IMDRF International Medical Device Regulators Forum

Stakeholder Forum
Stakeholder Session

WHO Regulatory Update

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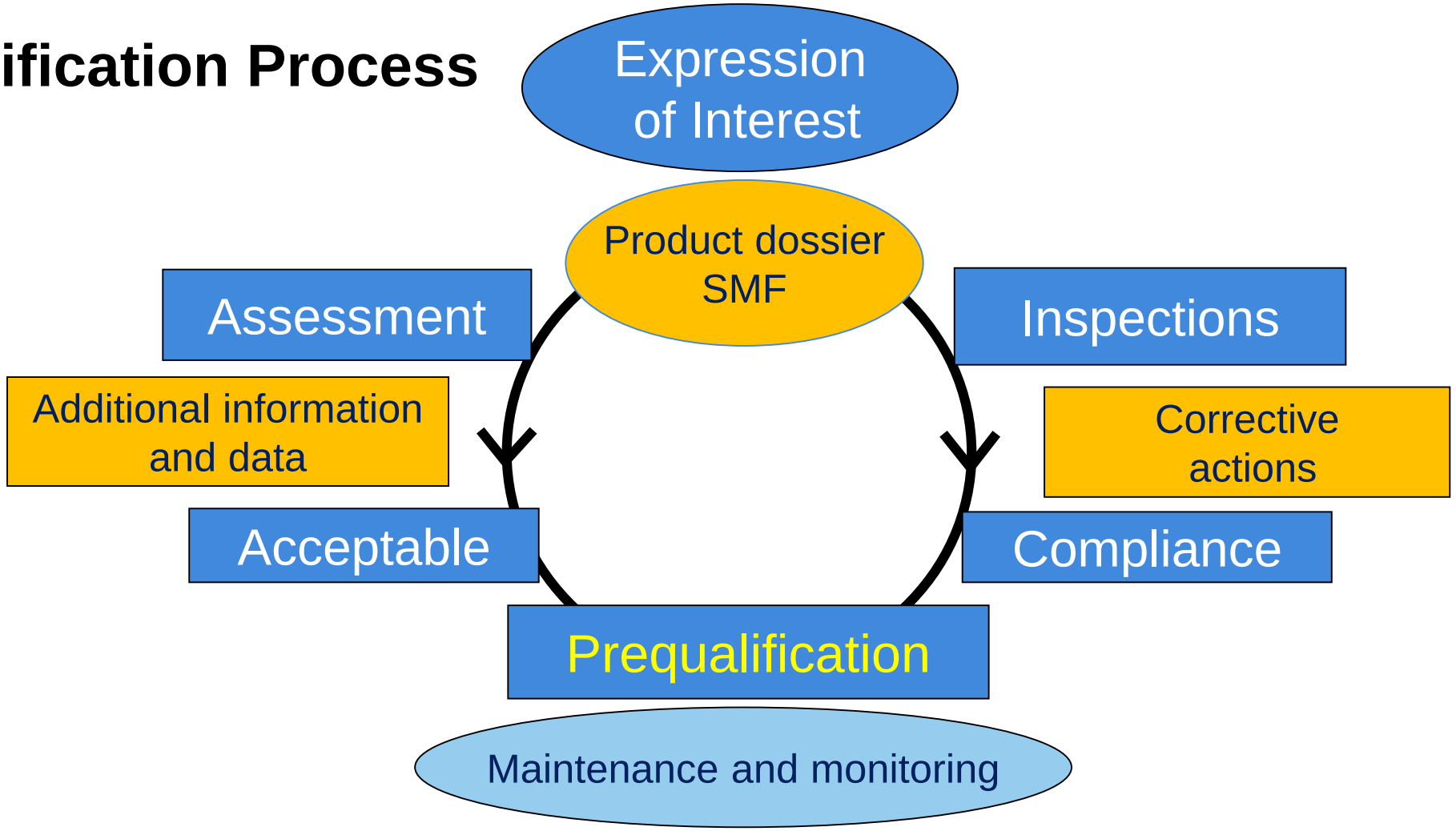
Overview

- Background:
  - WHO: Prequalification establishment
- PQT - Dx Assessment
- PQT - Safety
- PQT – Inspections

Diagnostics	Medicines	Vaccines	Vector Control
❑ *Origin*: Substandard performance of HIV assays in sub-Saharan Africa → *Response*: HIV Test Kit Evaluation Programme (1988)	❑ *Origin*: Request by WHO MS to assess the quality, safety and efficacy of low-cost and new FDCs HIV/AIDS generic medicines	❑ *Origin*: Request by UNICEF and PAHO to evaluate quality, safety and efficacy of vaccines in the context of national immunization programmes	❑ *Origin*: WHOPES set up in 1960 for evaluation of pesticides for public health. In 2015, WHO initiated reforms to foster innovation, improve efficiency, assure quality and align with other PQ programmes
❑ *PQ beginning*: **2010**	❑ *PQ beginning*: **2001**	❑ *PQ beginning*: **1987**	❑ *PQ beginning*: **2017**

