Vaccine PQ Overview

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Prequalification Team
Regulation of Medicines and other Health Technologies
Essential Medicines and Health Products
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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

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### 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)
WHO PREQUALIFICATION PROGRAMME

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

RHT

PQT

TSN

RSS

SAV

Increased access to quality products

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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
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)

1. Submission of application for PQ
2. Screening (30 days + 90 days if there is critical PSPQ non-compliance)
3. 270 days internal time
4. Streamlined based on SRA approval and sharing of NRA reports
5. 90 days internal time
6. Submission of variation
7. Screening
8. 90 days internal time
9. Streamlined based on SRA approval and sharing of NRA reports
10. 90 days internal time

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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

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<th>Quality</th>
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<td><strong>Quality</strong></td>
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<tr>
<td>Incomplete dossier</td>
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<tr>
<td>Lack of data at commercial scale</td>
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<tr>
<td>No history of characterization</td>
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<td>Master and Working cell banks</td>
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<td>Novel devices: eg, nasal administration</td>
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<th>Clinical</th>
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<td>Lack of clinical consistency data, unclear ethical oversight</td>
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<td>Clinical trial comparator product not acceptable</td>
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<td>Lack of access to data and/or old data not meeting current GCP</td>
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<td>Lack of registration of CTs</td>
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<th>Programmatic</th>
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<tr>
<td>Deviation Programmatic suitability criteria (PSPQ): eg, non autodisable prefilled syringes, stability profile and VVM</td>
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<th>GMP</th>
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<td>Quality systems Manufacturing process</td>
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### 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
- Regulatory
- Post-PQ monitoring
- Quality, safety and efficacy

Publication of PSPQ criteria and establishment of Standing committee on PSPQ

Briefing on PQ expectations (workshops and webinar)
Guidance documents
Pre-submission meetings

Consolidated investigation, reporting and communication in response to quality or safety concerns

Collaboration agreements with National Regulatory Authority of record for PQ
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

- New technologies
  - New opportunities for global supply

- New products
  - Assessment Guidelines
  - Regulatory actions

- New presentations
  - PSPQ
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
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 (e.g., 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, e.g., 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)]

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/pspq_v140512.pdf

Clinical
http://who.int/entity/biologicals/vaccines/clinical_evaluation/en/index.htm
http://who.int/biologicals/vaccines/nonclinal_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 sterile pharmaceutical products, Annex 6, WHO TRS 961, 2011
Thank you