WHO Prequalification of In Vitro Diagnostics

Dossiers requirements for WHO Prequalification Assessment

R Meurant

Prequalification Team – Diagnostics
Department of Essential Medicines & Health Products
World Health Organization


Omega
Rapid Test
Uni-Gold

General Purpose of a Dossier

- The dossier contains a subset of the technical documentation held by the manufacturer
- The dossier reflects the status of the IVD at a particular moment in time
- It allows the manufacturer to demonstrate that the IVD to which it applies conforms to the *Essential Principles of Safety and Performance of Medical Devices* as defined by GHTF

Essential Principles (GHTF)

- Medical devices should be designed and manufactured in such a way that, when used under the conditions and for the purposes intended and,
- where applicable, by virtue of the technical knowledge, experience, education or training, and the medical and physical conditions of intended users,
- they will perform as intended by the manufacturer and not compromise the clinical condition or the safety of patients, or the safety and health of users or, where applicable, other persons,
- provided that any risks which may be associated with their use constitute acceptable risks when weighed against the benefits to the patient and are compatible with a high level of protection of health and safety.

Purpose of a Dossier for PQ

- It should also provide sufficient information to inform the PQ Inspection team regarding:
  - Sites responsible for design and manufacture to enable planning of inspection/s
  - Information regarding the maturity of the manufacturer's QMS
- It should provide sufficient information to determine the regulatory version submitted to PQ and to ensure the data in the dossier is relevant to this version
- Most importantly it should demonstrate that the Mx has considered the safety and performance in WHO Member States.

STED Summary Technical Documentation

- GHTF recognised the advantage of having a consistent, summarised or abridged set of technical documentation used for selected premarket and post-market conformity assessment activities.
- This technical documentation subset is intended to have sufficient detail to allow the RA/CAB to fulfil its obligations.
- GHTF provided a dossier structure known as the Summary Technical Documentation
- WHO first international body to adopt the STED format
- Level of detail to be submitted is in line with GHTF risk classification requirements for Class D (high risk)