WHO responded to the need of procurement agencies and WHO Member States for quality-assured health products, by creating and applying quality-assurance mechanisms

Prequalification Process



Update on Dx Assessment

Expanding the scope of prequalification

- Consultation conducted in Q4 2018 – Q1 2019: Feedback received from several stakeholders
- New methodology developed for determining priority – reflecting
  - EDL listing
  - WHO guidelines
  - Burden of disease (DALYs *Disability adjusted life years i.e. heart disease, stroke, neonatal disorders*)
  - Priority diseases (Blueprint diseases [*i.e. Ebola, Zika, Lassa fever],* eradicable diseases and NTDs (*Neglected Tropical Diseases*)
  - Associated health interventions (availability of curative treatment, preventative management and containment strategies).
- WHO to finalize priority ranking and communicate on new eligibility and timelines
- In the meantime HBV VL (Viral Load) will be added, expected in Q1 2020

PQ abridged assessment

- Procedure in place since 2014
- Leverages existing stringent reviews
- Undergoing revision
  - To reflect changes in regulations in jurisdictions recognized as performing stringent reviews
  - To explore opportunities to add new jurisdictions recognized as performing stringent reviews
  - To reflect evolving international harmonization initiatives,
    - IMDRF's Medical Device Single Audit Programme (MDSAP)
  - Amended procedure expected early 2020

2019 Prequalification technical specifications development

Documents developed based on:

- international recognized best practice and standards
- using a consultative process during development to ensure
  - acceptance by manufacturers
  - confirmation on the practicality to implement

2019 Prequalification technical specifications development

- TSS documents planned for consultation and public comment in 2019
  - **focus Hepatitis B/C**

TSS 13	**Rapid diagnostic tests to detect hepatitis B surface antigen (HBsAg)**
TSS 14	**Immunoassays to detect hepatitis B surface antigen (HBsAg)**
TSS 15	**In vitro diagnostic (IVDs) medical devices used for the quantitative detection of Hepatitis B nucleic acid**

- TSS documents planned for 2019/2020

TSS 16	**In vitro diagnostic (IVDs) medical devices used for the quantitative detection of Haemoglobin**

2019 Prequalification technical specifications development

- Finalized Technical Specification Series (TSS) to be published in 2019

TSS 7	**Rapid diagnostic tests to detect hepatitis C antibody or antigen**
TSS 8	**Immunoassays to detect HCV antibody and/or antigen**
TSS 9	**Immunoassays to detect HIV antibody and/or antigen**

- In addition, PQ published three draft TSS for public comment

TSS 10	**In vitro diagnostic (IVDs) medical devices used for the qualitative and quantitative detection of Hepatitis C RNA**
TSS 11	**In vitro diagnostic (IVDs) medical devices used for the quantitative detection of HIV-1 nucleic acid**
TSS 12	**In vitro diagnostic (IVD) medical devices used for the qualitative detection of HIV-1 and HIV-2 nucleic acid**

PQDx IVD product dossiers – ToC format

- To date, WHO PQ applications, product dossiers have been provided and **reported** using **STeD format**
- WHO PQ Diagnostic Assessments to implement **ToC format** for dossiers and review reports:

  Pilot, Q3/4 2019:

  – as part of the Collaborative Registration Procedure for IVDs, a ToC-format dossier report has been generated and distributed to pilot participants

  – Dossier requirements, and dossier review documents being updated to reflect ToC

  Transition period, 2020:

  – Manufacturers requested to provide product dossiers in either STeD or ToC format; dossier reviews to be reported using ToC report templates

  – Training for assessors, and guidance for manufacturers, to be provided

  Implementation, 2021:

  – All product dossiers to be submitted in ToC format.

WHO reportable changes to prequalified medical devices

- WHO has published in Q2 2019 the final guidance document on management and classification of changes to a prequalified male circumcision device.

https://www.who.int/diagnostics_laboratory/180627_draft_mcd_guidance_for_comments_v01.4.pdf?ua=1

- WHO will launch a call for public comments of the guidance document on management and classification of changes to a prequalified in vitro diagnostic in Q3-Q4 2019.

https://apps.who.int/iris/bitstream/handle/10665/251915/WHO-EMP-RHT-PQT-2016.01-eng.pdf;jsessionid=A72C5B2D716245C92299ED653B367AD2?sequence=1

