20

World Health Organization

Technical specifications series for submission to WHO prequalification – diagnostic assessment

TSS-20 In vitro diagnostic medical devices used for the qualitative detection of SARS-CoV-2 nucleic acid

- multiplex (dual or triple viral target) NAT for the qualitative detection of SARS-CoV-2 nucleic acid
- internal control
- POC and lab based
- lab professionals and trained HC workers
- open and closed systems

! For **open platform NATs** which claim multiple kits/instrumentation for NA extraction and/or amplification: additional requirements may apply

- symptomatic subjects (& asymptomatic)
- specimen type: NPS, OPS, ANS, MTS (sputum)

Scope of TSS-21

World Health Organization

Technical specifications series

for submission to WHO prequalification – diagnostic assessment

TSS-21 SARS-CoV-2 antigen rapid diagnostic tests for professional use and self-testing

- Rapid Immunochromatographic test, Lateral flow test
- Qualitative detection of SARS-CoV-2 antigen (typically N)
- POC or self-test
- Symptomatic subjects
- NPS, OPS, ANS, MTS
- With or without reader
- Swabs must be provided with the test kit
- Controls recommended, but optional (can be sold separately)

PQ-IVD TSS in development

TSS-22 Haemoglobin point of care analysers

- Expansion of PQ: non-communicable diseases (NCD), risk class B
- Technical consultation (Apr 2021 → June 2023): 18 experts
- Public comment period: planned Q1 2024

Intended Use
professional use
screening for anaemia, monitoring of haemoglobin levels
diagnosis of anaemia/aid in the diagnosis of anaemia
capillary blood, venous blood

TSS-23: RDTs to detect mycobacterial lipoarabinomannan (LAM) antigen

- Technical consultation (Jan 2024): approx. 15 experts
- Public comment period: planned Q1 2024

Intended Use (based on GTB Policy update on LF LAM, 2019)
professional use
aid in the diagnosis of TB in individuals with signs and symptoms of TB (pulmonary or extrapulmonary)
HIV positive with CD4 count < 100cells/µL or seriously ill
urine

PQ-IVD TSS under revision

TSS-3: Malaria rapid diagnostic tests, 2nd edition

- Technical consultation: June 2023
- Public comment period: planned Q1 2024

Scope of the revision:

- Format changes → align with IMDRF ToC chapter numbering
- Availability of WHO International Standard for Pf & Pv (analytical studies)
- Clinical evidence to support claim for the detection of parasites with HRP2/3 deletions (applicable to all IVDs that detect Pf non-HRP antigens, e.g. LDH)

TSS-3, 2nd edition: Analytical Studies

- Limit of Detection (LOD) reported in IU/µL
  - First WHO International Standard for Plasmodium falciparum antigens NIBSC code: 16/376
  - First WHO International Standard for Plasmodium vivax antigen (LDH) NIBSC code: 19/116
- RDTs with a claim for “pan-specific” detection of Plasmodium species
  - LOD estimated with WHO IS **and** PF parasites with HRP2/3 deletions
- Metrological traceability
- Validation of control line
- High dose hook effect
- Qualification of usability

TSS-3, 2nd edition: Clinical studies

- For IVDs detecting non-HRP antigen (independent of a claim to detect HRP2/3 deletion mutants):
  - Supporting clinical evidence must be provided with HRP2/3 deletion specimens (prospective study)
  - Testing algorithm to establish reference result: **microscopy** and PCR (differentiation of species)

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PQ-IVD TSS planned for 2024/2025

unicef | UNFPA | World Health Organization

PRE PANDEMIC

WHO Prequalification of In Vitro Diagnostics Update

Issue 28
Q4 2019

IN THIS ISSUE:

1. PREQUALIFIED IVDs
2. EXPANSION OF THE PREQUALIFICATION OF IN VITRO DIAGNOSTICS SCOPE

2020: Haemoglobin (point of care) and glucose meters and test strips **& HbA1C POC**

2021: Tuberculosis, yellow fever, dengue fever, gonorrhoea and chlamydia **TB-LAM (consultation Jan 2024) & tNGS (TB-DR)**

2022: Measles, rubella, leishmaniasis and schistosomiasis **NTD (Leishmaniasis & Filariasis) ERPD**

2023: Mycoplasma genitalium and onchocerciasis

Planned TSS (new & revisions)

- TSS-4: In vitro diagnostic medical devices used for the detection of high-risk human papillomavirus (HPV) types in cervical cancer screening (mRNA, self-collection)
- TSS-6: Syphilis rapid diagnostic tests (self-testing)
- Open platform molecular tests (bridging studies)
- Sexually transmitted infections
    - TSS: Neisseria gonorrhoeae POC
    - TSS: Chlamydia trachomatis POC
- Tuberculosis
    - TSS: TB next-generation sequencing technologies for the detection of mutations associated with drug resistance in Mycobacterium tuberculosis complex

Changes to prequalified and EUL-listed IVD products

Helena Ardura & Fatima Gruszka
In Vitro Diagnostics Assessment Team
Prequalification Unit

Content

- PQ of IVDs: aim & scope
- PQ assessment components
- PQ assessment requirements
- PQ decision
- Post-PQ activities
- Reporting changes to PQ
- Examples of reportable changes
- WHO guidance documents
- PQDx Public Report
- CR reports

PQ of IVDs: aim & scope

The aim of PQDx is to promote and facilitate access to safe, appropriate and affordable IVDs of good quality.

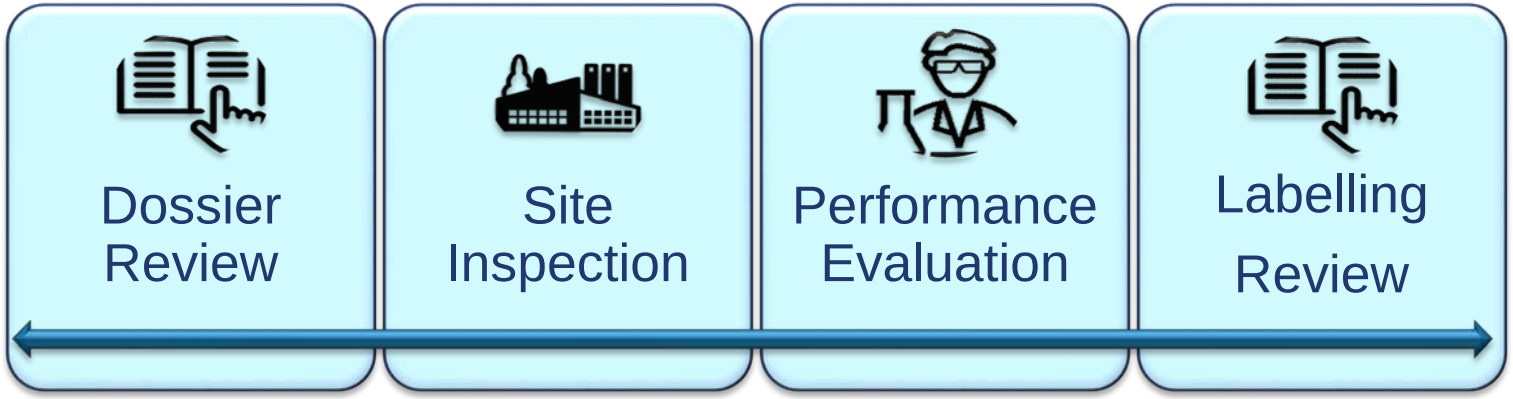
Focus is placed on IVDs for priority diseases and their suitability for use in resource-limited settings.

- Cholera
- G6PD
- Hepatitis B
- Hepatitis C
- HIV
- HPV
- Malaria
- SARS-CoV-2
- Syphilis
- Tuberculosis

PQ assessment components

- A comprehensive assessment of an IVD through a standardized procedure aimed at determining if the product meets WHO prequalification requirements.

- The prequalification assessment process components:



PQ assessment requirements

- To meet the Essential Principles of Safety and Performance of Medical Devices and IVD Medical Devices (GHTF/SG1/N41:2005) and to maintain this compliance throughout their entire lifecycle. Reassessment of the compliance to these essential principles is done through reviewing the changes made to the product.

