Collaborative procedure for registration of PQed vaccines

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Outline

• Strategic priorities
• Activities to facilitate access of vaccines
• Collaborative procedure for facilitating registration of PQed vaccines
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
### Access

<table>
<thead>
<tr>
<th>Access</th>
<th>Single standard of quality (WHO recommended requirements)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Consolidated investigation, reporting and communication in response to quality or safety concerns</td>
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<tr>
<td></td>
<td>Implementation of an expedited/facilitated registration procedure for prequalified vaccines in receiving countries</td>
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<tr>
<td></td>
<td>Mechanisms to minimize wastage of vaccines, facilitate outreach (VVMs, MDVP, CTC)</td>
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</tbody>
</table>

Facilitate access to quality products for developing countries
Contribution development of Controlled Temperature Chain Project Optimize: PATH/WHO

Mali, polio campaign, Photos: WHO/Olivier Ronveaux

National cold room during the campaign

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

<table>
<thead>
<tr>
<th>Manufacturers</th>
<th>Regulators</th>
<th>WHO</th>
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<tbody>
<tr>
<td>Studies to enable on label use of vaccines under CTC and regulatory submissions</td>
<td>Regulatory pathways</td>
<td>CTC Guidelines (Norms)</td>
</tr>
<tr>
<td>Review data for licensing under CTC</td>
<td>Work w/regulators to define Regulatory Pathways and prequalification (vPQ)</td>
<td>Field studies to show programmatic challenges, opportunities and impact of CTC (EPI-IVB)</td>
</tr>
</tbody>
</table>
## 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)
Registration of prequalified vaccines
Rationale

Although WHO prequalified vaccines are thoroughly assessed and manufacturers are inspected according to WHO/international standards, NRAs of importing countries have to be register the vaccine. Slow registration due to insufficient resources delays availability of vaccines.

Registration of PQd vaccines could be facilitated by closer cooperation among WHO, NRAs and manufacturers.
Rationale

Prerequisite of facilitated national registration is the communication of confidential data and therefore procedure must be well defined and agreed by all participating parties. Common assessment and inspections are useful practice, but not always are applicable.
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
EXPEDITED LICENSE PROCEDURE (1)

Why is an expedited procedure for registration of WHO prequalified vaccines being proposed?
Because... this is how UN supplied vaccines are evaluated

<table>
<thead>
<tr>
<th>Aspects considered</th>
<th>Exporting Country NRA</th>
<th>WHO prequalification procedure</th>
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<tbody>
<tr>
<td>Chemico pharmaceutical and biological</td>
<td>Exhaustive review</td>
<td>Review of summary information</td>
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<tr>
<td>Non-clinical data</td>
<td>Exhaustive review</td>
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</tr>
<tr>
<td>Clinical data</td>
<td>Relevance of data for exporting country</td>
<td>Relevance of data to UN target population</td>
</tr>
<tr>
<td>GMP</td>
<td>Compliance with National standard</td>
<td>Compliance with WHO standard</td>
</tr>
<tr>
<td>Consistency testing</td>
<td>Sometimes</td>
<td>Always</td>
</tr>
<tr>
<td>Schedule, co-administration</td>
<td>Relevance to exporting country</td>
<td>Relevance to UN population</td>
</tr>
<tr>
<td>Stability profile &amp; shelf life</td>
<td>Suitability for exporting country</td>
<td>Suitability for UN target population + VVM</td>
</tr>
<tr>
<td>Applicability of multidose vial policy</td>
<td>---</td>
<td>Assessed</td>
</tr>
<tr>
<td>Presentation</td>
<td>Highly flexible</td>
<td>Critical: vials and AD syringes</td>
</tr>
<tr>
<td>Shipping boxes</td>
<td>---</td>
<td>Validation assessed</td>
</tr>
</tbody>
</table>

Copenhagen, Denmark  23-26 November 2015
EXPEDITED LICENSE PROCEDURE (2)

Why is an expedited procedure for registration of WHO prequalified vaccines being proposed?

– Save resources that can be targeted to other activities (i.e. strengthening post-marketing surveillance, focusing on the detailed review of non-prequalified vaccines)

– Accelerate the registration procedure without disrupting the supply of the vaccines
Accelerated national registration of WHO-prequalified pharmaceutical products and vaccines.

<table>
<thead>
<tr>
<th>Vaccines</th>
<th>Pharmaceuticals</th>
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<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

Manufacturers

Agreement

Facilitated license

Copenhagen, Denmark | 23-26 November 2015
Principles of the procedure

1. Procedure is voluntary for manufacturers and NRAs and providing benefits to both parties.
2. With consensus from manufacturer, full PQ PSF and site audit report plus initial testing results will be shared with interested NRAs to facilitate national regulatory decisions making (registrations, variations, withdrawals).
3. No interference with national legislation, decision making process and regulatory fees – but PQ expertise is available to NRAs.
Principles of the procedure

4. Since there is agreement to share reports, the registration dossier should be in principle the same as the PSF approved by PQ.

5. Each participating authority commits to adopt registration decision within 90 days after having access to full PQ reports.

