Vaccine PQ Overview

Ms Carmen Rodriguez

Prequalification Team
Regulation of Medicines and other Health Technologies
Essential Medicines and Health Products
World Health Organization
Geneva, Switzerland
E-mail: vaccprequalification@who.int

WHO Cluster: Health Systems and Innovation

HEALTH SYSTEMS AND INNOVATION

Assistant Director General (ai.): Hans Troedsson

Department of Essential Medicines and Health Products (EMP)

Director: Suzanne Hill

Innovation, Access and Use (IAU)

Coordinator: Sarah Garner

- Promote affordable access to quality, safe and effective medicines, vaccines, diagnostics and other medical devices
- Determine WHO Model List of Essential Medicines (EML) and EML for Children (EMLc)
- Stimulate innovation for products to treat diseases affecting developing countries
- Make recommendations on regulation of controlled substances

Regulation of Medicines and other Health Technologies

Head: Emer Cooke

- Assist countries to strengthen regulation, including post-marketing surveillance
- Develop international technologies standards & norms
- Eliminate substandard and falsified medicines
- Facilitate access to quality-assured, safe and effective health products through prequalification mechanisms
- Ensure capacity building at all levels

About RHT and current focused areas

Regulation of Medicines and other Health Technologies (RHT)

Head: Emer Cooke

Technologies Standards and Norms (TSN)

Acting Coordinator Emer Cooke

- Set global written standards (recommendations & guidelines) & nomenclature (INN);
- Global measurement standards*;
- Quality assurance for Medicines Quality Control (QC) labs

*Including: biotherapeutics; blood products; in vitro diagnostic; medical devices; Vaccines , vector control products

Regulatory Systems Strengthening (RSS)

Coordinator Mike Ward

- Strengthen regulatory system; Benchmarking
- Capacity building:
  - GMP
  - Laboratory QS systems
- Harmonization initiatives
- Collaborative registration
- ICDRA support
- Technical assistance
- Laboratory testing
- Local Production

Prequalification Team (PQT)

Coordinator Deus Mubangizi

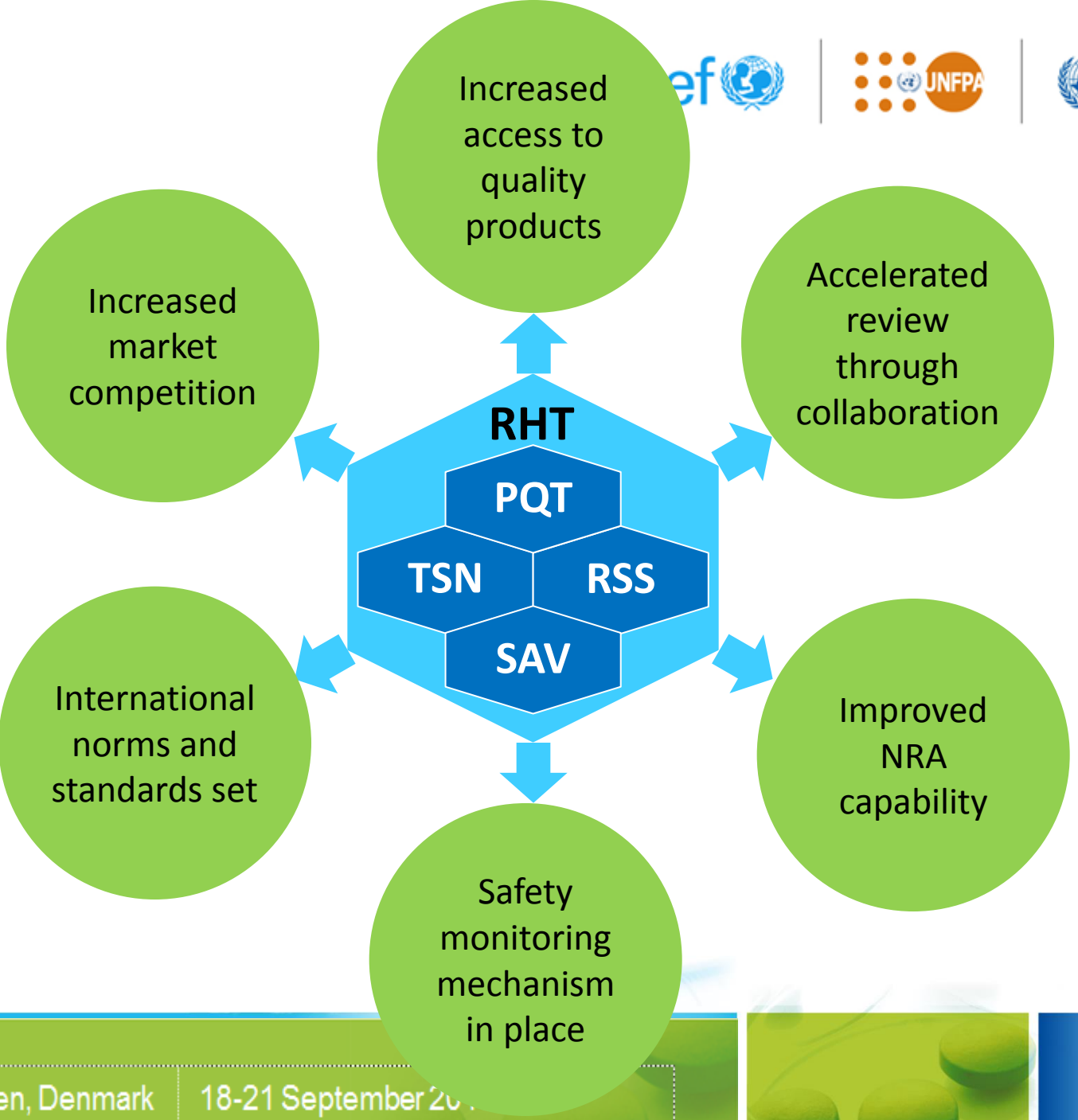
Prequalification (PQ) of medicines, vaccines, diagnostics, medical devices & vector control products:

- Dossier assessments
- Inspection
- PQ of medicines QC laboratories
- Scientific advice
- Training
- EUAL procedures for candidate vaccines, therapeutics and IVDs

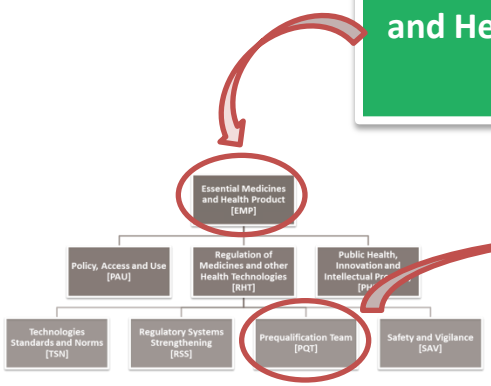
Safety and Vigilance (SAV)

Coordinator Clive Ondari

- Global surveillance & monitoring, including substandard & falsified medical products
- Coordination of global response to health / safety events
- Policies, norms, standards & guidelines
- Classify medicines & assign defined daily doses (ATC/DDD)


Increased access to quality products
Accelerated review through collaboration
Improved NRA capability
Safety monitoring mechanism in place
International norms and standards set
Increased market competition
RHT
PQT
TSN
RSS
SAV

Structure of the Prequalification Team



Essential Medicines and Health Products [EMP]