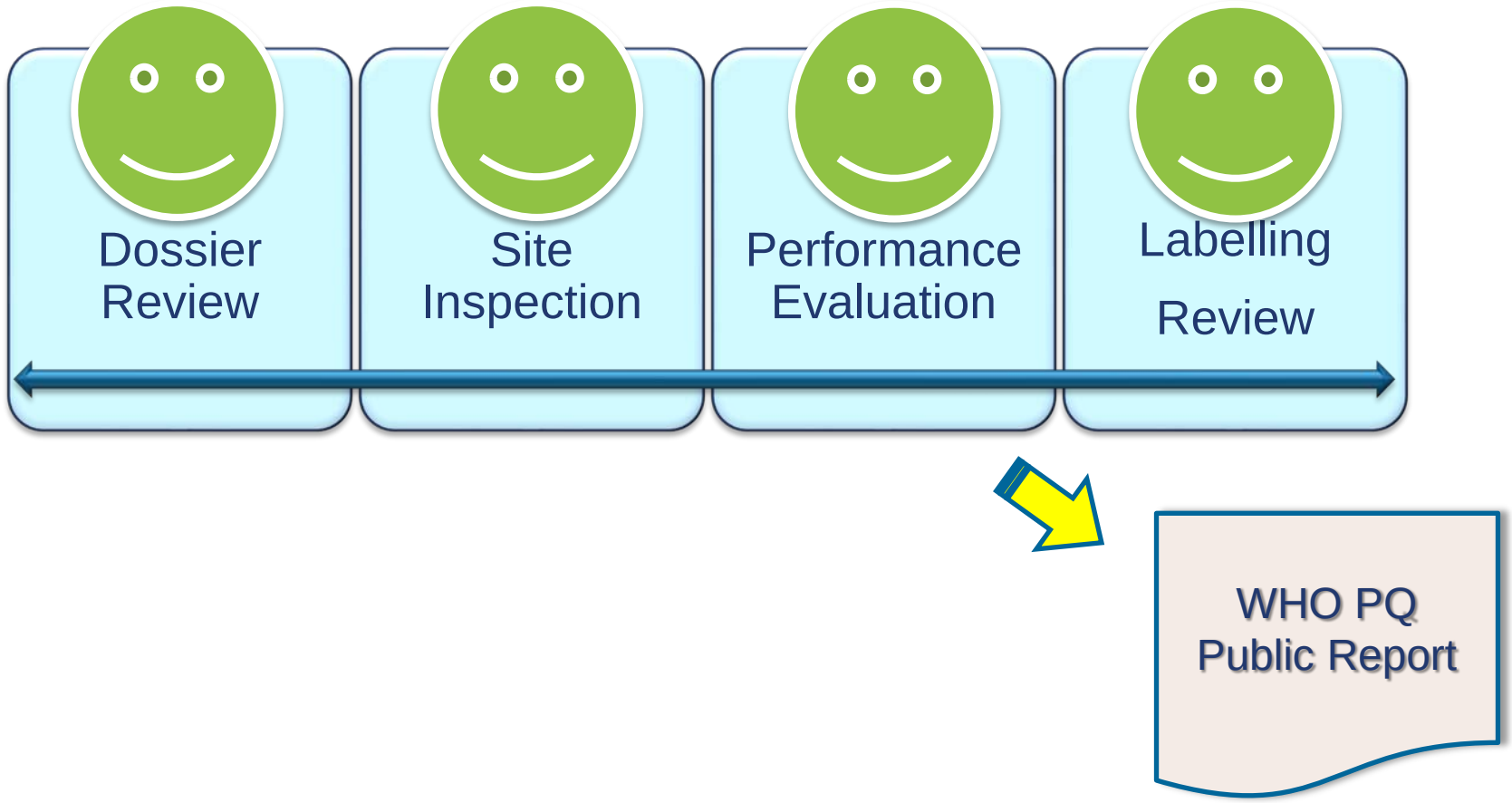
  e.g. 1st essential principle:

5.1.1 Medical devices and IVD medical devices should achieve the performance intended by their manufacturer and should be designed and manufactured in such a way that, during intended conditions of use, they are suitable for their intended purpose. They should be safe and perform as intended, should have risks that are acceptable when weighed against the benefits to the patient, and should not compromise the clinical condition or the safety of patients, or the safety and health of users or, where applicable, other persons.

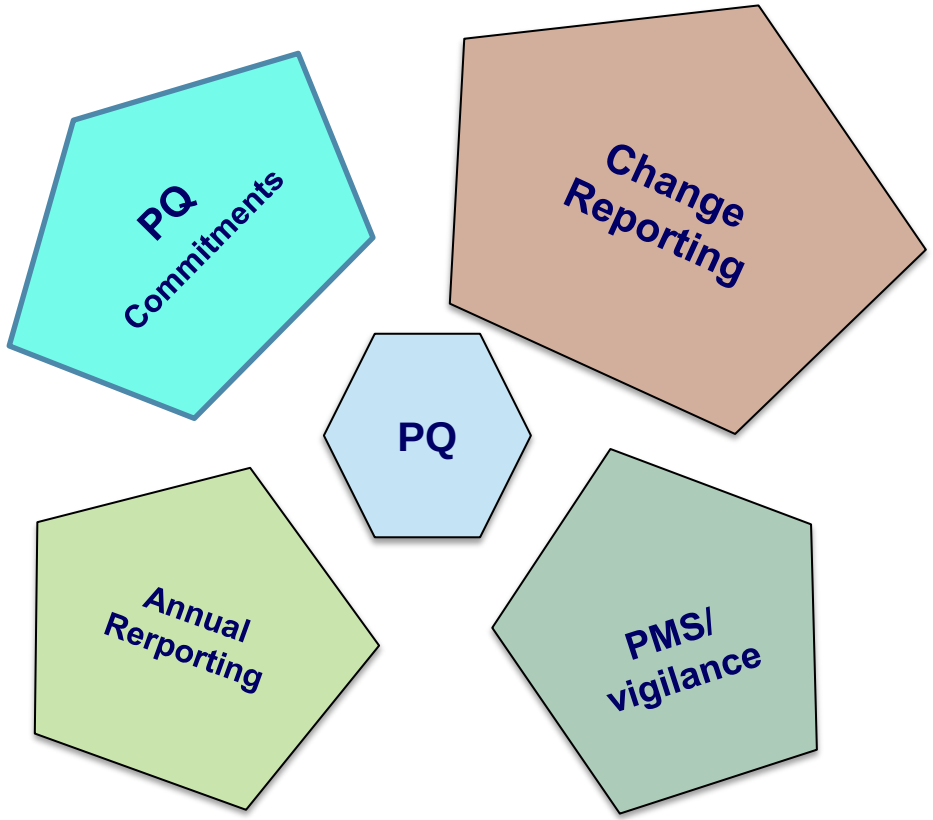
PQ assessment requirements

- To meet relevant WHO TSS requirements to the analyte & assay type
- To present evidence of a fully implemented quality management system based on International Standards:
  - IVD design & manufacture meets ISO 13485
  - Risk management meets ISO 14971
- To pass laboratory evaluation
- Labelling in agreement with international standards & PQ

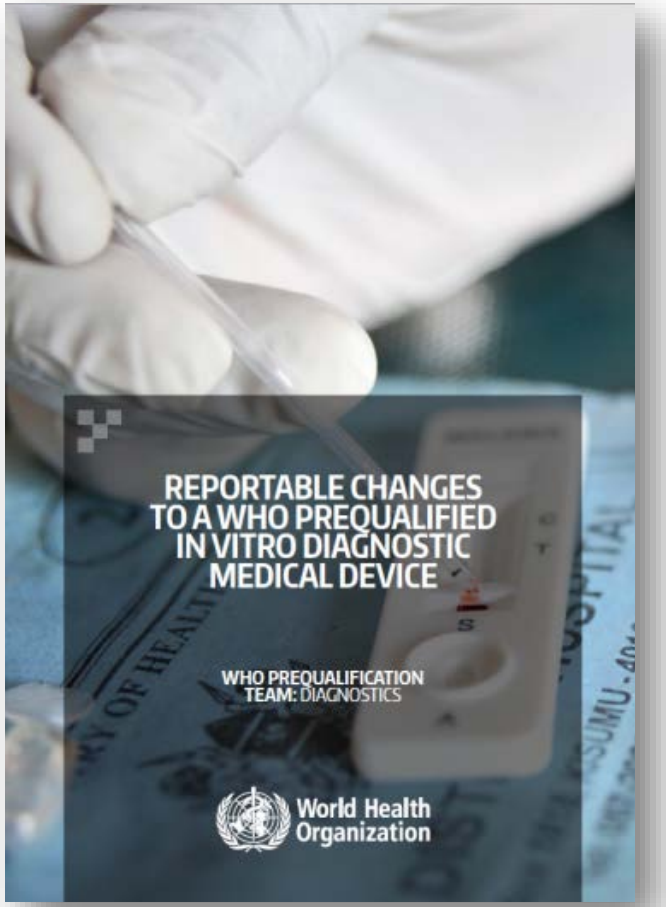
PQ assessment components



Post-Prequalification Activities
Maintenance of PQ status



Reporting changes to PQ

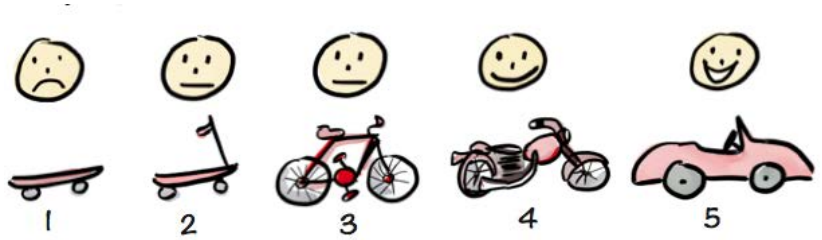


Notification and submission of planned changes to prequalified IVDs relating to:

- Product (e.g. materials used)
- Manufacturing
- QMS

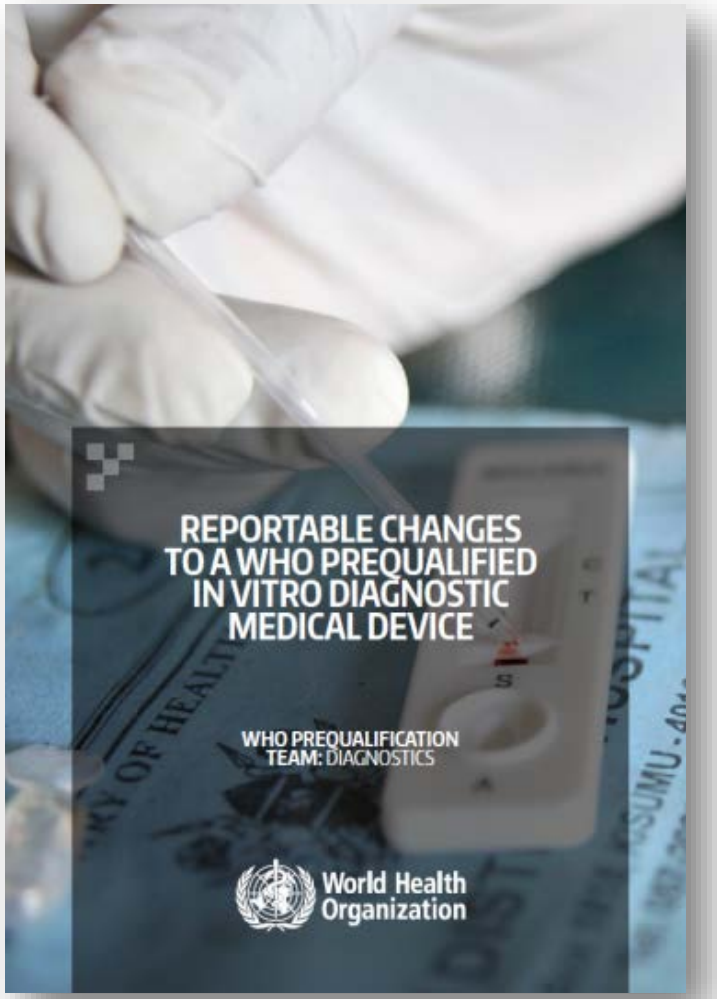
Changes reported to WHO

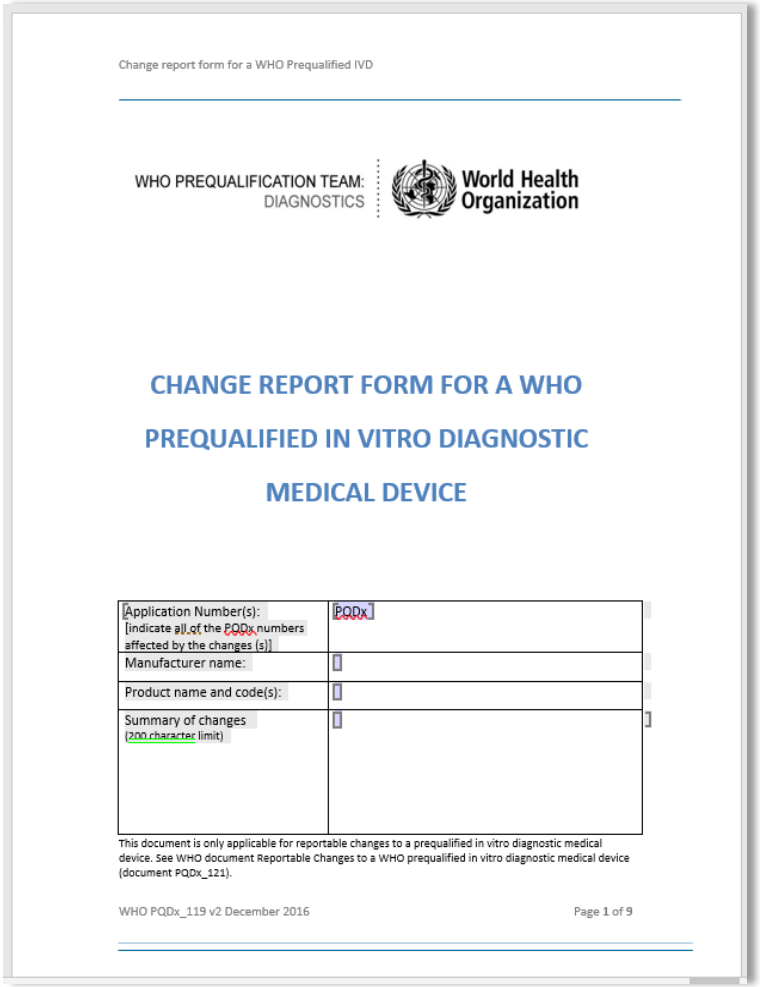
Year	PQ	EUL
2016*	33	N/A
2017	39	N/A
2018	50	N/A
2019	53	N/A
2020	60	13
2021	76	23
2022	59	14
2023	83	7



Reporting changes to PQ

Guidance document





Change report form for a WHO Prequalified IVD

WHO PREQUALIFICATION TEAM: DIAGNOSTICS

World Health Organization

CHANGE REPORT FORM FOR A WHO PREQUALIFIED IN VITRO DIAGNOSTIC MEDICAL DEVICE

[Application Number(s): [indicate all of the PQDx numbers affected by the changes (s)]	PQDx
Manufacturer name:	
Product name and code(s):	
Summary of changes (200 character limit)	

This document is only applicable for reportable changes to a prequalified in vitro diagnostic medical device. See WHO document Reportable Changes to a WHO prequalified in vitro diagnostic medical device (document PQDx_121).

WHO PQDx_119 v2 December 2016 Page 1 of 9

https://extranet.who.int/prequal/vitro-diagnostics/changes-prequalified-ivds

Overview of change reporting procedure

1. Manufacturer submits Change Report Form along with supporting evidence

2. PQDx coordinates the selection of independent reviewer qualified for the specific review (evidence + template report)

3. Reviewers produce an assessment report with recommendations for PQDx

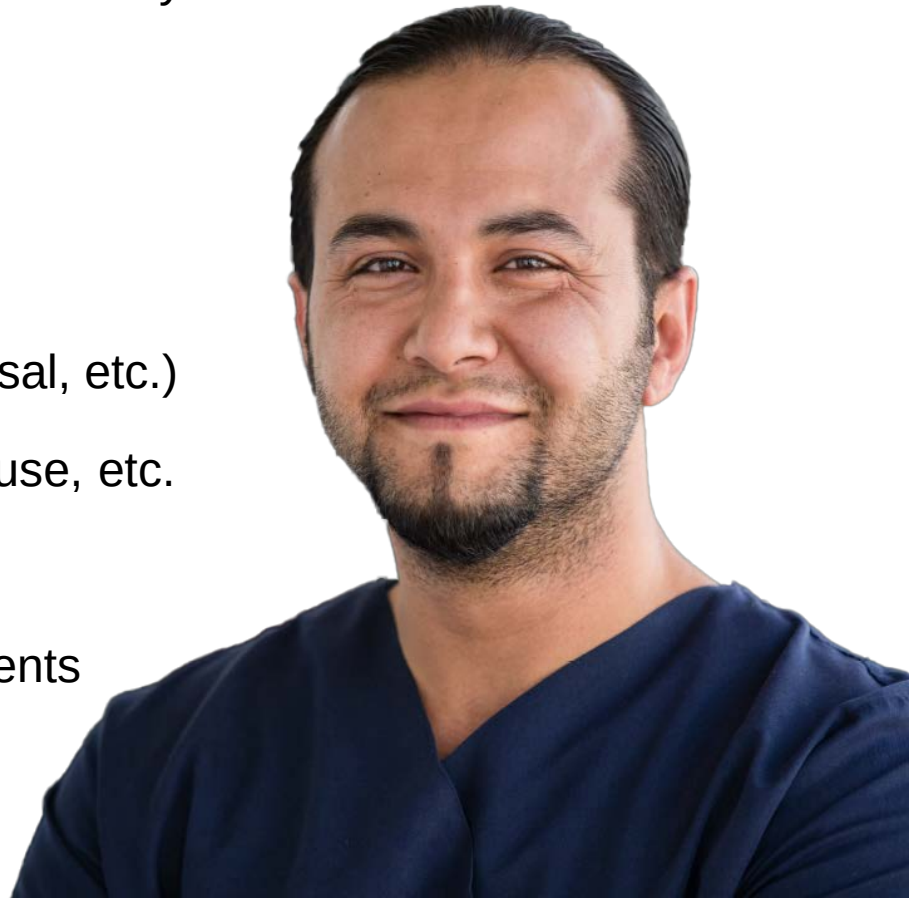
4. PQDx team sends a decision letter to the manufacturer based on the conclusions of the reviewer and available evidence on whether the change request is accepted, rejected, additional information is required, or a new PQ application is needed.

