Vaccine assessment for prequalification

Briefing on Vaccine Prequalification for manufacturers
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Olivier Lapujade
World Health Organization, EMP/RHT/PQT
lapujadeo@who.int
Outline

- Vaccine regulation
- Overview on Prequalification
- Challenges PQ
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 (system + 6, 4 or 3 regulatory functions implemented)
- 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)
WHO concept of Vaccine Regulation

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
Required functions according to vaccine source

<table>
<thead>
<tr>
<th>Vaccine Source</th>
<th>MAA &amp; licensing</th>
<th>PMS</th>
<th>Lot release</th>
<th>Lab access</th>
<th>Regulatory Inspections</th>
<th>Authorization &amp; monitoring CT</th>
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<tbody>
<tr>
<td>UN agency supply</td>
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<td>Direct purchase</td>
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<td>Producing country</td>
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Regulatory System

Exporting country NRA+ WHO-PQ

All countries where CTs are performed
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)
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
- Inform of WHO of problems that may impact the quality, safety, efficacy or timely supply of product
- Report serious AEFI
- 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 audit to manufacturing facilities
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
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
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
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 AEFIIs (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
## Past and current challenges

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<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  
Inappropriate devices: 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
- Post-PQ monitoring
- Regulatory
- 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-PQ monitoring
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