Prequalification Team Coordinator

Coordinator's office

Vaccines Assessment

Medicines Assessment

Diagnostics Assessment

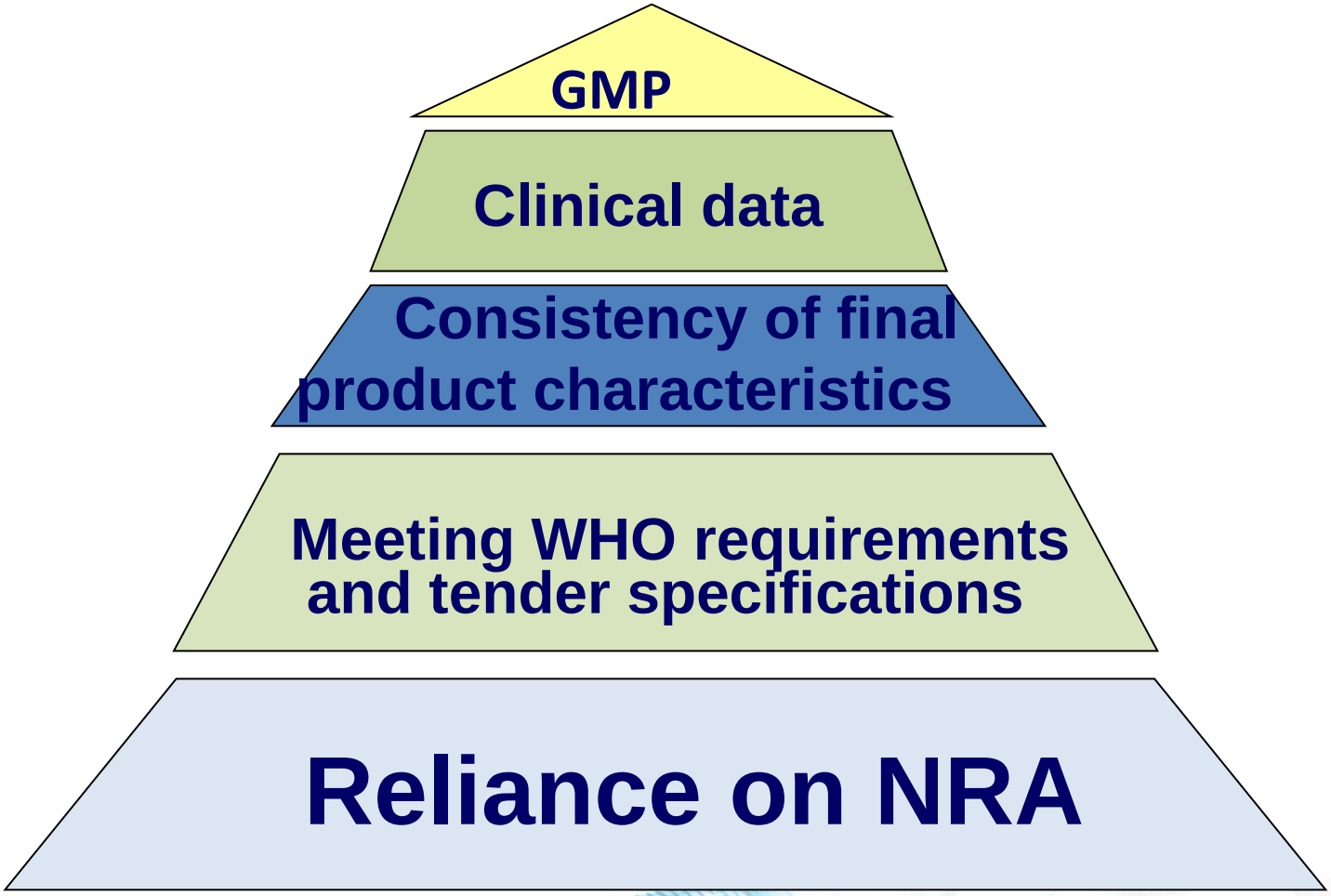
Vector Control Assessment

Inspections

WHO vaccines prequalification

- A service provided to UN purchasing agencies.
- Provides independent opinion/advice on the quality, safety and efficacy of vaccines for purchase
- Ensures that candidate vaccines are suitable for the target population and meet the needs of the programme
- Ensures continuing compliance with specifications and established standards of quality

Principles


GMP
Clinical data
Consistency of final product characteristics
Meeting WHO requirements and tender specifications
Reliance on NRA

Pre-conditions for PQT-VXA evaluation

Reliance on the National Regulatory Authority (NRA) of the exporting country

- **NRA evaluated by WHO NRA Global Benchmarking Tool**
- **NRA's status needs to be sustained over time**
- **Continued regulatory oversight by NRA is required as well as communication with WHO about potential problems with the vaccine**
- **Agreements are established with the NRAs for information exchange when a vaccine is about to be prequalified**

Pre-conditions for PQT-VXA evaluation

- **Vaccine is licensed/registered by the responsible NRA (or EMA article 58 scientific opinion)**
- **There are WHO guidelines/recommendations approved by the ECBS are available for the type of vaccine (published in the WHO Technical Report Series)**
- **Listed in the PQ vaccine priority list**

Pre-submission and Dossier Review

- Pre-submission meetings with manufacturers interested in submission are available and encouraged

- Notification of intended submission

- Dossier Submission
  - Product Summary File
  - Common Technical Document

- Screening
- Acceptance decision

Prequalification process

- Scientific review of quality dossier
- Scientific review of clinical data
- Testing of samples
- Consultation with responsible NRA
- Inspection to manufacturing facilities

