Quality assurance for essential medicines and health products: moving towards an harmonized approach

Prequalification of vaccines

David Wood QSS/EMP/WHO
12 December 2012
A growing portion of vaccines procured by the UN come from emerging market country manufacturers

*2011 – 2012 Data from UNICEF based on awards already made
WHO Approval of the State Food and Drug Administration, China
(announced on 1 March 2011)
Implications of Approval of the State Food and Drug Administration, China

Vaccines from China are eligible for WHO prequalification

- 22 March 2011 meeting attended by more than 30 vaccine manufacturers from China
- Strong interest in supply to global market through WHO PQ and UN procurement
- Priorities being established for PQ submissions from China
Vaccines prequalified by WHO: Status 2011 (assured quality)

- **15** industrialized country mfrs
  - Australia
  - Belgium
  - Canada
  - Denmark
  - France
  - The Netherlands
  - Germany
  - Hungary
  - Italy
  - Japan
  - Rep. of Korea
  - Switzerland
  - Sweden
  - United Kingdom
  - USA

- **8** emerging economy country mfrs
  - Brazil
  - Bulgaria
  - Cuba
  - India
  - Indonesia
  - Russia
  - Senegal
  - Thailand

- **29** manufacturers

- **131** pre-qualified vaccines

- Used in **124** countries

- **64% total population**
WHO prequalification process

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

Revised procedure in place from January 2012
Vaccine prequalification - reliance on NRA

- The responsible National Regulatory Authority (usually that of the producing country) is **independent and functional**.
- Meets all the critical indicators required for prequalification purposes following a WHO independent assessment.
- The status of the NRA is reassessed at regular intervals.
Revised vaccines PQ procedure

- Introduced option for increased collaboration with mature National Regulatory Authorities (NRAs) following a risk-based approach
  - Collaborative agreements are being negotiated with eligible NRAs
  - WHO will retain responsibility for ensuring compliance with UN tender specifications and programme needs
  - WHO will also continue to be responsible for the continuous monitoring of the quality and safety of products, and also for a targeted testing programme
Revised vaccines PQ procedure (2)

• The revised procedure defines critical and desirable programmatic characteristics of vaccines and provides a clear review mechanism
  – clear message to manufacturers on what is required for prequalification
  – reduced timeframe for PQ is expected

• Clear definition of desirable product characteristics expected to facilitate the development of vaccines better suited for the countries and circumstances in which they are expected to be introduced
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: e.g. 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>
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<tr>
<td>Review data for licensing under CTC</td>
<td>CTC Guidelines(QSS)</td>
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<tr>
<td>Work w/regulators to define Regulatory Pathways and prequalification (QSS)</td>
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<td>Field studies to show programmatic challenges, opportunities and impact of CTC (EPI)</td>
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Some challenges
## Status of National Regulatory Authority, 2011

<table>
<thead>
<tr>
<th>Main source of vaccines</th>
<th>Functional</th>
<th>Not functional</th>
<th>Total</th>
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<tbody>
<tr>
<td>1. Producing</td>
<td>35 (80%)</td>
<td>9</td>
<td>44</td>
</tr>
<tr>
<td>2. Procuring</td>
<td>21 (44%)</td>
<td>27</td>
<td>48</td>
</tr>
<tr>
<td>3. UN agency</td>
<td>4 (4%)</td>
<td>98</td>
<td>102</td>
</tr>
<tr>
<td>Total</td>
<td>60 (4%)</td>
<td>133</td>
<td>194</td>
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Increased reports from field of quality defects

White sediment sticking to vaccine vials of DTwP-Hib-HBV vaccine
Potential solutions
Options being explored

- Intensified support to NRAs
  - support for expedited approval of PQd vaccines
  - global standards
  - especially for post-marketing surveillance capacity

- Intensified risk mitigation evaluations of manufacturers
  - quality management systems
Early introducers in 2010: Accelerated registration of MenAfriVac in Burkina Faso, Benin and Mali with support from WHO/QSS

Two Implementation workshops for other countries in meningitis belt conducted in 2011 in Kenya (11 English speaking) and Burkina Faso (10 French speaking)
  - 11 countries have since registered the Men A (MenAfrivac Vaccine, SII), equivalent to a completion rate of approximately 50%. Regular follow up with remaining countries to assist implementation of the procedure as required.

But…..PROCEDURE APPLIED TO ALL VACCINES IN NIPs

- Implementation workshop in Kenya (2012 English speaking) for registration of tetravalent, rotavirus and pneumococcal vaccines
- Implementation workshop in Philippines (2012) for registration of pentavalent vaccine
Development of global written standards by WHO (2010 - 2014)

- Cell substrates
  - YFV
  - Hep B
  - Vaccine lot release

- OPV (TRS 904, 910)
  - DTP (TRS 800) + Combo
  - Malaria (new)
  - JE LA

- IPV (TRS 926)
  - Typhoid vaccines
  - Regulatory Risk Assessment

- Dengue (TRS 932)
  - BCG (TRS 745, 771)
  - aP (TRS 878)

- Nonclinical evaluation of adjuvanted vaccines (new)
  - Biologicals derived by DNA tech (TRS 814)
Launch of Global Vaccine Safety Initiative
(November 2012)

- Facilitating development of systems for interaction between governments, multilateral agencies, and manufacturers
- Strengthen vaccine safety monitoring in all countries.
- Provide advice on vaccine safety issues, through the Global advisory committee on vaccine safety
- Strengthen countries ability to evaluate vaccine safety signals.
- Facilitate strengthening of regional and global technical support platforms
- Develop vaccine safety communication plans at country level
- Advocate for establishment of a legal, regulatory and administrative framework for PV
- Develop internationally harmonized tools and methods for vaccine pharmacovigilance
- Global Vaccine Safety Initiative
Facilitating access through… Support to manufacturers

● Published points to consider documents
  – Guideline for the preparation of the Product Summary File for Vaccine prequalification (WHO/IVB/06.16)
  – Clinical considerations for evaluation of vaccines for prequalification: Points to consider for manufacturers of human vaccines (web doc)
  – Environmental monitoring of clean rooms in vaccine manufacturing facilities: Points to consider for manufacturers of human vaccines (web doc draft)
  – Guide to Master Formulae (web doc)

● Points to consider documents under development
  – Validation of Production Processes for Vaccines and other Biologicals: Compliance Expectations
  – Risk analysis for deviations management
  – Variations (likely to be merged with NSB document)
through ... Support to manufacturers: India 3-5 Oct/12

India, Iran, Egypt and Bangladesh
Further information

- [www.who.int/immunization](http://www.who.int/immunization)
- [http://www.who.int/immunization_standards/](http://www.who.int/immunization_standards/)
- [www.who.int/biologicals](http://www.who.int/biologicals)
- [www.who.int/vaccine_safety](http://www.who.int/vaccine_safety)