WHO vaccines prequalification overview
Copenhagen – 3 Dec 2019

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World Health Organization
Outline

• Introduction
• Principles
• Pre-conditions for PQ evaluation for Vaccines
• Conditions for prequalification
• Prequalification process
• Post Prequalification activities
• Technical assistance and capacity building
• Preparing for success for PQ
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Introduction

"Access to Medicines, Vaccines and Pharmaceuticals (MVP)"
Assistant Director General: Dr. Mariângela Batista Galvão Simão

Innovation, Access and Use

• Innovation/research & Development
• Intellectual property
• Evidence-based selection of Model List of Essential Medicines
• Pricing, Health technology assessment (HTA)
• Procurement and supply chain management
• Improved use of medicines and health products

Regulation of Medicines and other Health Technologies (RHT)
Head: Emer Cooke

- Technologies Standards and Norms (TSN)
- Regulatory Systems Strengthening (RSS)
- Prequalification Programme (PQT)
- Safety and Vigilance (SAV)
Introduction

RHT’s main activities supporting best practices, quality and access

- **Norms & Standards**: Establish/maintain international standards; Promote unified standards, as well as a global nomenclature.
- **Regulatory System Strengthening**: Strengthen NRAs for capacity building/efficiencies, promote harmonization, reliance, best practices & integrate framework for new products.
- **Prequalification**: Assure safe, effective & quality health products for public health challenges.
- **Safety & Vigilance**: Respond to and minimizing health risks from medical products by proactive, end-to-end, actionable, smart safety surveillance.

**Cross Cutting Challenges**
- AMR
- Benchmarking tools
- Data integrity
- Emergency preparedness
- Environmental issues
- Local production
- Non-communicable diseases
- Paediatric medicines
- Shortages
- Substandard & Falsified

Copenhagen, Denmark 2 – 5 December 2019
Introduction

Assessment pathways for vaccines and other biologicals

Prequalification (PQ)

- Response to the need of procurement agencies and Member States for quality-assured health products, by creating and applying quality-assurance mechanisms
- Reliance on “Stringent Regulatory Authority” possible

Risk based assessments time limited

- Licensed/PQ vaccine for emergency use (i.e. fractional dose)
- Emergency use and assessment listing EUAL
- Stockpiles: smallpox and polio
- Snake antivenom
Introduction

Purpose of WHO Vaccines PQ Programme

✓ 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.
Introduction

PQ is not a regulatory body
Introduction

• PQ of Vaccines
  • started 1987, originally request by UNICEF and PAHO to evaluate quality, safety and efficacy of vaccines in the context of national immunization programmes,
  • 148 vaccines prequalified to-date (238 presentations)
• Facilitates registration in developing countries
• Countries can rely on PQ assessment, inspection, lot testing, etc.
• PQ can also rely on other assessments
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Principles

- Reliance on NRA
- Meeting WHO requirements and tender specifications
- Consistency of final product characteristics
- Clinical data
- GMP
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Pre-conditions for PQ evaluation for Vaccines

- Reliance on the 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
  - Streamlined or abridged procedure also possible

- Vaccine is licensed/registered by the responsible NRA

- 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
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Conditions for prequalification (1)

Ongoing oversight and commitments by the NRA

Lot to lot release

- Inspections at regular intervals.
- Inform WHO of serious GMP deviations

Post-marketing surveillance for safety and efficacy
- Inform WHO in case of reports of serious AEFI

Inform WHO in case of withdrawals or recalls of lots and license suspensions
Conditions for prequalification (2)

Commitments from the manufacturer

- Report variations to WHO
- Report serious AEFI
- Communicating with WHO
  - Inform of WHO of problems that may impact the quality, safety, efficacy or timely supply of product
  - Provide regular updates of safety profile
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Prequalification process (1)

- Pre-submission meetings with manufacturers interested in submission are available and encouraged
- Notification of intended submission
- Dossier Submission
  - Product Summary File (until end 2021)
  - Common Technical Document (mandatory from Jan 2022)
- Screening
- Acceptance decision
Prequalification process (2)

Prequalification process

• Scientific review of quality dossier
• Scientific review of clinical data
• Testing of samples
• Consultation with responsible NRA
• Site audit of manufacturing facilities
Prequalification process (3)

Programmatic Suitability for PQ (PSPQ):
Ensure that vaccines used in low and middle income countries can be used safely and effectively, given the constraints and conditions of their immunization systems.
Prequalification process (4)

Programmatic Suitability for PQ (PSPQ):

• Objectives:
  ✓ Judge the programmatic suitability against defined mandatory, critical and preferred characteristics

• Benefits:
  ✓ Give clear directions to vaccine manufacturers before PQ submission
  ✓ Reduce decision making time
Prequalification process (5)

PSPQ criteria

Mandatory

- Compliance is compulsory
- Failure to meet this characteristic will prevent the vaccine to be further considered for pre-qualification

Critical

- Compliance is also compulsory
- However, deviations in vaccine characteristics will be reviewed by the Programmatic Suitability for WHO Prequalification (PSPQ) Standing Committee
- Under special circumstances exceptions can be granted to vaccines that deviate from the critical characteristics.
- Decision can only be taken by the PQ Secretariat and will include consideration of recommendations from the PSPQ Standing Committee and consideration of topics such as public health need and access to vaccines.
Prequalification process (6) - flowchart

Dossier submission

Screening

NRA functionality/maturity level 3

Programmatic suitability

Dossier review

Laboratory testing

Prequalification decision

Inspection

Follow-up inspection

CAPA¹

Copenhagen, Denmark 2 – 5 December 2018
## Prequalification process (7)

### Critical requirements for PQ

<table>
<thead>
<tr>
<th>Quality</th>
<th>Clinical</th>
<th>Programmatic</th>
<th>Regulatory</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Stability data at accelerated conditions to allow implementation of VVM</td>
<td>• Clinical expectations (immunogenicity / efficacy / safety)</td>
<td>• Compliance with Programmatic suitability criteria (PSPQ):</td>
<td>• Registration by functional NRA</td>
</tr>
<tr>
<td>• Manufacturing and QC data</td>
<td></td>
<td>• Relevance to preferred target product profile.</td>
<td>• Compliance with global standards and PSPQ (i.e., monodose vs multidose presentations), Non-auto-disable syringes</td>
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Prequalification process (8): 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
Prequalification process (9)

As part of the evaluation procedure, consultation with NRA

- To discuss 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
- Informal agreement for information sharing with WHO recorded in Consultation report
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Post Prequalification activities

• Variations
• Annual Report evaluation
• Reassessment (frequency defined on risk analysis basis)
• Targeted testing program with contracted laboratory: once a year testing of samples of lots shipped to countries to ensure continuing compliance with specifications
• Monitoring/Investigation of vaccine quality and cold chain complaints
• Monitoring/investigation of Adverse Events following immunization (AEFI) (with collaboration of the responsible NRA)
• Collaborative National Registration
• Technical Review of tenders for UNICEF
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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
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Preparing for success for PQ

- Where is the vaccine to be manufactured?
- What is the status of the NRA in that country?
- Are programmatic suitability and PQ conditions met?
- What are the expected timelines for CT, regulatory submission, PQ submission?
- Is there a need to develop WHO (ECBS) guidelines/recommendations?
- Inclusion on priority list – prepare in advance
Thank you