PQ procedure

1. **Standard procedure**
2. **Abbreviated/streamlined**
3. **Fast track procedure:**

Applicable to licensed vaccines (marketing authorization available) that are part of the routine immunization programmes or those that are used only as an emergency response, but not applicable in the case of novel vaccines not yet introduced or recently introduced into the routine immunization

Prequalification process: timelines (excluding applicant response times)

Submission of application for PQ → Screening (30 days + 90 days if there is critical PSPQ non compliance) → 270 days internal time

Streamlined based on SRA approval and sharing of NRA reports → 90 days internal time

Submission of variation → Screening → 90 days internal time

Aspects considered during evaluation of vaccines for WHO Prequalification

- **Production**
- **Quality Control**
- **Clinical development, including data relevant to target population for supply through UN agencies**
- **Compliance with WHO recommendations and UN tender specifications including labels and inserts**
- **Compliance with GMP**
- **Programmatic suitability**

Role of NRA during PQ process

As part of the evaluation procedure, consultation with NRA discusses:

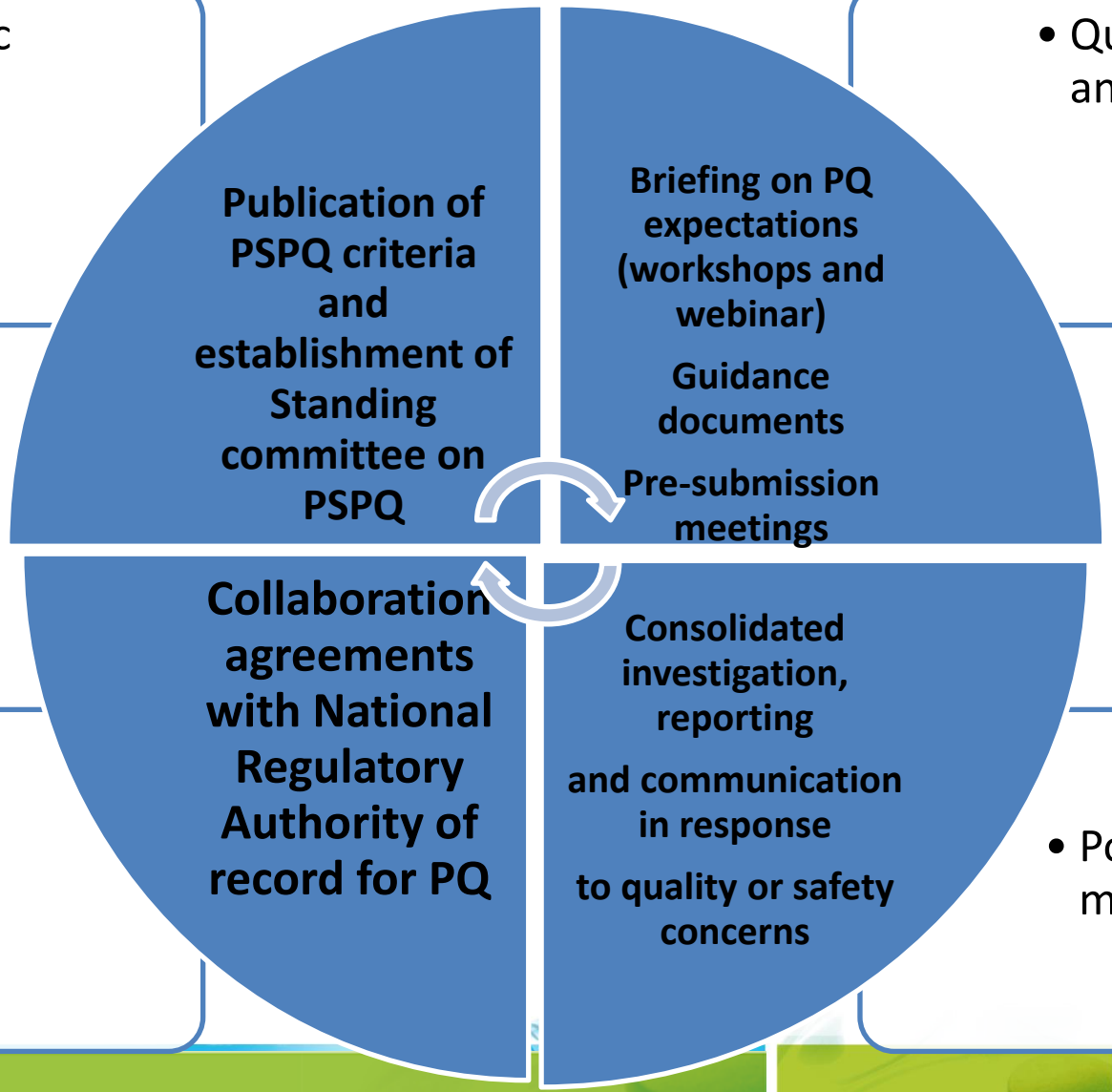
- Regulatory status of the concerned vaccine/s
- Clinical performance in country of manufacture if used
- Quality evaluation, outcome of recent GMP inspections
- Compliance with specifications (trends from lot release data)
- Regulatory actions concerning the vaccine/s

