

Stakeholder Forum Stakeholder Session

WHO Regulatory Update

Joey Gouws, Group Lead: Inspections 17 September 2019



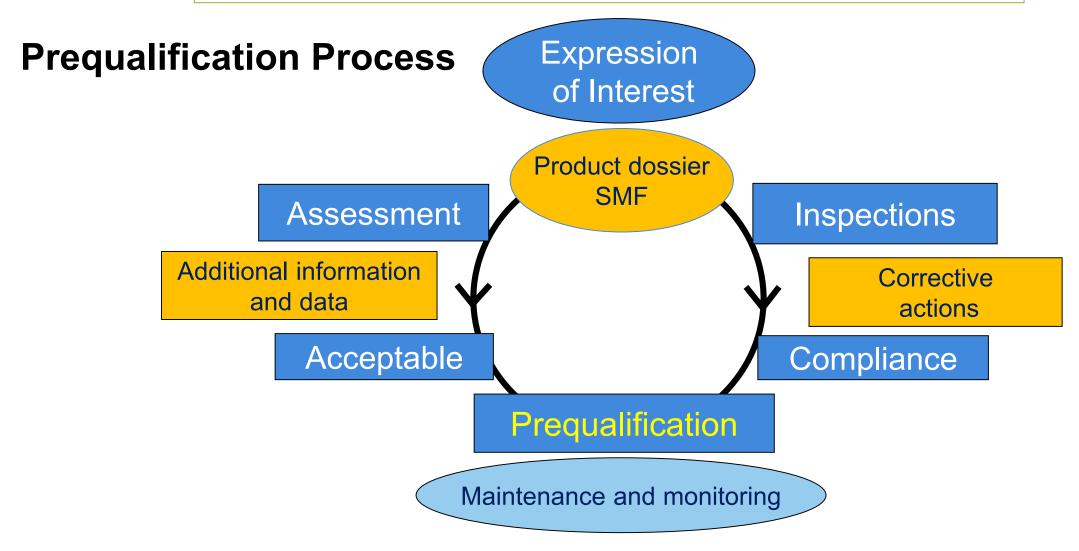
Overview

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

Diagnostics	Medicines	Vaccines	Vector Control
 □ <u>Origin</u>: 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 qualityassured health products, by creating and applying quality-assurance mechanisms







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

		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



ПОСТРЕГИСТРАЦИОННЫЙ НАДЗОР ЗА МЕДИЦИНСКИМИ ИЗДЕЛИЯМИ ДЛЯ ДИАГНОСТИКИ IN VITRO

Organisation norticle to to Sant

LIGNES DIRECTRICES POUR LA SURVEILLANCE POST COMMERCIALISATION DES DISPOSITIFS MÉDICAUX DE DIAGNOSTIC IN VITRO (DIV)

> World Health Organization

POST-MARKET SURVEILLANCE OF IN VITRO DIAGNOSTICS



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

2	Search	(a) [Advanced Search] Browse Coding Tool Special Views Info
	 ▼ ICD-11 - Mortality and Morbidity Statistics ▶ 01 Certain infectious or parasitic diseases 	Foundation Id : http://id.who.int/icd/entity/850137482
	02 Neoplasms	23 External causes of morbidity or mortality
	 03 Diseases of the blood or blood-forming organs 04 Diseases of the immune system 	Description
	 05 Endocrine. nutritional or metabolic diseases 06 Mental. behavioural or neurodevelopmental disorders 07 Sleep-wake disorders 08 Diseases of the nervous system 09 Diseases of the ear or mastoid process 11 Diseases of the circulatory system 12 Diseases of the respiratory system 13 Diseases of the skin 14 Diseases of the skin 15 Diseases of the skin 15 Diseases of the nusculoskeletal system or connective tissue 16 Diseases of the genitourinary system 	The WHO definition of an 'injury' is: 'injuries are caused by acute exposure to physical agents such as mechanical energy, heat, electricity, chemicals, and ionizing radia interacting with the body in amounts or at rates that exceed the threshold of human tolerance. In some cases, (for example, drowning and frostbite), injuries result from sudden lack of essential agents such as oxygen or heat'. Injuries may be categorized in a number of ways. However, for most analytical purposes and for identifying and intervention opportunities. It is especially useful to categorize injuries according to whether or not they were deliberately inflicted and by whom. Commonly used categorize intervention and (i.e. accidental) entitonal (i.e. deliberate): interprisonal (e.g. assult and homicide) self-harm (e.g. abuse of drugs and alcohol, self-mutilation, suicide) legal intervention (e.g., action by police or other law enforcement personnel): war, civil insurrection and disturbances (e.g., demonstrations and riots) undetermined intent Regarding the collection of events that cause injuries, as et of definitions apply. See section 'Definition related to transport accidents'.
	 17 Conditions related to sexual health 18 Pregnancy, childbirth or the puerperium 19 Certain conditions originating in the perinatal period 	
J	 20 Developmental anomalies 21 Symptoms, signs or clinical findings, not elsewhere classified 22 Injury, poisoning or certain other consequences of external causes 23 External causes of morbidity or mortality 	
	 Unintentional causes Intentional self-harm Assault Undetermined intent Exposure to extreme forces of nature Maltreatment Legal intervention Armed conflict Causes of healthcare related harm or injury 	Release Notes



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

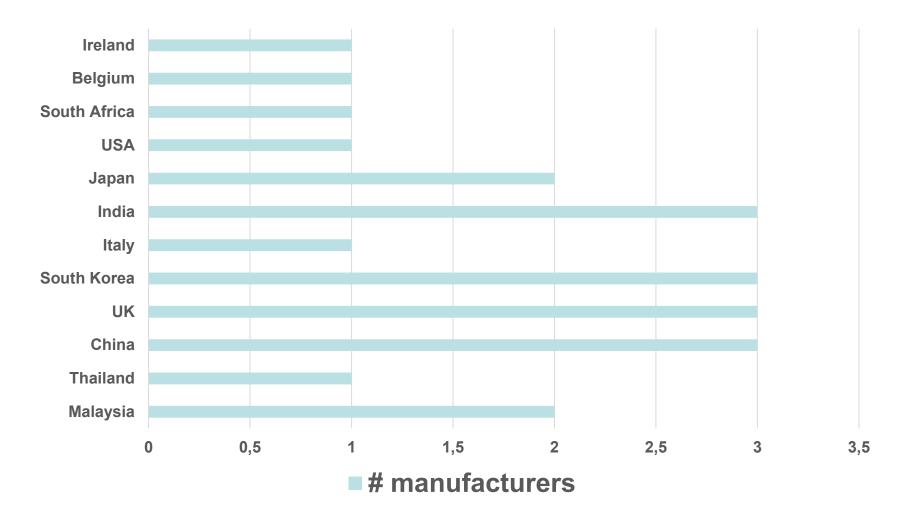
August 2018 – August 2019

- 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