Change assessment target timelines

Assessment stage	Maximum time allowed (calendar days) in which to provide a response	
	WHO	Manufacturer
Change notification screening	30	N/A
Submission of additional data	N/A	30
Screening of additional information	30	N/A
Change assessment	60	N/A
Submission of additional information	N/A	Up to 6 months
Review of additional information and acceptance decision		N/A

Examples of reportable changes

- New certification or change of certification body for ISO 13485
- **Change of registration to EU IVDR**
- Shelf-life extension
- Addition of intended use (self-testing)
- Addition of a new specimen (saliva, nasal, etc.)
- Addition of manufacturing site, warehouse, etc.
- Automation of production line
- Introduction of new equipment/instruments



Examples of reportable changes

- Add a new supplier of materials/components:
  - Change to the specimen transfer device (i.e. loops to inverted cups).
  - Change of blood lancets, from simple steel sterile lancets to safety lancets.

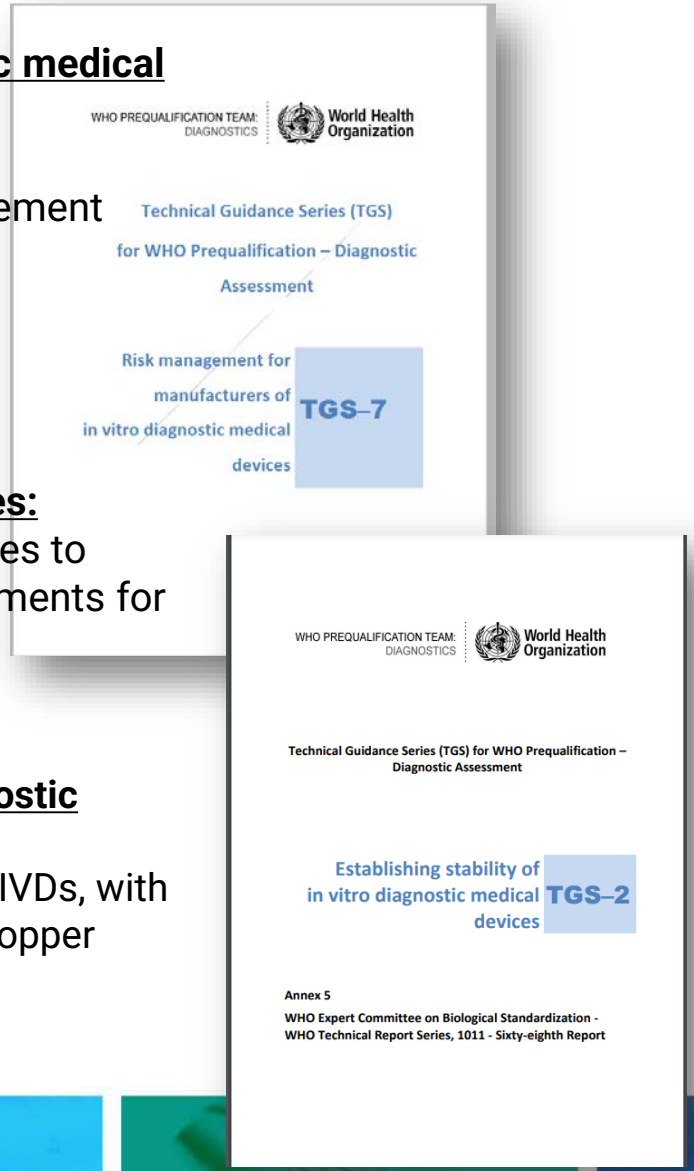
- Changes to the IFU and labels:
  - Labelling update to reflect the new manufacturer name and/or address.
  - Rebranding, change of name of the product.
  - Addition of label elements in preparation for IVDR.
  - Correction of typographical errors.

Other WHO guidance documents: TGS & TSS

TGS 7 Risk management for manufacturers of in vitro diagnostic medical devices:
Guidance to help manufacturers of IVDs develop appropriate risk management within their quality management system before compiling a product dossier for submission to WHO and in preparation for site inspection as part of WHO prequalification assessment.

TGS 2 Establishing stability of in vitro diagnostic medical devices:
Provides IVD manufacturers with guidance on possible approaches to determining stability and describes WHO prequalification requirements for stability testing.

Annex to TGS 2 Establishing component stability for in vitro diagnostic medical devices:
Recommendations for establishing the stability of components for IVDs, with examples on the change from establishing stability for multi-use dropper bottles to establishing stability for single-use vials.



Other WHO guidance documents: TGS & TSS

TSS 1 - Human immunodeficiency virus (HIV) rapid diagnostic tests for professional and/or self-testing

TSS 2 - In vitro diagnostic medical devices to identify glucose-6-phosphate dehydrogenase (G6PD) activity

TSS 3 - Malaria rapid diagnostic tests

TSS 4 - In vitro diagnostic medical devices used for the detection of high-risk human papillomavirus (HPV) types in cervical cancer screening

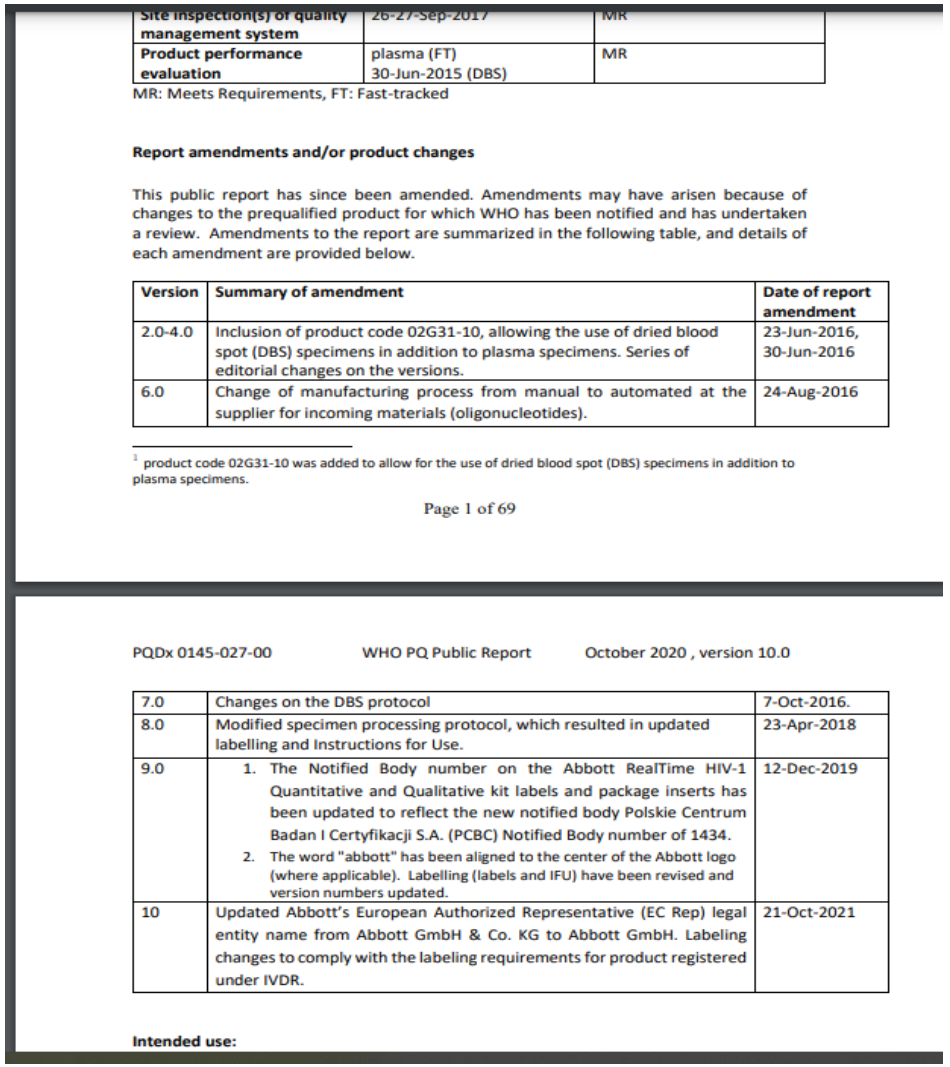
TSS 5 - Rapid diagnostic tests used for surveillance and detection of an outbreak of cholera…

…TSS 21

PQDx Public Report

WHO PQDx Public Report is updated to reflect any changes due to the change request.

<u>Product is/remains eligible for WHO and UN procurement</u>



Site inspection(s) of quality management system	26-27-Sep-2017	MR
Product performance evaluation	plasma (FT) 30-Jun-2015 (DBS)	MR

MR: Meets Requirements, FT: Fast-tracked

Report amendments and/or product changes

This public report has since been amended. Amendments may have arisen because of changes to the prequalified product for which WHO has been notified and has undertaken a review. Amendments to the report are summarized in the following table, and details of each amendment are provided below.

