WHO PQ: Vaccine PQ overview

Olivier Lapujade
Vaccines & Immunization Devices Assessment Team (VAX)
Prequalification Team Unit (PQT)
Regulation and Prequalification Department (RPQ)
Access to Medicines and Health Products Division (MHP)
World Health Organization
Geneva, Switzerland

E-mail: vaccprequalification@who.int
Outline

• Introduction

• Overview on Prequalification process :
  ➢ Pre-conditions for PQ evaluation
  ➢ Conditions for PQ
  ➢ Process
  ➢ Monitoring
  ➢ Timelines

• Advantages of having PQed vaccines
Access to Medicine and Health Products organigram

Health Products Policy and Standard (HPS)
- Unit Technical standards & specifications (TSS)
- Unit INN & classification of medical products
- Unit Expert Com on Drug Dependence
- Unit Medicines selection, IP, affordability
- Unit Access to assistive technology
- Global guidance on rational/optima use
- Monitoring, implementation & reporting
- Transparency & governance

Regulation and Prequalification (RPQ)
- Unit Prequalification (PQ)
  - Office of the Unit Lead
    - Inspection Services
    - IVD Assessment
    - Medicines Assessment
    - Vaccines & Immunization Devices Assessment
    - Vector Control Products Assessment
- Unit Regulation and Safety (REG)
  - Office of the Unit Lead
    - Regulatory Systems Strengthening
    - Regulatory Convergence and Networks
    - Facilitated Product Introduction
    - Laboratory Network and Services
    - Pharmacovigilance
    - Incidents and SF Medical Products

Office of the Director
- Cross-cutting Lead Product Safety
- Cross-cutting Lead Local Production and Industry Support

Version June 2020
Access to Medicine and Health Products organigram

Health Products Policy and Standard (HPS)
- Unit Technical standards & specifications (TSS)
- Unit INN & classification of medical products
- Unit Expert Com on Drug Dependence
- Unit Medicines selection, IP, affordability
- Unit Access to assistive technology
- Global guidance on rational/optima use
- Monitoring, implementation & reporting
- Transparency & governance

Regulation and Prequalification (RPQ)
- Unit Prequalification (PQ)
  - Office of the Unit Lead
    - Inspection Services
    - IVD Assessment
    - Medicines Assessment
    - Vaccines & Immunization Devices Assessment
    - Vector Control Products Assessment
- Unit Regulation and Safety (REG)
  - Office of the Unit Lead
    - Regulatory Systems Strengthening
    - Regulatory Convergence and Networks
    - Facilitated Product Introduction
    - Laboratory Network and Services
    - Pharmacovigilance
    - Incidents and SF Medical Products

Cross-cutting Lead
- Technical Coordination
- Product Safety
- Local Production and Industry Support

Office of the Director

Version June 2020
WHO Goal for vaccines regulation

Ensure that “100%” of vaccines used in all national immunization programmes are of assured quality

Definition of “Vaccines of Assured quality”

- National Regulatory Authority (NRA) independent from vaccine manufacturer & procurement system
- NRA is functional or at least maturity level 3
- No unresolved reported problem with vaccine

WHO guidance by Experts Committee on Standardization of Biologicals (ECBS) recommendations on safety, efficacy and quality issued in WHO Technical Report Series (TRS)
Prequalification (PQ) of Vaccines by WHO

– 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,
  • 157 vaccines prequalified (250 presentations) on 8 March 2022
– Facilitates registration in developing countries
– Countries can rely on PQ assessment, inspection, lot testing, etc.
– PQ can also rely on other assessments

Vaccine PQT website: https://extranet.who.int/pqweb/vaccines
Purpose of WHO vaccines prequalification 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.
Principles

Reliance on NRA

Meeting WHO requirements and tender specifications

Consistency of final product characteristics

Clinical data

GMP
Pre-conditions for PQ evaluation

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

- NRA must be assessed as functional/at least ML3 as a result of successful evaluation using the WHO NRA assessment tool
- NRA’s functional/at least ML3 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
WHO concept of Vaccine Regulation

Before 2015

National Regulatory System: Governance + six regulatory functions

1. Marketing Authorization (MA) and Licensing Activities
2. Post-marketing activities including surveillance of Adverse Events Following Immunization (AEFI)
3. NRA Lot Release
4. Laboratory access
5. Regulatory Inspections
6. Authorization/Approval of Clinical Trials
WHO recommended regulatory functions for Medicines and Vaccines based on product lifecycle since 2015.

