Prequalification overview.
Outline

• WHO PQ process
• PQ of vaccines:
  • Principles and conditions
• PQ process
• PSPQ
• Past and current challenges
• Post-PQ monitoring activities
• PQ of immunization devices and equipment
Through the prequalification process, WHO has made available numerous quality-assured products to WHO Member State markets.

At the close of 2016, PQT's list of prequalified products included:

- **Medicines**
  - 416 FPPs
  - 100 APIs
  - 41 QCLs

- **Diagnostics**
  - 64 IVDs
  - 2 MCDs

- **Vaccines**
  - 147 Vx
  - 310 ImDs

- **Vector control**
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 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
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
Prequalification process: the Past

- PQ vaccines extensively used
- Immunization programmes

- Novel vaccines/new combinations licensed by industrialized countries

- Container closure PFS
- Composition
- Stability profile
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.

Nicaragua, rotavirus delivery. Photo: Gates Foundation

Mali, polio campaign. Photos: WHO/Olivier Ronveaux
Programmatic Suitability for Prequalification

- 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
Vaccine characteristics that will affect pre-qualification

Mandatory

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

Critical

• Compliance with PSPQ criteria 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.
Vaccine characteristics that are unique

Unique (characteristics not otherwise specified)

- Are reviewed by the PSPQ Standing Committee
- May be pre-qualified if considered suitable by the PQ Secretariat on the advice of the PSPQ Standing Committee
Submission Screening and Standing Committee Assessment

• Upon receipt, dossiers are screened for completeness and compliance with the required format and contents by the PQ secretariat.

• Dossiers are also screened for compliance with programmatic suitability criteria:
  • If mandatory characteristics are not met, the dossier is rejected.
  • If there is a deviation from a “critical” criterion or if a unique characteristic is identified, the vaccine will be referred to the PSPQ standing committee for independent review.

http://www.who.int/immunization_standards/vaccine_quality/pspq2_v140512.pdf
### Past and current challenges

<table>
<thead>
<tr>
<th>Quality</th>
<th>Clinical</th>
<th>Programmatic</th>
<th>GMP</th>
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| 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
- Regulatory
- Post-PQ monitoring
- Quality, safety and efficacy

Publication of PSPQ criteria and establishment of Standing committee on PSPQ
Collaboration agreements with National Regulatory Authority of record for PQ
Briefing on PQ expectations (workshops and webinar)
Guidance documents
Pre-submission meetings
Consolidated investigation, reporting and communication in response to quality or safety concerns

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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: AVAREF
Prequalification of immunization devices and equipment
Scope Prequalification
immunization devices and equipment

Three steps cycle

Standards and Innovation
- Identify requirements
- Develop and maintain performance specifications and verification protocols

Prequalification
- Immunization devices
- Cold chain equipment

Post- PQ monitoring
- Monitor products and inform new requirements

Innovation 3 + 2
- Product performance validation protocol (field monitoring and field testing)
- Target product profile
STANDARDS, GUIDELINES & INNOVATION

Develop product Specifications that suit the environmental, infrastructural and socio-economic context of countries (LMICs) for procurement by UN Agencies

Develop verification protocols to test the candidate products against the specifications

Develop guidelines for manufacturers on how to apply for prequalification for each category of product

Develop guidelines for countries in the PQS catalogue on how to go about the selection of the various equipment available

Shipping guidelines revision Consultation process
PRE-QUALIFICATION

Expression of interest from the manufacturer – a letter explaining the manufacturers intentions and any specific questions from the manufacturers

Invitation to apply for PQ

List of documents, samples and/or laboratory tests to be submitted for the pre-qualification

Dossier examination

Prequalification
Categories of Devices

1. E001 – Cold Rooms and Freezer Rooms
2. E002 – Transport
3. E003 – Refrigerators and Freezers
4. E004 – Cold boxes and vaccine carriers
5. E005 – Coolant packs
6. E006 - Temperature monitoring devices
7. E007 - Cold chain accessories
8. E008 - Injection devices for immunization
9. E010 - Waste management equipment
10. E013 - Injection devices for therapeutic purposes
Prequalification of Immunization equipment

# of products

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<thead>
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PRE-QUALIFICATION FIELD PERFORMANCE EVALUATION

Introduced in 2016

Generic field evaluation protocol published

Applies to new technology

Purpose is to have a minimum of field performance data before prequalification
POST-QUALIFICATION MONITORING

• Systematic feedback from the field on equipment performance and failures
• Serves as an important information source for the development of future product TPPs
• Currently there is no active system in place
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/pspq2_v140512.pdf"

- Clinical
  - "http://who.int/entity/biologicals/vaccines/clinical_evaluation/en/index.htm"
    - "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,
WHO GMP for sterile pharmaceutical products, Annex 6, WHO TRS 961, 2011