Assuring vaccine quality: Overview of Prequalification

DCVMN meeting
Sao Paulo UNICEF, Copenhagen 8-9 October 2014
Carmen Rodriguez Hernandez
World Health Organization, EMP/RHT/PQT
rodriguezhernandezc@who.int
Outline

- Overview on Prequalification
- Programmatic suitability for PQ
- Strategic priorities
- Activities to facilitate access of vaccines:
  - Polio eradication and end game strategy
  - Activities to facilitate license of IPV and bOPV
- Path forward
- Technical assistance and capacity building
Prequalification

- Ensures the quality, efficacy and safety of medicines, vaccines and immunization devices and diagnostics.
- Medicines:
  - Prequalification programme for medicines (finished dosage forms)
  - Prequalification of active pharmaceutical ingredients (APIs)
  - Prequalification of quality control (QC) laboratories
  - Expanding access to priority essential medicines: HIV/AIDS, tuberculosis, Malaria, Reproductive Health and some other disease categories (e.g. NTD)
- Vaccines and immunization devices:
  - Ensures that candidate vaccines are suitable for the target population and meet the needs of the programme
Prequalification is NOT stand alone activity
Many other technical work areas support and link to prequalification (medicines, vaccines, diagnostics and medical devices)

- Outside EMP – Disease oriented departments/programs, IVB Department, Strategic Advisory Group of Experts (SAGE) on Immunization; Regional and Country Offices
- Inside EMP – Norms and standards work/Quality Assurance, Safety/Vigilance, Activities to combat SFFC medical products, NRA strengthening, Policy, Innovation and technology transfer

New prequalification team: five functional groups

- **PQT Coordinator**
  - Inspections services
    - Deus Mubangizi
  - Technical assistance and laboratory services
    - Milan Smid
- Medicines assessment
  - Matthias Stahl
- Vaccines assessment
  - Carmen Rodriguez
- Diagnostics assessment
  - Irena Prat
WHO uses the same scientific principles to assess the products' safety, quality and efficacy/performance as well-resourced national regulators:

- Scientific assessment of documentary evidence for quality, safety and efficacy
- Assessment of suitability for use of the vaccine in the intended settings
- Site inspections for GMP, GLP and GCP
- Control of variations to products and their manufacturing processes
- Post-approval monitoring of quality and safety
Extensive multilayer collaboration: working with regulators … for regulators

- Not duplicating work done by stringent regulatory authorities
  - SRA approval of new and generic products – abridged procedure
  - US FDA tentative approvals – based on confidentiality agreement including in the PQ products list
  - European Medicines Agency (EMA) – Art 58 … and beyond
  - Collaboration with EDQM, in particular in the area of APIs (confidentiality agreements with US FDA, EDQM, EMA …)

- Active participation and involvement of
  - Regulatory authority experts from well resourced and less resourced settings WORKING TOGETHER for common goal
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 as a result of successful evaluation using the WHO NRA assessment tool
NRA’s functional 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 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)
Prequalification process

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

Revised procedure in place from January 2012
Role of NRA during PQ process

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
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
Why is Vaccines PQ important for user countries and its NRAs?

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 audits, 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
Programmatic suitability and its assessment

- Vaccines produced in developed countries may not have taken into account programmatic challenges in developing countries.
- **Examples:**
  - 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
Programmatic suitability

- **Objectives of PSPQ**
  - Judge the programmatic suitability against defined mandatory, critical and preferred characteristics

- **Benefits of PSPQ**
  - Give clear directions to vaccine industry before submission
  - Reduce decision making time
Strategic priorities

- Secure the supply base for priority medicines
- Facilitate access to quality products for developing countries
- Improve efficiency of the prequalification procedure
- Expand portfolio according to needs and options for introduction
Supply Security

Monitor closely the performance of prequalified vaccines including FU audits and conducting production capacity assessments.

Actively seek for additional sources for priority vaccines.