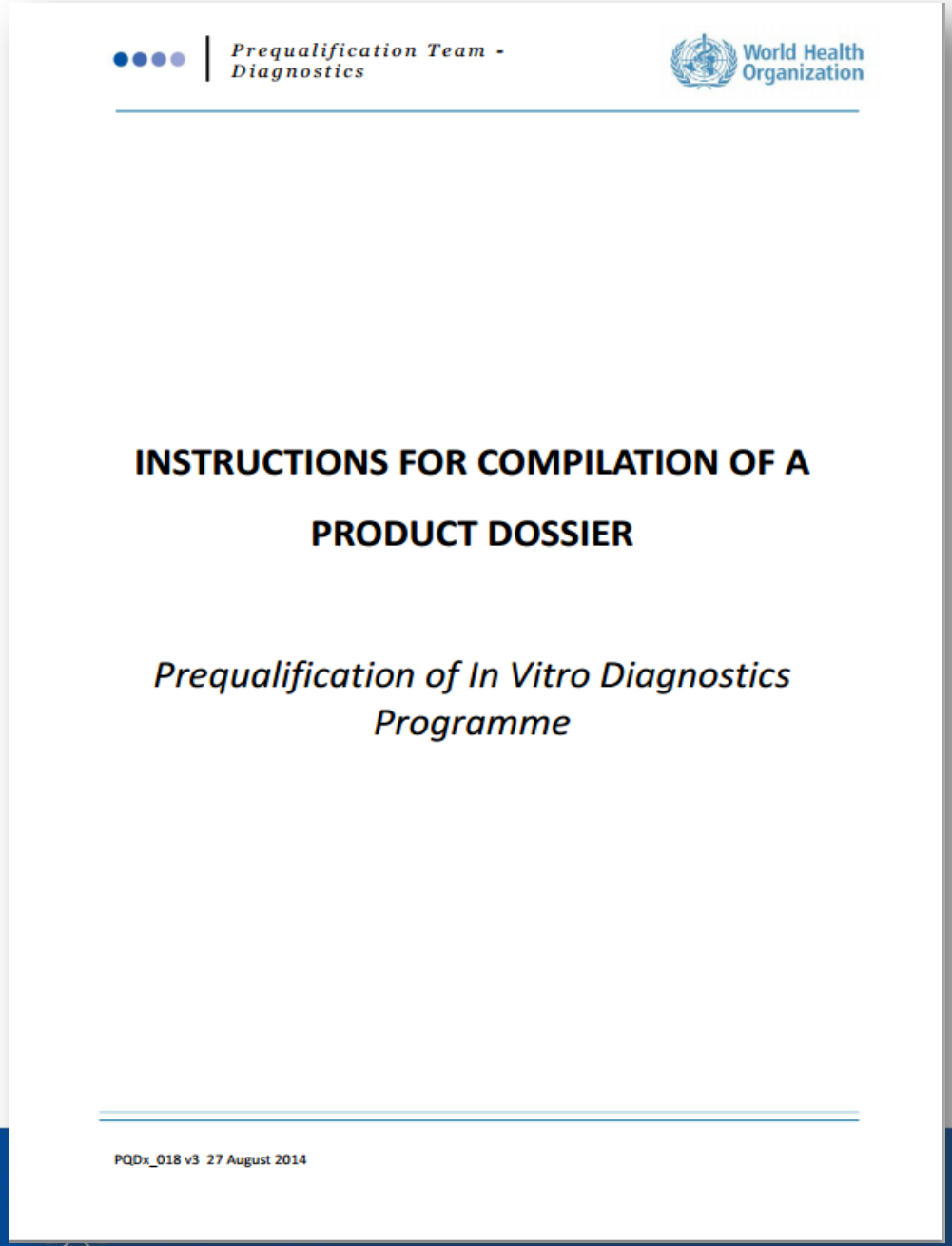
Table of Contents

IMDRF IVD MA ToC

IVD Market Authorization Table of Contents

- An internationally harmonized, modular, format for use when filing medical device submissions to regulatory authorities for market authorization
- Goal is to have an electronic submission format while minimizing regional divergences and indicating where regional variation exists.
- Works together with a classification document to determine level of detail required
- More granularity than STED
- WHO Dossier requirements revised to align with ToC (not yet the same order)