Past and current challenges

Quality	Clinical	Programmatic	GMP
Incomplete dossier Lack of data at commercial scale No history of characterization Master and Working cell banks Novel devices: eg, nasal administration	Lack of clinical consistency data, unclear ethical oversight Clinical trial comparator product not acceptable Lack of access to data and/or old data not meeting current GCP Lack of registration of CTs	Deviation Programmatic suitability criteria (PSPQ): eg, non autodisable prefilled syringes, stability profile and VVM	Quality systems Manufacturing process
Regulatory	National Vs WHO requirements: Test methodologies and GMP Schedules and target population Monodose Vs multidose presentation (preferred)		

Past/current Challenges and solutions

- Programmatic suitability criteria
- Quality, safety and efficacy



- Regulatory
- Post-PQ monitoring

Post Prequalification WHO Activities

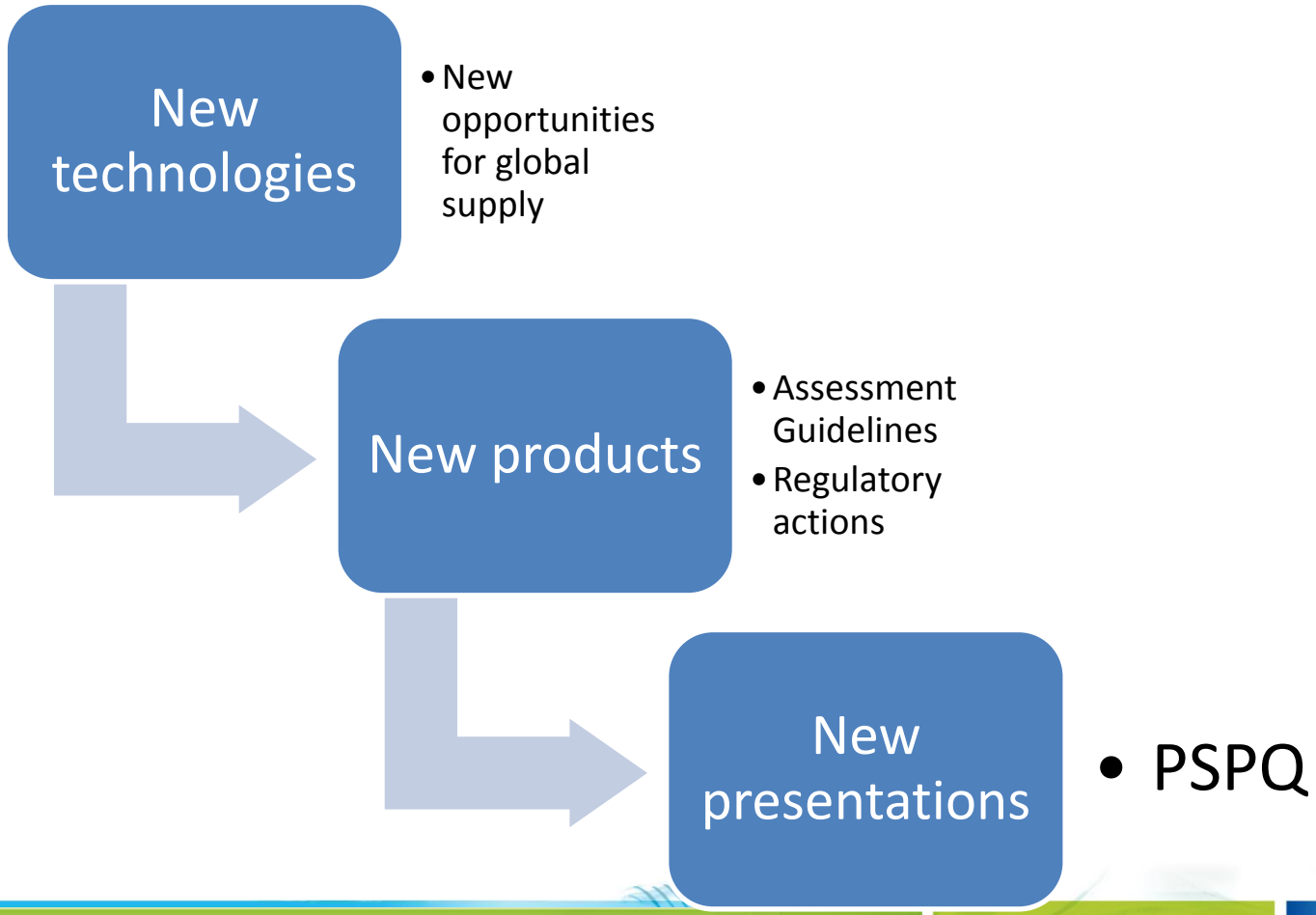
- Variations
- Annual Report evaluation
- Reassessment
- Targeted testing program
- Monitoring/Investigation of vaccine quality and cold chain complaints
- Monitoring/investigation of Adverse Events following immunization (AEFI)
- Collaborative National Registration
- Technical Review of tenders for UNICEF