Version	Summary of amendment	Date of report amendment
2.0-4.0	Inclusion of product code 02G31-10, allowing the use of dried blood spot (DBS) specimens in addition to plasma specimens. Series of editorial changes on the versions.	23-Jun-2016, 30-Jun-2016
6.0	Change of manufacturing process from manual to automated at the supplier for incoming materials (oligonucleotides).	24-Aug-2016

[1] product code 02G31-10 was added to allow for the use of dried blood spot (DBS) specimens in addition to plasma specimens.

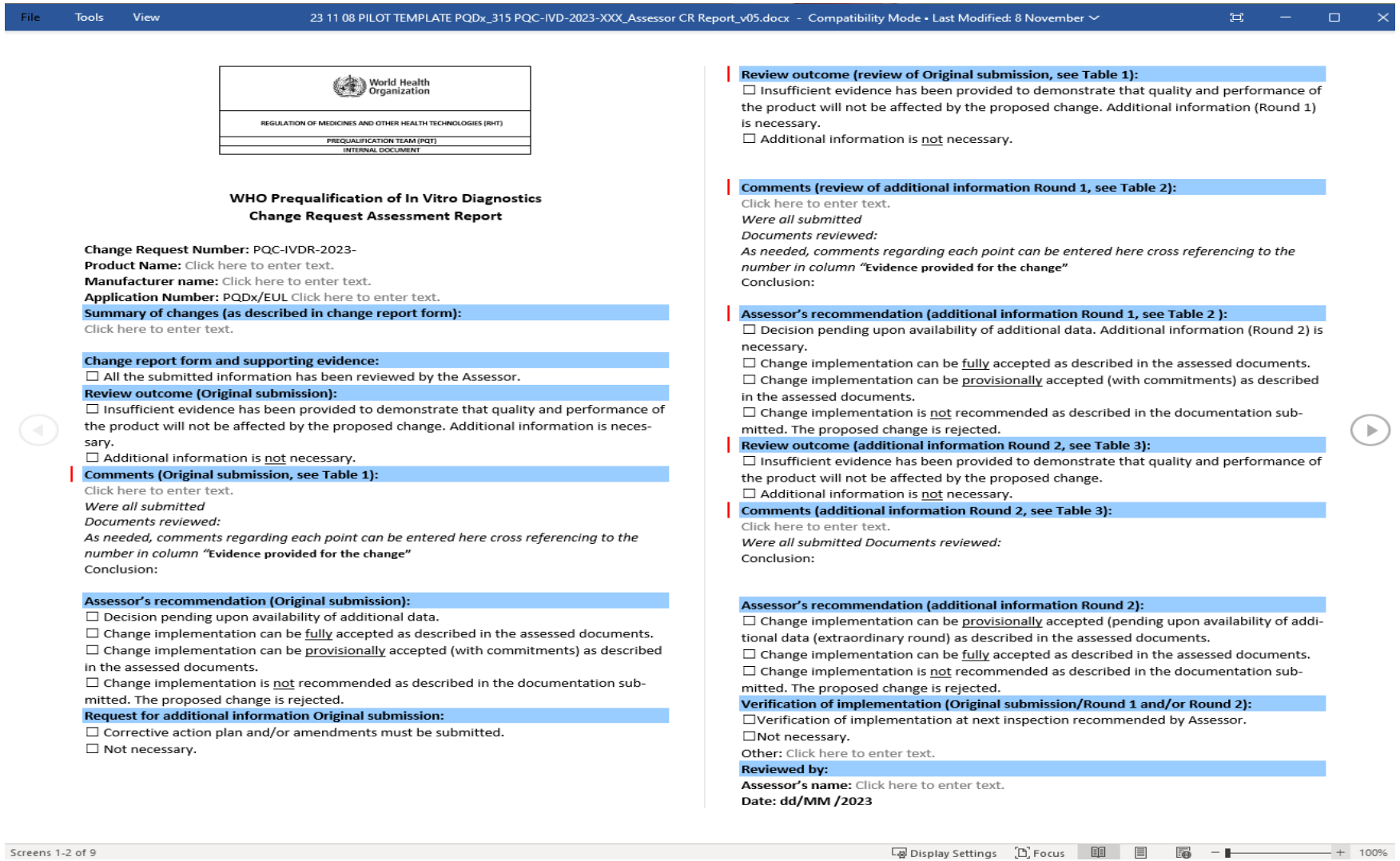
Page 1 of 69

PQDx 0145-027-00 WHO PQ Public Report October 2020 , version 10.0

7.0	Changes on the DBS protocol	7-Oct-2016.
8.0	Modified specimen processing protocol, which resulted in updated labelling and Instructions for Use.	23-Apr-2018
9.0	1. The Notified Body number on the Abbott RealTime HIV-1 Quantitative and Qualitative kit labels and package inserts has been updated to reflect the new notified body Polskie Centrum Badan I Certyfikacji S.A. (PCBC) Notified Body number of 1434. 2. The word "abbott" has been aligned to the center of the Abbott logo (where applicable). Labelling (labels and IFU) have been revised and version numbers updated.	12-Dec-2019
10	Updated Abbott's European Authorized Representative (EC Rep) legal entity name from Abbott GmbH & Co. KG to Abbott GmbH. Labeling changes to comply with the labeling requirements for product registered under IVDR.	21-Oct-2021

Intended use:

Assessment report template



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World Health Organization

REGULATION OF MEDICINES AND OTHER HEALTH TECHNOLOGIES (RHT)

PREQUALIFICATION TEAM (PQT)

INTERNAL DOCUMENT

WHO Prequalification of In Vitro Diagnostics
Change Request Assessment Report

Change Request Number: PQC-IVDR-2023-
Product Name: Click here to enter text.
Manufacturer name: Click here to enter text.
Application Number: PQDx/EUL Click here to enter text.

Summary of changes (as described in change report form):
Click here to enter text.

Change report form and supporting evidence:
☐ All the submitted information has been reviewed by the Assessor.

Review outcome (Original submission):
☐ Insufficient evidence has been provided to demonstrate that quality and performance of the product will not be affected by the proposed change. Additional information is necessary.
☐ Additional information is not necessary.

Comments (Original submission, see Table 1):
Click here to enter text.
Were all submitted
Documents reviewed:
*As needed, comments regarding each point can be entered here cross referencing to the number in column "**Evidence provided for the change**"*
Conclusion:

Assessor's recommendation (Original submission):
☐ Decision pending upon availability of additional data.
☐ Change implementation can be fully accepted as described in the assessed documents.
☐ Change implementation can be provisionally accepted (with commitments) as described in the assessed documents.
☐ Change implementation is not recommended as described in the documentation submitted. The proposed change is rejected.

Request for additional information Original submission:
☐ Corrective action plan and/or amendments must be submitted.
☐ Not necessary.

Review outcome (review of Original submission, see Table 1):
☐ Insufficient evidence has been provided to demonstrate that quality and performance of the product will not be affected by the proposed change. Additional information (Round 1) is necessary.
☐ Additional information is not necessary.

Comments (review of additional information Round 1, see Table 2):
Click here to enter text.
Were all submitted
Documents reviewed:
*As needed, comments regarding each point can be entered here cross referencing to the number in column "**Evidence provided for the change**"*
Conclusion:

Assessor's recommendation (additional information Round 1, see Table 2):
☐ Decision pending upon availability of additional data. Additional information (Round 2) is necessary.
☐ Change implementation can be fully accepted as described in the assessed documents.
☐ Change implementation can be provisionally accepted (with commitments) as described in the assessed documents.
☐ Change implementation is not recommended as described in the documentation submitted. The proposed change is rejected.

Review outcome (additional information Round 2, see Table 3):
☐ Insufficient evidence has been provided to demonstrate that quality and performance of the product will not be affected by the proposed change.
☐ Additional information is not necessary.