WHO Specific Dossier Requirements



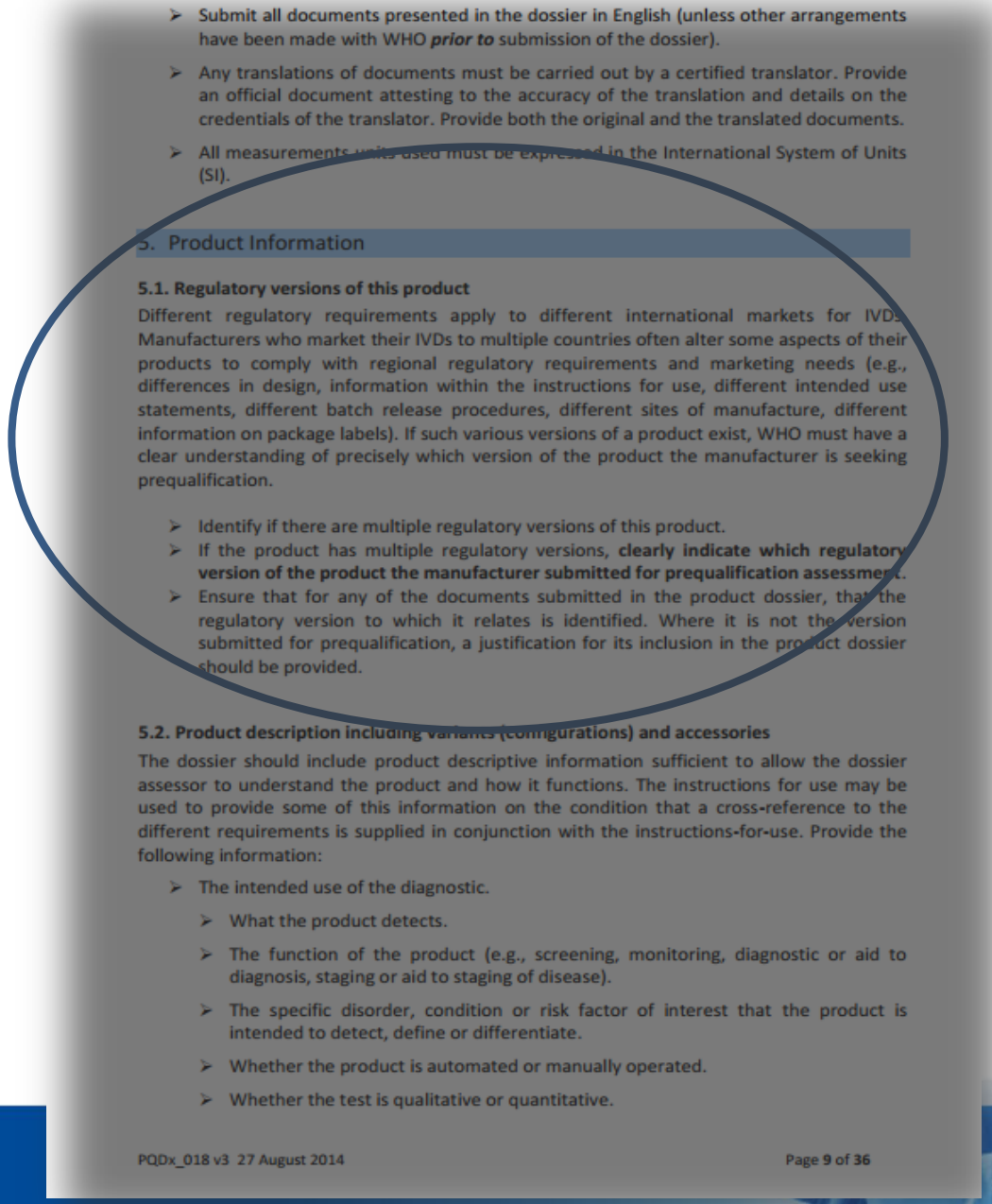
Prequalification Team - Diagnostics

World Health Organization

INSTRUCTIONS FOR COMPILATION OF A PRODUCT DOSSIER

Prequalification of In Vitro Diagnostics Programme

PQDx_018 v3 27 August 2014



- Submit all documents presented in the dossier in English (unless other arrangements have been made with WHO ***prior to*** submission of the dossier).
- Any translations of documents must be carried out by a certified translator. Provide an official document attesting to the accuracy of the translation and details on the credentials of the translator. Provide both the original and the translated documents.
- All measurements units used must be expressed in the International System of Units (SI).

5. Product Information

5.1. Regulatory versions of this product

Different regulatory requirements apply to different international markets for IVDs. Manufacturers who market their IVDs to multiple countries often alter some aspects of their products to comply with regional regulatory requirements and marketing needs (e.g., differences in design, information within the instructions for use, different intended use statements, different batch release procedures, different sites of manufacture, different information on package labels). If such various versions of a product exist, WHO must have a clear understanding of precisely which version of the product the manufacturer is seeking prequalification.

- Identify if there are multiple regulatory versions of this product.
- If the product has multiple regulatory versions, **clearly indicate which regulatory version of the product the manufacturer submitted for prequalification assessment**.
- Ensure that for any of the documents submitted in the product dossier, that the regulatory version to which it relates is identified. Where it is not the version submitted for prequalification, a justification for its inclusion in the product dossier should be provided.

5.2. Product description including variants (configurations) and accessories

The dossier should include product descriptive information sufficient to allow the dossier assessor to understand the product and how it functions. The instructions for use may be used to provide some of this information on the condition that a cross-reference to the different requirements is supplied in conjunction with the instructions-for-use. Provide the following information:

- The intended use of the diagnostic.
  - What the product detects.
  - The function of the product (e.g., screening, monitoring, diagnostic or aid to diagnosis, staging or aid to staging of disease).
  - The specific disorder, condition or risk factor of interest that the product is intended to detect, define or differentiate.
  - Whether the product is automated or manually operated.
  - Whether the test is qualitative or quantitative.