**Product Lifecycle**

**Pre-Marketing**
- Pre-clinical
- Clinical
- Production & Quality Control

**Post-Marketing**
- Marketing and sales
- Post-Marketing

**Common Regulatory Functions**
- Next steps: Medical devices, Blood & (2017)

**Non Common Regulatory Functions**
- (vaccine)

**National Regulatory System**
- National Regulatory System (RS)
- Regulatory Inspection (RI)
- Laboratory access and Testing (LA)
- Clinical Trial's Oversight (CT)
- Vigilance (PV)
- Licensing premises (LI)
- Registration & marketing authorization (MA)
- Market surveillance and Control (MS)
- NRA Lot release (LR)
### WHO GBT Performance Maturity Levels

<table>
<thead>
<tr>
<th>ISO 9004</th>
<th>WHO GBT</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>No formal approach</td>
</tr>
<tr>
<td>2</td>
<td>Reactive approach</td>
</tr>
<tr>
<td>3</td>
<td>Stable formal system approach</td>
</tr>
<tr>
<td>4</td>
<td>Continual improvement emphasized</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>ISO 9004</th>
<th>WHO GBT</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Some elements of regulatory system exist</td>
</tr>
<tr>
<td>2</td>
<td>Evolving national regulatory system that partially performs essential regulatory functions</td>
</tr>
<tr>
<td>3</td>
<td>Stable, well-functioning and integrated regulatory system</td>
</tr>
<tr>
<td>4</td>
<td>Regulatory system operating at advanced level of performance and continuous improvement</td>
</tr>
</tbody>
</table>

- Can be considered as functional if rely on other regulators for some specific functions
- Target of WHA Resolution 67.20
- Advanced/reference Regulatory Authorities

---

[https://www.who.int/tools/global-benchmarking-tools](https://www.who.int/tools/global-benchmarking-tools)
Pre-conditions for PQ evaluation

- Vaccine is licensed/registered by the responsible NRA (Scientific opinion by EMA accepted)

- WHO guidelines/recommendations approved by the ECBS are available (published in the WHO Technical Report Series)

- Listed in the vaccine priority list (low priority vaccines may be postponed depending on workload and no priority vaccines will not be reviewed)
Conditions for prequalification

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 PQ evaluation

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
Prequalification process

• Scientific review of quality dossier
• Scientific review of clinical data
• Testing of samples
• Consultation with responsible NRA
• Site inspection to manufacturing facilities

https://www.who.int/immunization_standards/vaccine_quality/TRS_978_61st_report_Anne_x_6_PQ_vaccine_procedure.pdf
Monitoring performance of PQd vaccines

• Targeted testing by WHO contracted labs: Once a year testing of samples of lots shipped to countries to ensure continuing compliance with specifications

• Monitoring and resolution of complaints and reports of AEFIs (with collaboration of the responsible NRA)

• Reassessments frequency defined on risk analysis basis
Role of NRA during PQ process

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

- 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
Programmatic suitability

Vaccines produced in developed countries may not have taken into account programmatic challenges in developing countries.

- Non auto-disable prefilled syringe presentations
- Stability of components in the event of cold chain breakdown

WHO PQT has **always considered programmatic suitability** but it was **in 2012 that a written guidance (PSPQ) was developed and put in place**

PSPQ procedure:  
https://apps.who.int/iris/bitstream/handle/10665/148168/WHO_IVB_14.10_eng.pdf
## Critical requirements for PQ

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

Dossier Submission
(only CTD format accepted since 1st Jan 2022)

Screening

NRA
Functional/Maturity level 3

PSPQ

1) CAPA
2) FU Inspection (if needed)

Dossier evaluation

Testing

Testing

Inspection

Inspection

Prequalification decision

270 days

Expedited procedure

Answers
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
- 90/100 days internal time
Why is Vaccines PQ important for: 
- user countries and its NRAs? 
- manufacturers 
  - It represents a source of vaccines of "assured quality"
  - In addition the evaluation is focused on programmatic needs
  - WHO follows up on complaints and reports of AEFIs and publishes the outcome of investigations
  - WHO monitors the quality of prequalified vaccines on a continuing basis, through testing of samples, reassessment of the products, targeted inspections, and delists vaccines if they do not meet the established specifications and/or standard
  - Opportunity for NRAs in user countries to save resources to focus on other priorities, since registration can be granted through a facilitated and shortened procedure

Manufacturers are advised to request pre-submission meeting(s) during the development of the vaccine.
Link to vaccine PQT webpage: https://extranet.who.int/pqweb/vaccines

Thank you