Comments (additional information Round 2, see Table 3):
Click here to enter text.
Were all submitted Documents reviewed:
Conclusion:

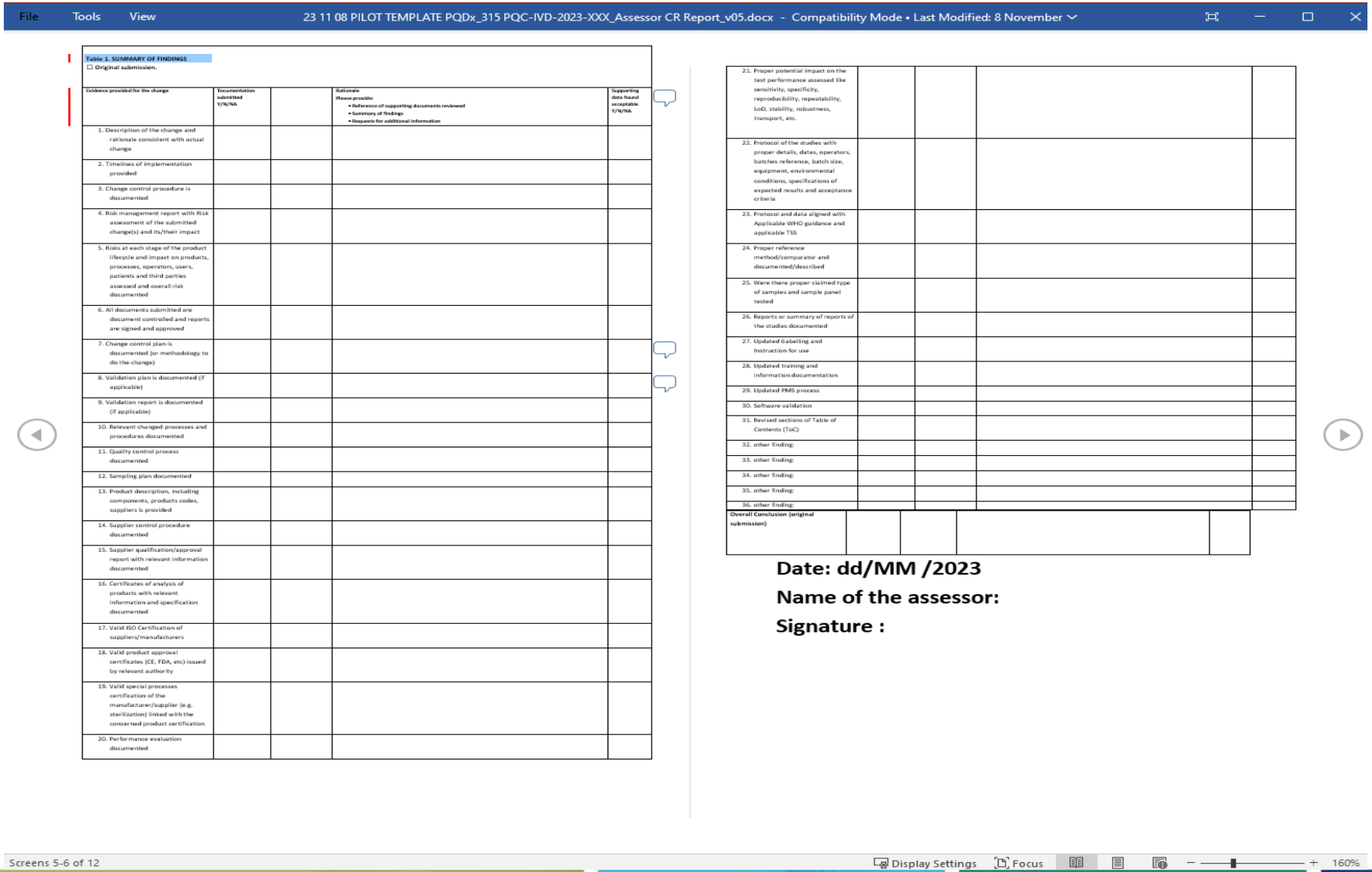
Assessor's recommendation (additional information Round 2):
☐ Change implementation can be provisionally accepted (pending upon availability of additional data (extraordinary round) as described in the assessed documents.
☐ Change implementation can be fully accepted as described in the assessed documents.
☐ Change implementation is not recommended as described in the documentation submitted. The proposed change is rejected.

Verification of implementation (Original submission/Round 1 and/or Round 2):
☐Verification of implementation at next inspection recommended by Assessor.
☐Not necessary.
Other: Click here to enter text.

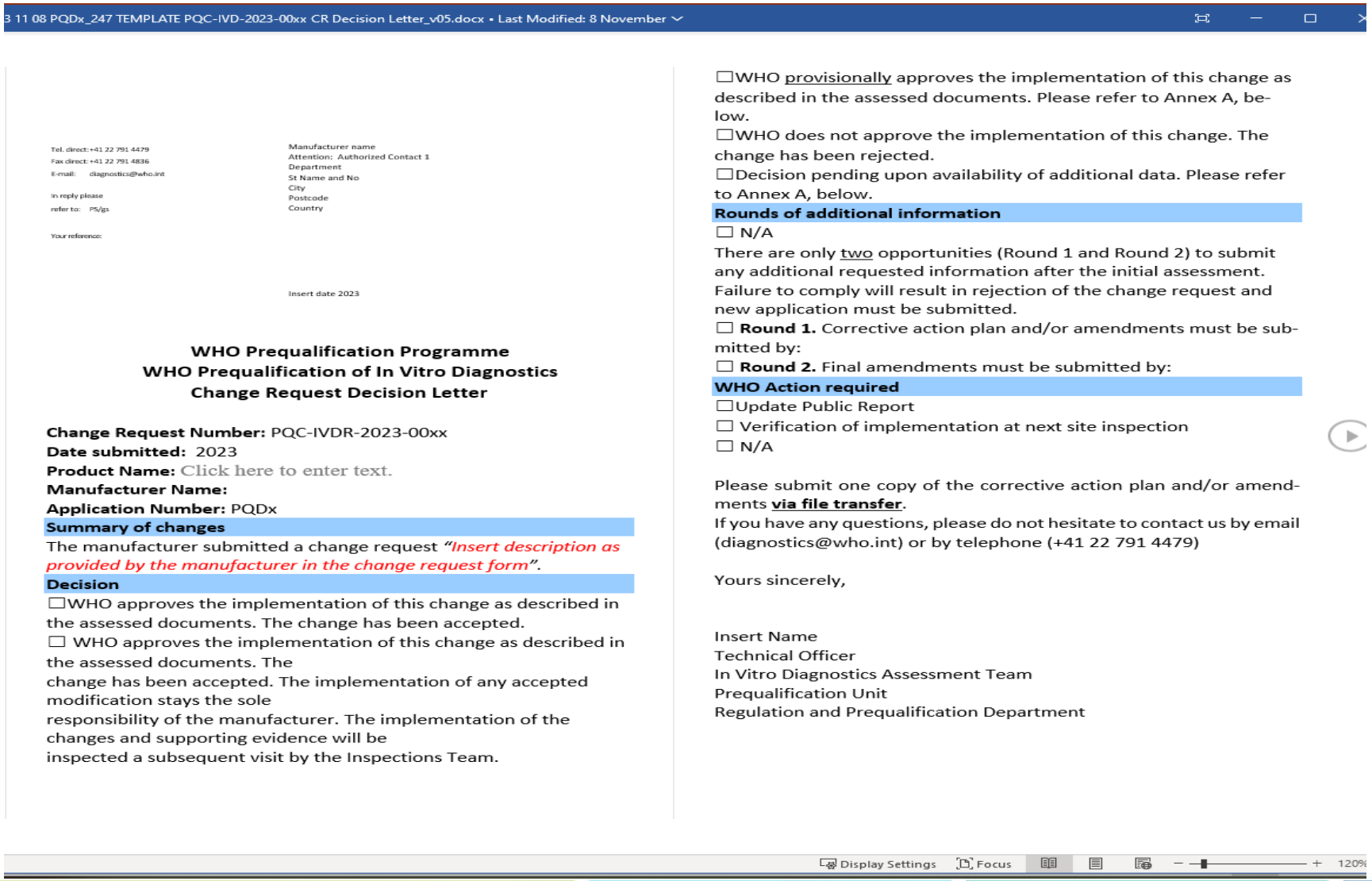
Reviewed by:
Assessor's name: Click here to enter text.
Date: dd/MM /2023

Screens 1-2 of 9 Display Settings Focus 100%

Assessment report template



Decision letter sent to the Manufacturer



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Tel. direct:+41 22 791 4479
Fax direct:+41 22 791 4836
E-mail: diagnostics@who.int

In reply please
refer to: PS/gs

Your reference:

Manufacturer name
Attention: Authorized Contact 1
Department
St Name and No
City
Postcode
Country

Insert date 2023

WHO Prequalification Programme
WHO Prequalification of In Vitro Diagnostics
Change Request Decision Letter

Change Request Number: PQC-IVDR-2023-00xx
Date submitted: 2023
Product Name: Click here to enter text.
Manufacturer Name:
Application Number: PQDx

Summary of changes

The manufacturer submitted a change request *"Insert description as provided by the manufacturer in the change request form"*.

Decision

☐WHO approves the implementation of this change as described in the assessed documents. The change has been accepted.
☐ WHO approves the implementation of this change as described in the assessed documents. The change has been accepted. The implementation of any accepted modification stays the sole responsibility of the manufacturer. The implementation of the changes and supporting evidence will be inspected a subsequent visit by the Inspections Team.
☐WHO provisionally approves the implementation of this change as described in the assessed documents. Please refer to Annex A, below.
☐WHO does not approve the implementation of this change. The change has been rejected.
☐Decision pending upon availability of additional data. Please refer to Annex A, below.