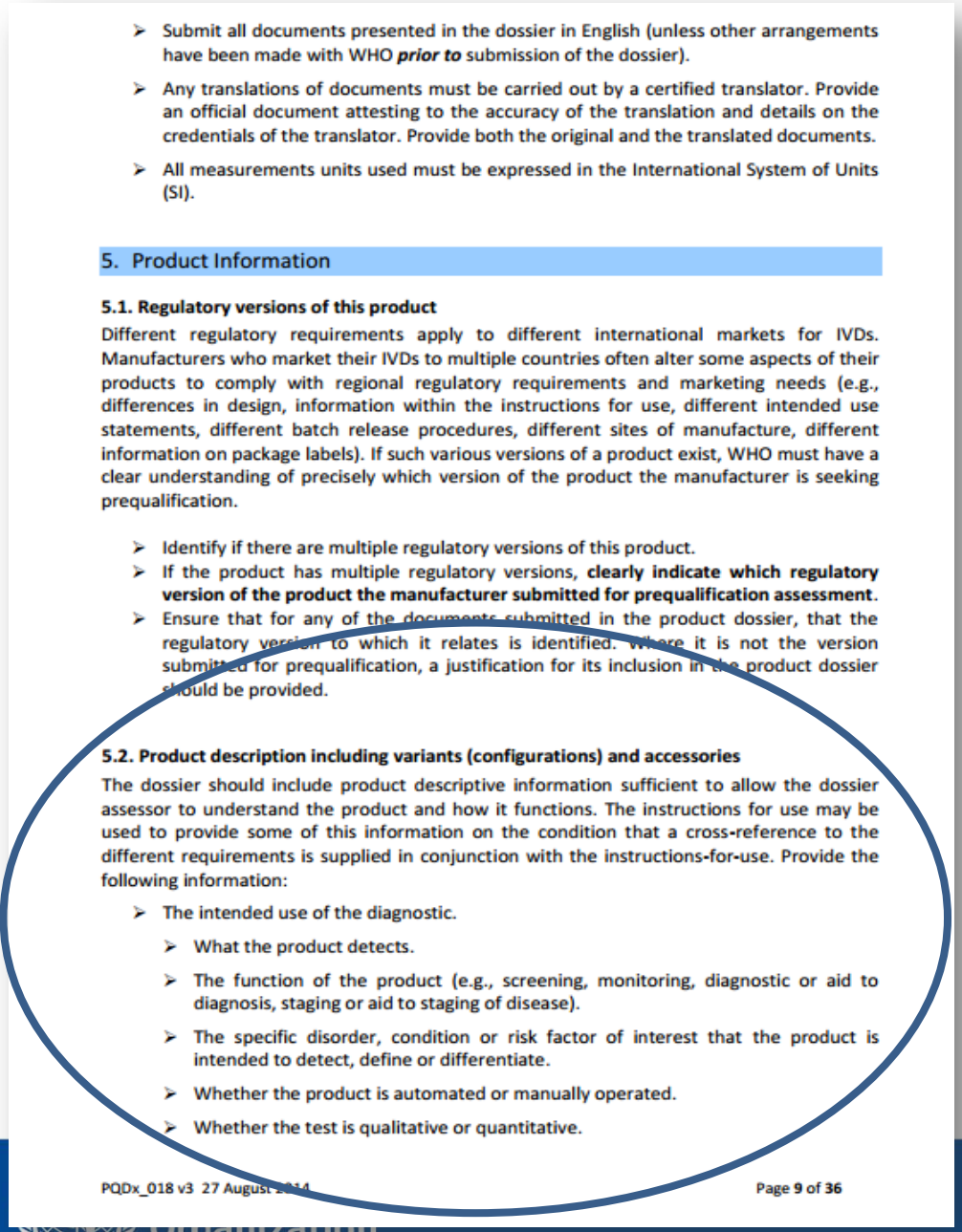
PQDx_018 v3 27 August 2014 Page 9 of 36

Regulatory Versions

You may not be getting identical twins!