6. The NRA has the right to:
   – decline to adopt procedure for specific products
   – decide differently from PQ, but keep PQ informed and clarify the reasons for deviation.
Key elements: Agreement

- NRA confirms to WHO PQ its interest to participate in collaborative procedure and respect its conditions
- One or two focal persons are designated at each interested NMRA, sign confidentiality undertaking and are given access to the WHO managed restricted access
Key elements: registration

Applicant submits dossier to NRA as per national procedures (content should be the same as that in the PSF)

Applicant pays fees to NRA as per national rules

Applicant informs WHO and gives written consent for WHO to share information

NRA makes a decision and informs PQ
Post-registration

Variations are communicated from WHO to NRA

If national rules on variations differ from WHO-PQ variations
NRA will inform PQ

WHO-PQ informs NRA about withdrawals, suspensions, delisting.
Win-win situation

NRAs
– Availability of WHO assessment and inspection outcomes to support national decisions
– Opportunity to learn from PQ assessors and inspectors
– Saving internal capacities

• WHO and UN agencies
  – Prequalified vaccines are available sooner
  – Feed-back on WHO prequalification outcomes

Manufacturers
  – Harmonized data for PQ and national registration
  – Accelerated and more predictable registration
Experience with the procedure for medicines: participating NRAs

Armenia
Botswana
Dem. Rep of Congo
Ethiopia
Georgia
Ghana
Kenya
Kyrgyzstan
Madagascar
Malawi

Mozambique
Namibia
Sierra Leone
Nigeria
Tanzania
Uganda
Ukraine
Zambia
Zanzibar
Zimbabwe
Steps of the procedure: agreement

- NMRA confirms to WHO PQP its interest to participate in collaborative procedure and respect its conditions
- One or two focal persons are designated at each interested NMRA, sign confidentiality undertaking and are given access to the WHO managed restricted access web-site
Joint collaborative procedure for pharmaceuticals and vaccines: Path forward

• Revised procedure published on the web
  http://www.who.int/immunization_standards/vaccine_quality/expedited_review/en/
• Discussion with stakeholders started
• Pilot for vaccines being used
• Endorsement by relevant expert committees expected in 2015
• Extension of current agreements with NMRAs to vaccines (potentially also Diagnostics)
• Based on collaboration agreements, full reliance on PQ as potential mechanism for accelerated registration of products for emergency use. Eg flu, Ebola
• Newcomers are welcome to participate!
The Strategic Advisory Group of Experts on Immunization (SAGE), recommended in 2012 the withdrawal of the type 2 component of oral polio vaccine (OPV) from routine immunization programmes in all countries, facilitated by the introduction of at least one dose of IPV.

Weekly epidemiological record wer 8901

The last case of wild poliovirus type 2 (WPV2) was seen in 1999.

88% of the total of the circulating vaccine derived poliovirus (cVDPV) cases in recent years were caused by the vaccine derived type 2 strain.

Introduction of IPV by 2015 and bOPV by 2016 in all countries.
Facilitating license of IPV: PQ pathway

WHO

NRA

Manufacturers

Agreement

Joint review

Facilitated license

Copenhagen, Denmark      23-26 November 2015
Path forward facilitating license of IPV

Joint review

AFRO countries
20-24 October 2014 Turkey

Francophone countries:
Benin, Burkina Faso, Cameroon, Cote d’Ivoire, Mali, Senegal, Togo

Anglophone countries:
Botswana, Ethiopia, Ghana, Sierra Leone, Tanzania, Uganda, Zambia, Zimbabwe: ENGLISH

SEARO countries
10-14 November Thailand

Bhutan, Myanmar and Sri Lanka

Copenhagen, Denmark | 23-26 November 2015
Facilitating license of other PQed vaccines

<table>
<thead>
<tr>
<th>Vaccine</th>
<th>Country</th>
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<tbody>
<tr>
<td>Pneumococcal vaccine Prevenar 13 Pfizer United States</td>
<td>Eritrea</td>
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<tr>
<td></td>
<td>Lesotho</td>
</tr>
<tr>
<td></td>
<td>Sudan</td>
</tr>
<tr>
<td>Inactivated polio vaccine SP France</td>
<td>Sudan</td>
</tr>
<tr>
<td>DTwP-hepatitis B-Hib vaccine Serum Institute of India (SII)</td>
<td>Nigeria</td>
</tr>
<tr>
<td>Measles SII</td>
<td>Nigeria</td>
</tr>
<tr>
<td>Tetanus SII</td>
<td>Nigeria</td>
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Access of vaccines

Regulatory Requirements

Access of vaccines eg polio, flu
Pandemic influenza preparedness

• Advocacy of collaborative procedure to facilitate registration of PQd vaccines

• Mapping of countries that have licensed seasonal and pandemic vaccines in all regions

• Mapping of countries accepting the collaborative procedure in all regions

• Development of criteria for facilitating registration of pandemic flu vaccines in an emergency situation.

• Joint reviews for facilitating license of prequalified seasonal flu vaccine with potential impact on pandemic flu vaccine
Regulatory challenges: Prequalification approach

- PQed Vaccines licensed by a functional National regulatory Authority
- Collaboration between PQ and NRA for information sharing (initial evaluation and Post-PQ)
- Prequalification assessment includes experts from different settings.
- Capacity building activities:
  - Participation in file review for PQ and rotational fellowship
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/