Procedure for Expedited Review of imported pre-qualified vaccines for use in national immunization programmes

Dr Nora Dellepiane/Dr Anil Kumar Chawla

WHO/HQ-Geneva, Switzerland
Expedited review procedure

It is a procedure recommended by WHO to facilitate and accelerate the registration of imported prequalified vaccines in user countries.
BACKGROUND
Features of vaccines supplied through UN agencies

- Vaccines of "ASSURED QUALITY"
- WHO PREQUALIFIED
- Ongoing regulatory oversight in place
- Ongoing monitoring of quality and safety by WHO
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

30 manufacturers

121 pre-qualified vaccines used in 124 countries

64% total population
United Nations supplied vaccines

124 countries

UNICEF 90

PAHO 34

70-80% waive registration requirement for many of the vaccines used in NIPs

All countries should fulfil the registration requirements and implement the pharmacovigilance function.
# National Regulatory Functions & vaccine supply source

<table>
<thead>
<tr>
<th>Regulatory functions</th>
<th>Source of vaccines</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>UN agency</td>
</tr>
<tr>
<td><strong>Regulatory system</strong></td>
<td>✓</td>
</tr>
<tr>
<td><strong>Marketing Authorization/Licensing</strong></td>
<td>✓</td>
</tr>
<tr>
<td><strong>Post marketing surveillance/AEFI</strong></td>
<td>✓</td>
</tr>
<tr>
<td><strong>Lot release</strong></td>
<td>Functions</td>
</tr>
<tr>
<td><strong>Laboratory access</strong></td>
<td>undertaken in producing countries</td>
</tr>
<tr>
<td><strong>Regulatory inspections</strong></td>
<td></td>
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<tr>
<td><strong>Regulatory Oversight of CT</strong></td>
<td>In countries that conduct clinical trials</td>
</tr>
</tbody>
</table>
Vaccines recommended by WHO to be procured & used

- WHO vaccines prequalification procedure ensures that vaccines meet WHO recommended standards and programmatic needs of NIPs.

NEVERTHELESS

- WHO vaccine prequalification procedure **DOES NOT REPLACE** the regulatory oversight role of the National regulatory Authority of the importing country.

- Upon request from a group of countries, WHO developed a procedure for Expedited Review of Imported Prequalified Vaccines for Use in National Immunization Programmes.
Expedited review procedure

- 6 countries from SEARO region considered a waste of time to invest resources in evaluating these vaccines
- They met with WHO HQ and RO in 2005
- Discussed need for registration in all countries
- Proposed a "facilitated process" for registration (MA) of imported prequalified vaccines

THIS GAVE BIRTH TO THE EXPEDITED REVIEW PROCEDURE, SUBJECT OF THIS WORKSHOP
THE PROCEDURE
Expedited procedure for registration of WHO prequalified vaccines - Major Gains

- 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
Countries that can benefit from the procedure

- Countries that source their vaccines through UN agencies (i.e. UNICEF)
- Countries that procure their vaccines directly but that require WHO prequalification as a basis for selection of vaccines for purchase
- Countries where the national regulations include provisions to shorten the normal regulatory approval process.
Manufacturer's Benefits

- Authorized use of the product in receiving country.
- Interaction with NRA for any follow up or investigation.
- Facilitation in collection of PMS data.
- Facilitation for enlarging the scope of registration.
Requirements for implementation

- Political decision
- Integration into the national regulations
- Technical expertise to review the submission
Steps of the Procedure (in brief)

1. Check prequalification status
2. Submit product samples, product inserts, NRA lot release certificates from the country of origin, a list of countries where the product is licensed and marketed, and summary lot protocols of three final lots.
3. Visual inspection of samples
4. Review protocols (check specifications), labels, boxes and inserts against WHO model. Ensure presence of VVM
5. Prepare report of compliance (non-compliance)
6. If compliant, issue Certificate of Approval
7. Inform manufacturer and WHO
8. If novel vaccine with limited clinical data, review of clinical data may be needed
- **Time lines**

  - 30 days for routine evaluation
  - 90 days if testing is required
  - 120 days if clinical Review is needed
Implementation of the procedure in the African Region

- Implementation started with the registration of the Meningococcal A conjugate vaccine
  - Burkina Faso, Niger and Mali first three countries to apply and register the vaccine
  - Implementation workshops carried out in 2011 in Kenya for anglophone and in Burkina Faso for francophone countries with special focus on meningococcal A conjugate vaccine
  - Implementation workshop carried out in 2012 in Kenya for anglophone countries with focus on DTP-Hep B, rotavirus and pneumococcal vaccines
Participating countries (two representatives per country):