- Relates to the information associated with a submission for approval by a regulatory authority.
- The submitted version is defined by all of the documentation related to development, manufacture, and intended use, labelling and post market surveillance of the product and all the documented evidence supporting the safety and performance claims associated with that submission.
- Any difference is considered to be a different regulatory version.
- Need to be sure how the data in the dossier relates to the product undergoing review.
- The FDA approved product may be different to the Rest of World (ROW) model!

Product Description



- Submit all documents presented in the dossier in English (unless other arrangements have been made with WHO ***prior to*** submission of the dossier).
- Any translations of documents must be carried out by a certified translator. Provide an official document attesting to the accuracy of the translation and details on the credentials of the translator. Provide both the original and the translated documents.
- All measurements units used must be expressed in the International System of Units (SI).

5. Product Information

5.1. Regulatory versions of this product

Different regulatory requirements apply to different international markets for IVDs. Manufacturers who market their IVDs to multiple countries often alter some aspects of their products to comply with regional regulatory requirements and marketing needs (e.g., differences in design, information within the instructions for use, different intended use statements, different batch release procedures, different sites of manufacture, different information on package labels). If such various versions of a product exist, WHO must have a clear understanding of precisely which version of the product the manufacturer is seeking prequalification.

- Identify if there are multiple regulatory versions of this product.
- If the product has multiple regulatory versions, **clearly indicate which regulatory version of the product the manufacturer submitted for prequalification assessment**.
- Ensure that for any of the documents submitted in the product dossier, that the regulatory version to which it relates is identified. Where it is not the version submitted for prequalification, a justification for its inclusion in the product dossier should be provided.

5.2. Product description including variants (configurations) and accessories

The dossier should include product descriptive information sufficient to allow the dossier assessor to understand the product and how it functions. The instructions for use may be used to provide some of this information on the condition that a cross-reference to the different requirements is supplied in conjunction with the instructions-for-use. Provide the following information:

- The intended use of the diagnostic.
  - What the product detects.
  - The function of the product (e.g., screening, monitoring, diagnostic or aid to diagnosis, staging or aid to staging of disease).
  - The specific disorder, condition or risk factor of interest that the product is intended to detect, define or differentiate.
  - Whether the product is automated or manually operated.
  - Whether the test is qualitative or quantitative.

PQDx_018 v3 27 August 2014 Page 9 of 36

- Goal – to have a comprehensive understanding of all aspects of the product/s included in the application
- The dossier assessor is a subject matter expert and will be able to ascertain from this description, the probability of the product being able to achieve its intended use, in the hands of intended users, in a safe manner
- For PQ applications, WHO expects photos of the kit and contents to be supplied.

Product Description

For HIV rapid tests, great attention is paid to certain aspects, especially those that impact on operational aspects…

- **Reading time frame**
- **Composition of different package sizes within an application**

Product Description

For HIV rapid tests, great attention is paid to certain aspects, especially those that impact on operational aspects…

- **Presence of a control line (consider what it does control)**
- **Clear markings/labelling of test and control lines**
- **Place for Pt ID**
- **Suitability of cassette design for addition of required volume of specimen (chance of spillage etc)**

Product Description

For HIV rapid tests, great attention is paid to certain aspects, especially those that impact on operational aspects…

Suitability of accessories

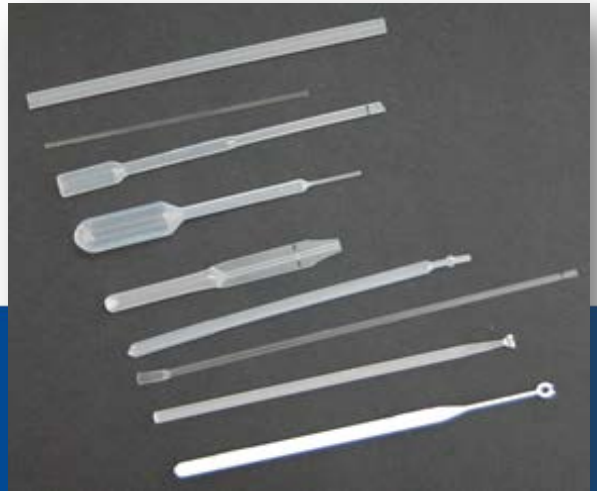
Specimen transfer devices

- Glass not ideal, need for calibration/accurate specimen volume,
- Need for precision pipettes
- Validation of chosen device