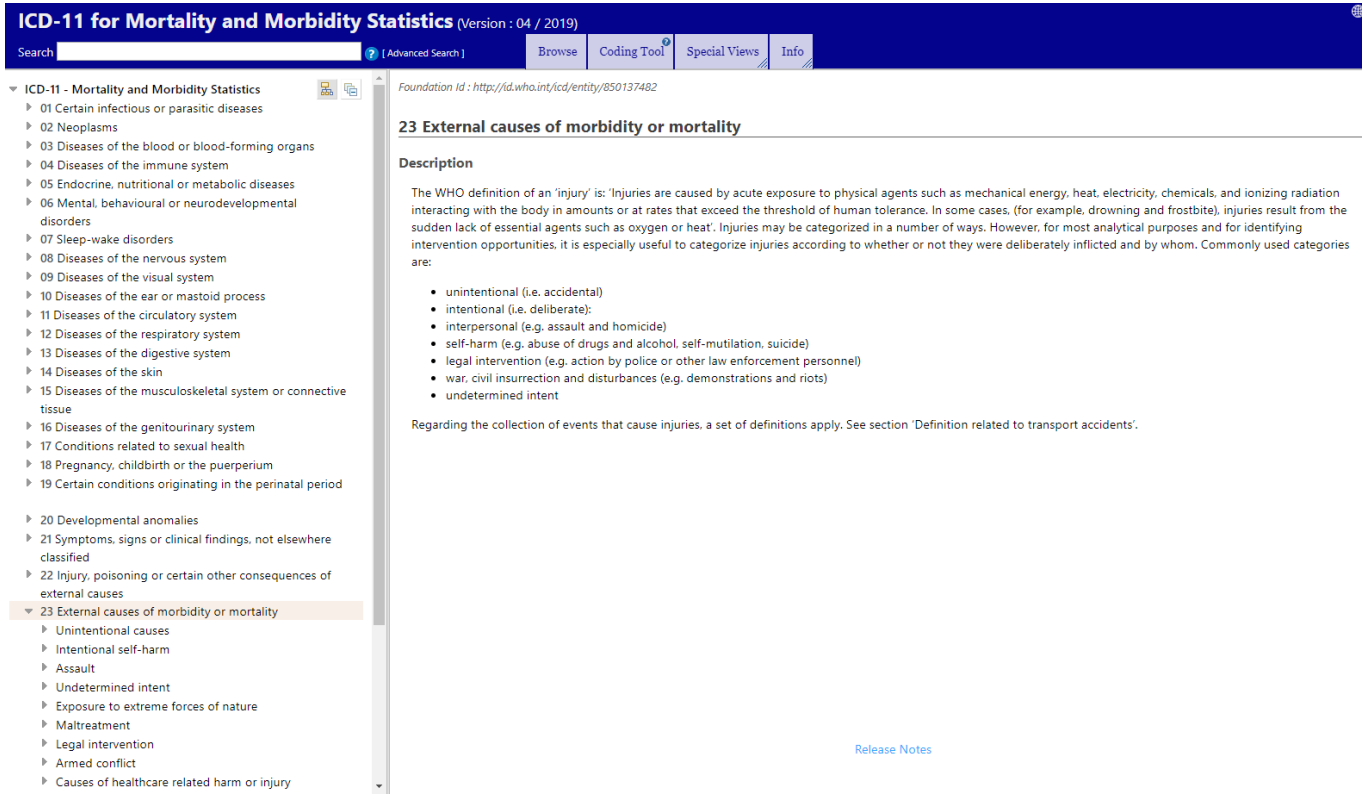
Update on Safety

WHO normative guidance

- Available in three languages
  - Spanish translation likely to be next
- Report templates harmonized with IMDRF and MEDDEV
- WHO offers 2-day workshop on how to engage stakeholder and implement guidance

How WHO will use IMDRF's adverse event reporting terminology

- WHO will add IMDRF AER terms to ICD-11
  - Taking advantage of ICD's governance, maintenance and translation functions
- WHO will host F2F meeting of AE reporting WG on 4-7 November 2019



Update on Inspection

Inspection types

- On site inspections
- Desk reviews
  - MDSAP inspection reports
    - Challenge limited due to delay in receiving reports
  - Stage 1 inspection – documents received from the manufacturer