Rounds of additional information

☐ N/A

There are only two opportunities (Round 1 and Round 2) to submit any additional requested information after the initial assessment. Failure to comply will result in rejection of the change request and new application must be submitted.
☐ **Round 1.** Corrective action plan and/or amendments must be submitted by:
☐ **Round 2.** Final amendments must be submitted by:

WHO Action required

☐Update Public Report
☐ Verification of implementation at next site inspection
☐ N/A

Please submit one copy of the corrective action plan and/or amendments **via file transfer**.
If you have any questions, please do not hesitate to contact us by email (diagnostics@who.int) or by telephone (+41 22 791 4479)

Yours sincerely,

Insert Name
Technical Officer
In Vitro Diagnostics Assessment Team
Prequalification Unit
Regulation and Prequalification Department

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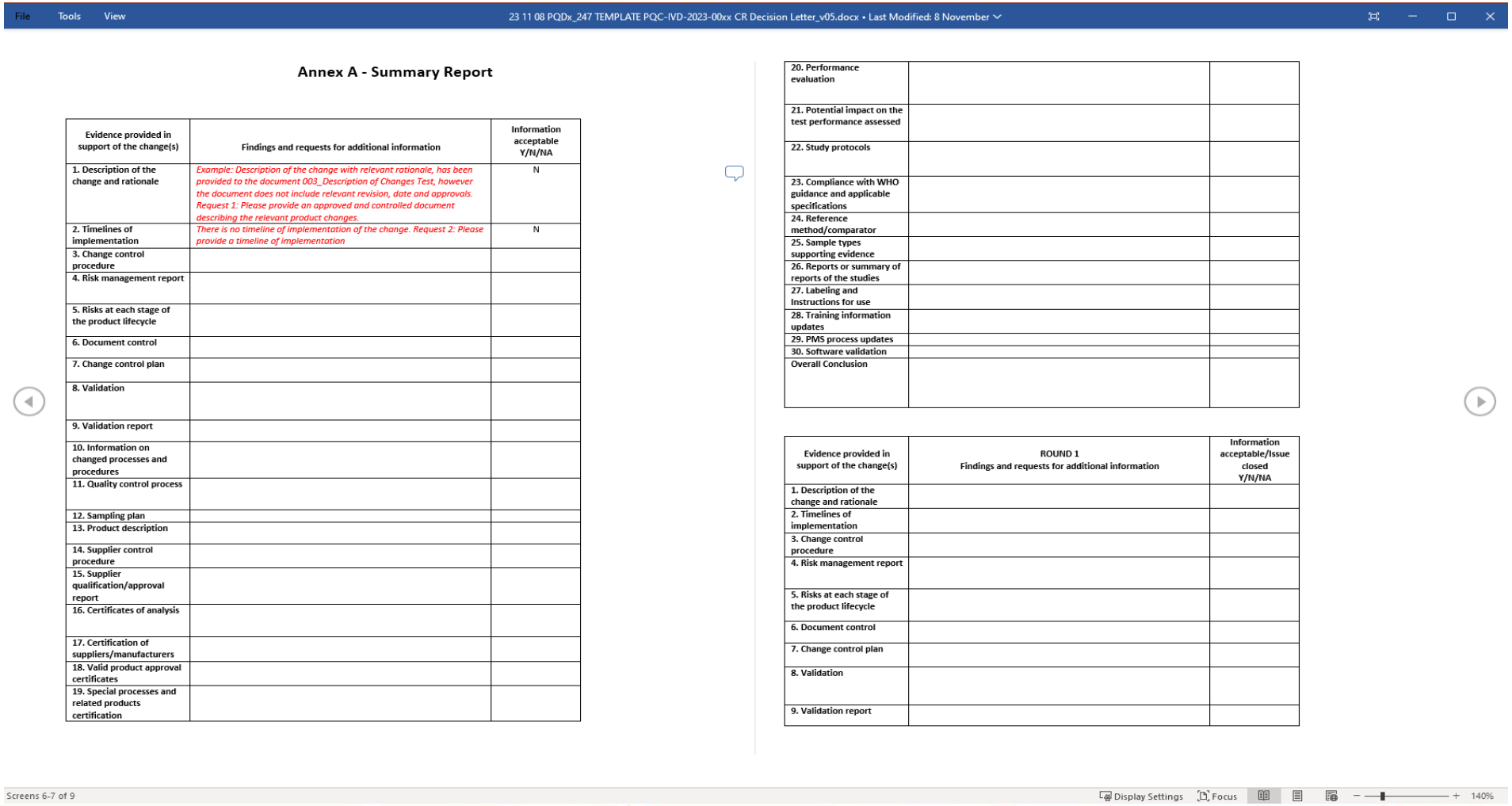
Decision letter sent to the Manufacturer



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Annex A - Summary Report

Evidence provided in support of the change(s)	Findings and requests for additional information	Information acceptable Y/N/NA
1. Description of the change and rationale	*Example: Description of the change with relevant rationale, has been provided to the document 003_Description of Changes Test, however the document does not include relevant revision, date and approvals. Request 1: Please provide an approved and controlled document describing the relevant product changes.*	N
2. Timelines of implementation	*There is no timeline of implementation of the change. Request 2: Please provide a timeline of implementation*	N
3. Change control procedure		
4. Risk management report		
5. Risks at each stage of the product lifecycle		
6. Document control		
7. Change control plan		
8. Validation		
9. Validation report		
10. Information on changed processes and procedures		
11. Quality control process		
12. Sampling plan		
13. Product description		
14. Supplier control procedure		
15. Supplier qualification/approval report		
16. Certificates of analysis		
17. Certification of suppliers/manufacturers		
18. Valid product approval certificates		
19. Special processes and related products certification		
20. Performance evaluation		
21. Potential impact on the test performance assessed		
22. Study protocols		
23. Compliance with WHO guidance and applicable specifications		
24. Reference method/comparator		
25. Sample types supporting evidence		
26. Reports or summary of reports of the studies		
27. Labeling and Instructions for use		
28. Training information updates		
29. PMS process updates		
30. Software validation		
Overall Conclusion		

Evidence provided in support of the change(s)	ROUND 1 Findings and requests for additional information	Information acceptable/Issue closed Y/N/NA
1. Description of the change and rationale		
2. Timelines of implementation		
3. Change control procedure		
4. Risk management report		
5. Risks at each stage of the product lifecycle		
6. Document control		
7. Change control plan		
8. Validation		
9. Validation report		

Screens 6-7 of 9 Display Settings Focus 140%

Collaborative Registration Procedure (CRP) For IVDs

Susie Braniff
PQT-IVD

Overview

- Principles of Reliance
- PQ Reports
- Collaborative Registration procedure
- NRAs participating
- 2023 update
- Support available form PQT

Principles of Reliance

The act whereby an authority in one jurisdiction gives significant weight to assessments performed by another regulatory authority or trusted institution, or to any other authoritative information, in reaching its own decision.

Collaborative Registration Procedure (CRP)

Collaboration between NRA, Manufacturer and WHO

Aims to accelerate country registration of prequalified IVDs through information sharing between WHO PQ and National Regulatory Authorities

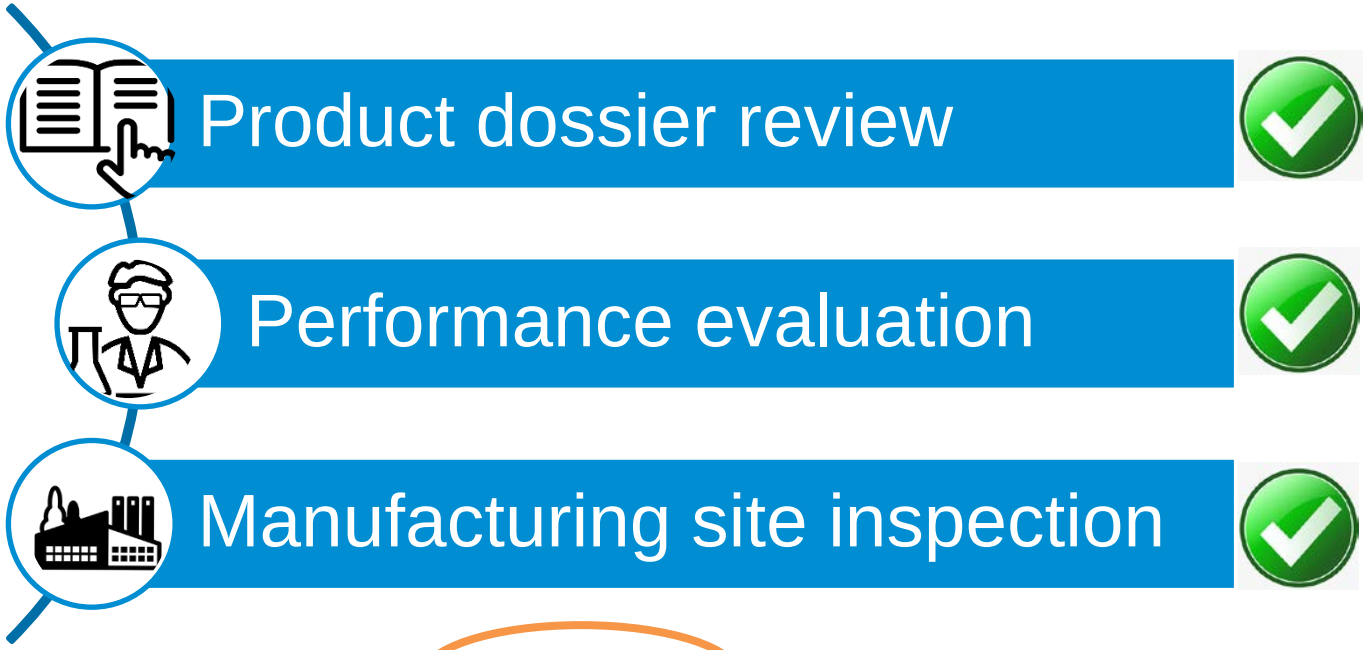
PRINCIPLES

- Voluntary for Mx of prequalified IVDs
- Product sameness must be guaranteed
- Confidentiality of data shared
- Target timeline: 90 days for NRA decision