Quality and packaging of the lancets

Presence of a desiccant

- How to know what it is for, action to take if colour change, composition



Product Description

For HIV rapid tests, great attention is paid to certain aspects, especially those that impact on operational aspects…

Technical skills required of staff:

- Reconstitution of reagents/buffers required
- Need for dilution calculations
- Number of steps required

What is the quoted rate of invalid runs

Provided stability claims vs anticipated conditions of use

Biological hazard (have control specimens been tested by NAT for HIV, HCV, HBV and/or heat inactivated)

Provision of a job aid and suitability of the IFU and other labelling

Instructions for Use, Job Aid and other Labelling

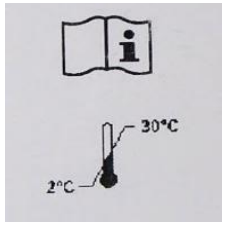
For HIV rapid tests, great attention is paid to certain aspects, especially those that impact on operational aspects…

Regulatory requirements

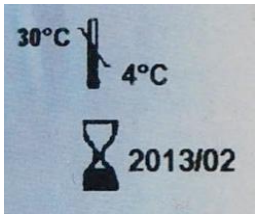
Takes into account the likely end user

- Language complexity
- Font
- Clarity of instructions
- Interpretation of results

Unambiguously identifies the product for PQ

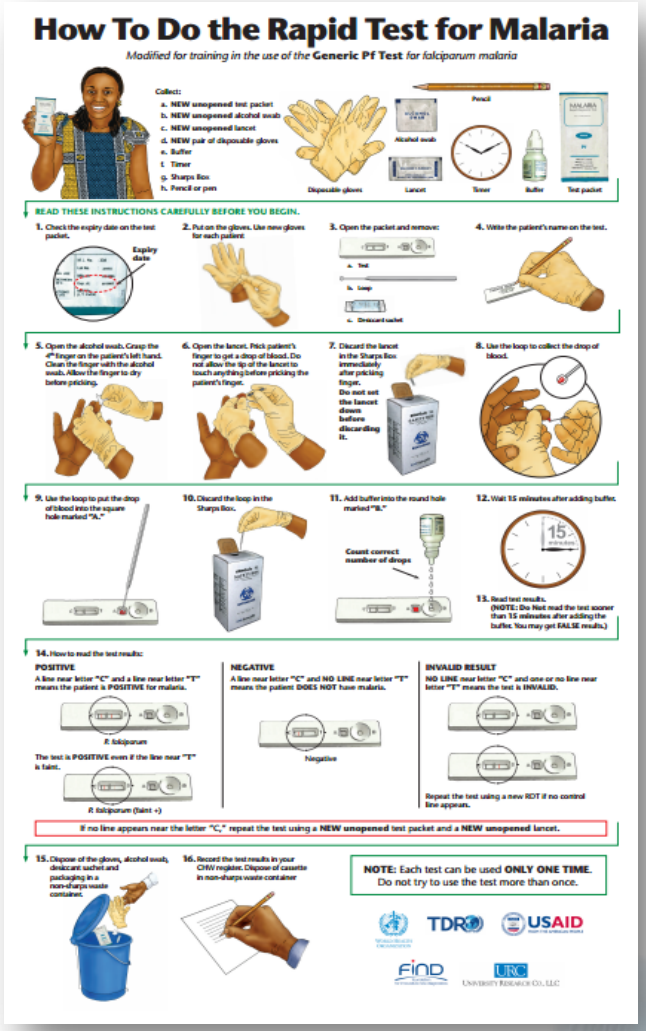


9.1 CORRECT



9.2 INCORRECT

9.3 INCORRECT



Other aspects of the dossier

For HIV rapid tests, great attention is paid to considering the end user as someone in a WHO Member State other than EU or US…

Risk Analysis

Analytical studies

- Reproducibility
- Robustness
- Genotypes/world wide panels
- Flex studies

Stability and transport stress

Clinical studies

- Where possible, studies to support the use of the assay in Africa, Asia etc

Thank You