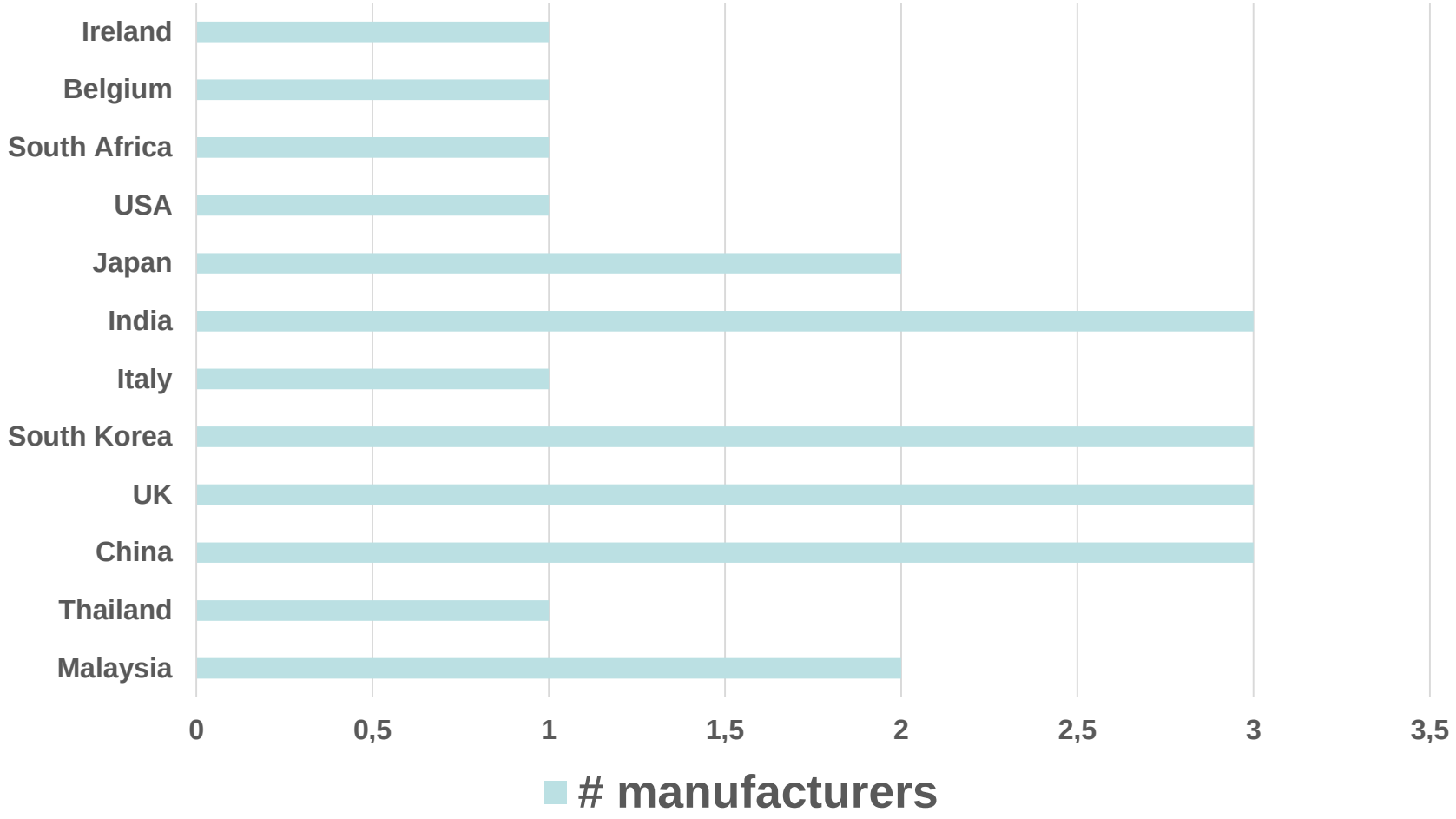
On site Inspections

August 2018 – August 2019

- 21 IVD inspections completed
- 1 Male circumcision device (MCD)
  - Number of products reviewed = total 45 products

	HIV	**HCV**	**Malaria**	**HBsAg**
Rapid	23	3	6	1
NAT *(nucleic acid test)*	6	1		
EIA (enzyme immunoassay)	1	3		
Combo	1			

Countries visited



Types of Non conformities identified

- **Level 5**
  - Data integrity:
    - falsification of batch manufacturing records (BMR)
    - Falsification of QC testing results
- **Level 4**
  - Planning of product realization
    - Risks throughout product realization were not always documented (full life cycle of the product)
    - Lack of verification and validation activities specific to the product and product requirements

Prequalification technical guidance specifications series

- TGS 6 - Panels for quality assurance and quality control of in vitro diagnostic medical devices:
  - Purpose:
    - to provide IVD manufacturers with guidance on possible approaches in preparing validation panels for quality assurance (QA) and quality control (QC).
    - describes the WHO Prequalification expectations in terms of the QA and QC information provided for prequalification assessment.

Prequalification technical guidance specifications series

- TGS 7 - Risk management for manufacturers of in vitro diagnostic medical devices:
  - Purpose:
    - to aid IVD manufacturers to develop appropriate risk management within their quality management system prior to:
      - compiling a product dossier for submission to WHO
      - in preparation for the site inspection.

Prequalification technical guidance specifications series

- TGS 8 - Quality control for in vitro diagnostic medical devices for WHO prequalification:
  - Purpose:
    - to aid IVD manufacturers in the development of Quality Control criteria focusing on:
      - identifying whether or not quality requirements for the product are being met
      - Identifying defects in the products that are produced.

END