WHO PQ REPORTS SHARED

- Dossier review & Change requests
- Site Inspection
- Performance Evaluation

Prequalification assessment



- Labelling review is conducted & the public report prepared
- The product is added to the list of WHO prequalified IVDs

➢ IVD is eligible for WHO and UN procurement & CRP

WHO PQ Assessment Reports

Dossier Review

Assessment of manufacturer's information:

- Product information
- Design and manufacturing
- Product performance specifications
  - Validation and clinical studies
- Labels
- Commercial history
- Regulatory history
- Quality management system

Site Inspection

On-site inspection findings:

- Scope of inspection
  - Objectives
  - Limitations
- Information about the manufacturer
- Inspection findings
  - Audit trails and sources of evidence
  - Evaluation and conclusions
  - List of non-conformities and observations
  - Grading of NCs

Performance Evaluation

Protocol & data provided:

- Product provided for evaluation
- Specimen panels tested
- Reference results
- Data Analysis
- Results
- Appraisal by laboratory technician
- Appendices containing data generated during the evaluation

+ Reports for approved changes

CRP Roles and Responsibilities

The Manufacturer

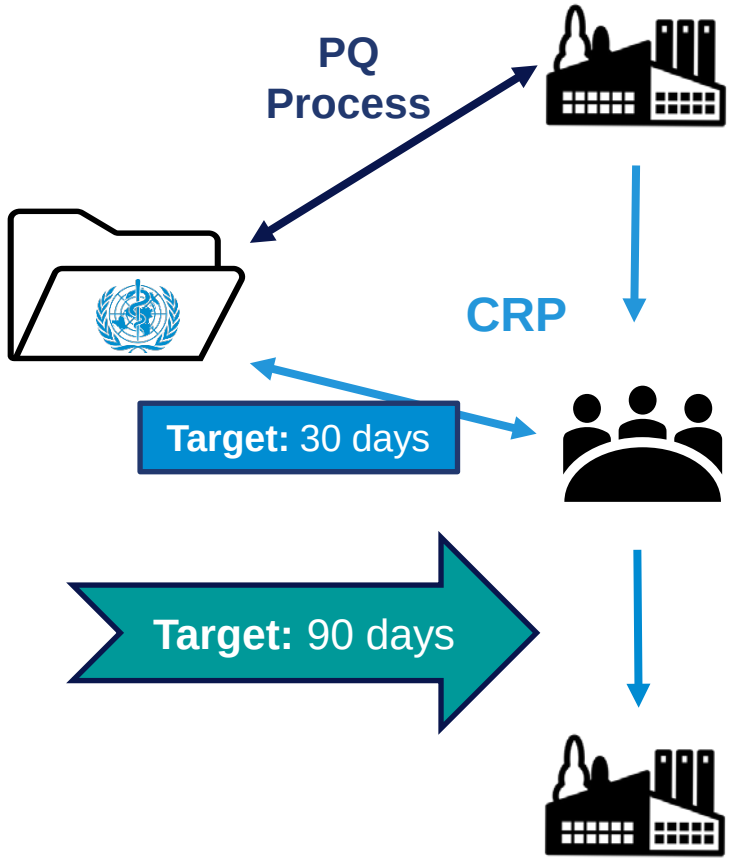
- Submit an expression of interest to the NRA
- Provide consent for WHO to share PQ reports
- Submit product dossier to NRA

WHO

- Make reports available to NRA via secure transfer
- Provide advocacy and support to regulatory authorities

The NRA

- Treat WHO PQ reports as confidential
- Issue a national regulatory decision within 90 days



NRAs participating in CRP for IVDs

Rwanda
Nigeria
Mauritania
Uganda
South Africa
Ethiopia
Tanzania
Kenya
Bhutan
Namibia
Malawi

Eritrea
Burundi
Gabon
Togo
DR Congo
Senegal
Zanzibar
Mozambique
Ivory Coast
Cameroon
Ghana

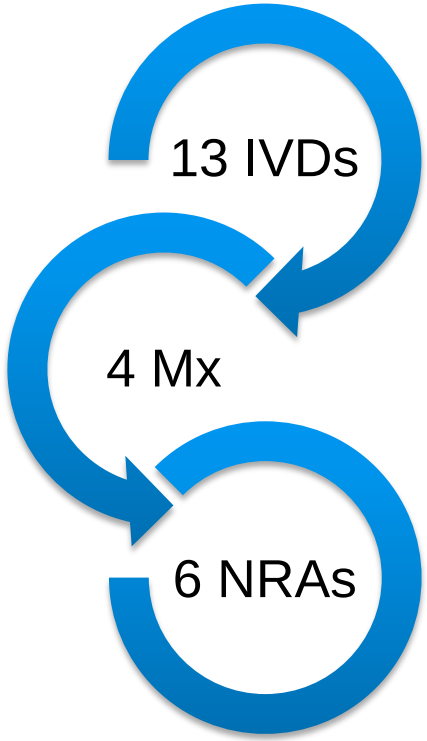
Thailand
Yemen
Cabo Verde
Togo
Angola
Zimbabwe
Botswana
Comoros

As of October 2023




2023 Update

- PQT received 21 requests to share reports
  - 100% reports provided within target 30-day timeframe
  - Average 9 days
- Change report provided for x IVDs
- Participated in CRP workshops & meetings
  - Indonesia, Ukraine, Kazakhstan, Francophone African countries

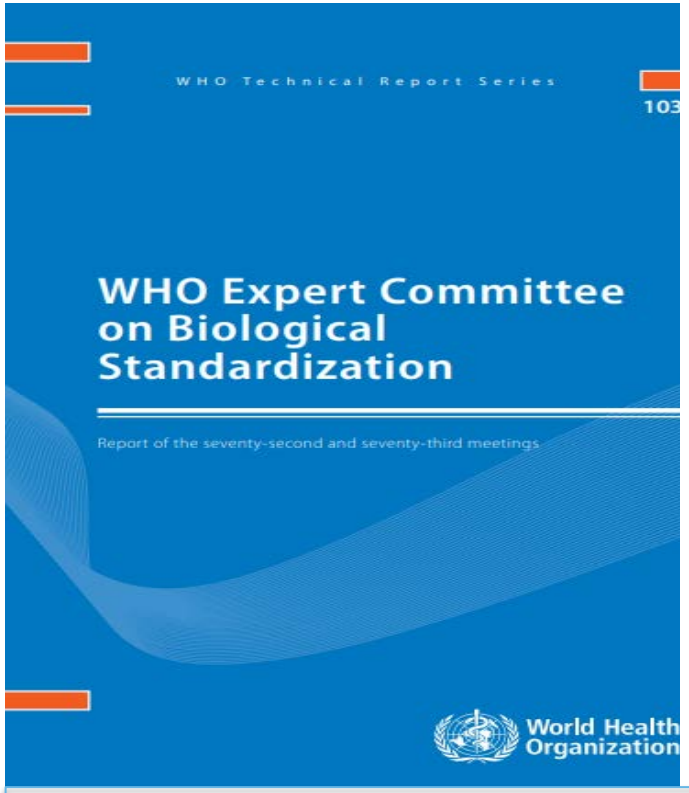


PQT-IVD support for CRP

- Preparation of CRP Dossier review reports for prequalified IVDs
  - Retrospectively prepared from assessment templates completed at the time of the review
  - Incorporate the CAP requests
  - Quarterly updates to summary of approved change requests
- Presentations in CRP Workshops and meetings with NRA
  - Including product specific workshops
- Discussions with manufacturers on CRP planning for products close to prequalification
- Inclusion of NRA assessors in PQ Joint Assessment Sessions

More information on the procedure

The CRP procedure is published on WHO website:



Annex 4

Collaborative procedure between the World Health Organization and national regulatory authorities in the assessment and accelerated national registration of WHO-prequalified in vitro diagnostics

1. **Introduction** 227
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Appendix 2 Consent of WHO prequalification holder for WHO to confidentially share information with the NRA under the Procedure 254

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Appendix 4 Report on post-registration actions in respect of a product registered under the Procedure 265

https://www.who.int/publications/i/item/9789240024373

Thank you

World Health Organization 75 HEALTH FOR ALL