Technical assistance and capacity building

- **Meetings with manufacturers at early stages of vaccine development. Advice on product characteristics and clinical development.**
- **PQ briefing workshops**
- **Support to IFPMA and DCVMN**
- **Support to regulatory networks: DCVRN, AVAREF**

New opportunities/ expanding the PQ scope

New opportunities



Expanding the PQ scope to other biologicals?

Products to be used in humanitarian emergencies, such as specific immunoglobulins or other biological products such as vaccines for treatment of intravesical cancer.

Monoclonal antibodies

Path forward (1)

Prequalification is not a one-off exercise but includes monitoring of quality on a continuous basis. Resources (financial and staff) are needed to ensure not only the quality, safety and efficacy of the medicinal products but also to ensure that quality is sustained and the benefit/risk ratio is still favorable over time.

- Mechanism to assess suitability
- Adequate standards for assessment

Path forward (2)

1. Public health interest
2. Development of a procedure that can also include other products that may be needed (eg other monoclonal antibodies, immunoglobulin, etc).
3. Definition of the principles applied for the initial assessment and also post-PQ/advice to ensure the sustainability of the quality, safety and efficacy
4. Consultation with relevant National regulatory authorities, eg USFDA, EMA, others
5. Resources: What mechanisms should be in place to secure resources to sustain the activities to ensure quality, safety and efficacy

Reference documents

PQT/VXA procedure [TRS 978, Annex 6 (2013]

http://www.who.int/entity/immunization_standards/vaccine_quality/TRS_978_61st_report_Annex_6_PQ_vaccine_procedure.pdf

PQ vaccines: Priority setting and Review

http://www.who.int/immunization_standards/vaccine_quality/pq_priorities/en/

Programmatic Suitability for Prequalification

http://www.who.int/immunization_standards/vaccine_quality/pspq2_v140512.pdf

Clinical

http://apps.who.int/prequal/info_general/documents/TRS850/WHO_TRS_850-Annex3.pdf

http://who.int/entity/biologicals/vaccines/clinical_evaluation/en/index.htm

http://who.int/biologicals/vaccines/nonclinial_evaluation_of_vaccines/en/

http://www.who.int/immunization_standards/vaccine_quality/pq_vaccine_evaluation/en/

Variations to prequalified vaccines

http://who.int/immunization_standards/vaccine_quality/variations_pq_vaccine/en/

HO contracted testing laboratories

http://www.who.int/immunization_standards/vaccine_quality/contracted_labs_vaccines/en/

Reference documents

Good Manufacturing Practice

WHO GMP for biological products, Annex 2, WHO TRS 999, 2016, http://who.int/biologicals/areas/vaccines/Annex_2_WHO_Good_manufacturing_practices_for_biological_products.pdf

WHO GMP for pharmaceutical products: main principles, Annex 2, WHO TRS 986, 2014

WHO GMP for sterile pharmaceutical products, Annex 6, WHO TRS 961, 2011

Thank you