Secure the supply base for priority vaccines for developing countries.

Establish risk mitigation strategies in case of failure of NRA.
Access

Facilitate access to quality products for developing countries

- Single standard of quality (WHO recommended requirements)
- Consolidated investigation, reporting and communication in response to quality or safety concerns
- Implementation of an expedited/facilitated registration procedure for prequalified vaccines in receiving countries
- Mechanisms to minimize wastage of vaccines, facilitate outreach (VVMs, MDVP, CTC)
Contribution development of Controlled Temperature Chain Project Optimize: PATH/WHO

Nicaragua, rotavirus delivery, Photo: Gates Foundation

Transport to health centre
Allow specific vaccines to be kept and administered at ambient temperatures, up to 40°C. For one, limited period of time immediately preceding administration. For vaccines meeting a number of stability conditions.

Current focus: vaccines administered during campaigns and special strategies: eg Meningo conjugate A, Yellow Fever, Pneumo, Hepatitis B, Rota, Cholera.

Manufacturers:
Studies to enable on label use of vaccines under CTC and regulatory submissions.

Regulators:
Regulatory pathways
Review data for licensing under CTC

WHO:
CTC Guidelines (Norms)
Work w/regulators to define Regulatory Pathways and prequalification (vPQ)
Field studies to show programmatic challenges, opportunities and impact of CTC (EPI-IVB)
Accelerated registration of WHO prequalified vaccines

**Objective**

Assist countries to adopt a facilitated, expedited procedure for the national registration of prequalified vaccines.

**Who can benefit**

Countries procuring through UN agencies and/or
Countries procuring directly but requiring WHO prequalification as a tender condition where the national regulations include provisions to shorten the normal regulatory approval process.
Implementation of Procedure for expedited review of imported prequalified vaccines for use in national immunization programmes (WHO/IVB/07.08)

Firstly used for registration of MenAfriVac in 26 countries of the belt
Accelerated national registration of WHO-prequalified pharmaceutical products and vaccines.

<table>
<thead>
<tr>
<th>Vaccines</th>
<th>Pharmaceuticals</th>
</tr>
</thead>
<tbody>
<tr>
<td>Procedure for expedited review of imported prequalified vaccines for use in national immunization programmes (WHO/IVB/07.08)</td>
<td>Collaborative procedure between the World Health Organization Prequalification of Medicines Programme and national medicines regulatory authorities in the assessment and accelerated national registration of WHO-prequalified pharmaceutical products.</td>
</tr>
<tr>
<td>Expert Committee on Biological standardization</td>
<td>Expert Committee on Specifications for Pharmaceutical Preparations</td>
</tr>
<tr>
<td>Firstly used for registration of MenAfriVac in 26 countries of the meningitis belt</td>
<td>Procedure in place since 2012 Collaborative agreements signed with 20 National Regulatory authorities 33 procedures finalized Details on <a href="http://www.who.int/prequal">www.who.int/prequal</a></td>
</tr>
</tbody>
</table>
Revision of procedure

WHO

NRA

Agreement

Facilitated license

Manufacturers
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
Summary

• Prequalification system ensures the quality, efficacy and safety of medicines, vaccines and immunization devices and diagnostics for global use.
• Assessment focused on programmatic needs
• Facilitate access to quality products for developing countries:
  • Control temperature chain
  • Shipping validation
  • Multidose vial policy
• The collaborative registration of PQed medicines is a work-sharing and confidential information sharing mechanism, which already produces results: in 80% of 33 procedures registration was granted in less than 90 days.
Relevant PQ information

http://www.who.int/immunization_standards/vaccine_quality/pq_system/en/
http://www.who.int/immunization_standards/vaccine_quality/pq_suppliers/en/
http://www.who.int/immunization_standards/vaccine_quality/ps_pq/en/
http://www.who.int/immunization_standards/vaccine_quality/expedited_review/en/