- English speaking: Uganda, Ghana, Nigeria, Rwanda, Tanzania, Guinea Bissau, Kenya, Ethiopia, Cameroon, the Gambia and Eritrea

- French speaking: Burkina Faso, Benin, Burundi, Central African Republic, Côte d'Ivoire, Gabon, Mauritania, Senegal, Tchad and Togo
Workshop 2012

Participating countries (two representatives per country):

- English speaking: Botswana, Ethiopia, the Gambia, Kenya, Malawi, Namibia, Uganda and Sierra Leone

- Focus: DTP-Hep B, rotavirus and pneumococcal vaccine with support from one manufacturer for rota and pneumo vaccines

Workshop for French speaking countries planned for 2013
Impact of the training

- 11 countries have since registered the Men A (MenAfrivac Vaccine, SII),
  - equivalent to a completion rate of approximately 50%. WHO is in the process of verifying the number of countries that have effectively used the procedure for registration of this vaccine.

- Regular follow up with countries to assist implementation of the procedure as required. In total, 22 countries have been approached for registration by the manufacturer by submitting Form 1A. WHO has issued Form 1B in all the cases. Thus there is 100% follow up rate from WHO.

- However, for the countries which have not completed the registration process, WHO has planned one to one follow up in last trimester of 2012.
Planned follow up in AFRO countries

- Two one on one follow up meetings are planned in November 2011 with AFR countries. There are two venues for these meetings i.e. South Africa and Benin. Two to four countries will be invited at each venue for this follow up meetings. The criteria for selection of participating countries is as follows:
  - Menafrivac registration still pending and introduction planned in the coming two years

- During these follow up meetings, the countries will be guided through the whole process using a mock application similar to what they are dealing with. This will ensure that they can go back to their countries and smoothly implement the procedure.
Implementation in other regions

- Implementation workshop conducted in EMRO in 2009
  - Two follow up meetings planned in October 2012 in this region.
    - Afghanistan NRA participants will be invited to WHO regional office in Cairo, Egypt. The country will be guided through the procedure using a mock application.
    - Visit to South Sudan, where a similar exercise will be carried out in NRA office or WHO country office.

- Implementation workshop to be carried out in the Philippines with 7 priority countries from the Region
Improvements introduced

- As the number of countries using the procedure increases,
- And since WHO commits to inform countries adopting the procedure about significant changes in the prequalification status
- A certain "automatization" of the process becomes necessary to ensure timely transmission of information to each adopting country for each vaccine type for which the procedure was followed
IMPLEMENTATION THROUGH INTERNET BASED APPLICATION
WHO Servers and Network

- Managed centrally
- High level Security
- Daily Back ups
- Restricted access and monitored 24X7
- Open access to external experts and organizations
- Through ADS account and authorization
Data base- Expedited Review Procedure

– Internet/Web based application

– Log in for NRA, Manufacturers and WHO

– All submissions and forms generation online through system except samples (Annex 1a, 1b, 1d and 1c)

– System generated emails to initiate action

– Monitoring and overall control by WHO
System for Expedited Review of Imported Prequalified Vaccines

This application is introduced to streamline the procedure for expedited review of imported prequalified vaccines for use in national immunization programs into an electronic system which facilitates and improves process oversight.

Access for Manufacturers’ and NRAs’ representatives...

1) Create an Application Directory Service (ADS) account:
   Use the link on the left toolbar "ADS Account" to create a new ADS account.

2) Request access using your ADS account:
   Log in using your newly created ADS account. From the left toolbar, use the link "Request" to request access to this system.

3) Log in:
   Once access is granted, you will receive a confirmation e-mail, and you will be able to use that same account to log in.

About the database:
* 9 Expedited Processes
* 251 Vaccines
* 132 Manufactures
* 218 NRAs
## System for Expedited Review of Imported Prequalified Vaccines

### Applications:

<table>
<thead>
<tr>
<th>Vaccine</th>
<th>Manufacturer</th>
<th>NRA</th>
<th>Form 1a</th>
<th>Form 1b</th>
<th>Form 1c</th>
<th>Updates</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diphtheria-Tetanus-Pertussis (whole cell)-Hepatitis B-Haemophilus influenza type b: Quinvaxem</td>
<td>Bema Biotech Korea Corp., Republic of Korea</td>
<td>Republic of Korea: Korea Food &amp; Drug Administration</td>
<td>Cancelled by manufacturer</td>
<td></td>
<td></td>
<td>0</td>
</tr>
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<td>Diphtheria-Tetanus-Pertussis (whole cell)-Hepatitis B-Haemophilus influenza type b: Quinvaxem</td>
<td>Bema Biotech Korea Corp., Republic of Korea</td>
<td>Ghana: Food and Drugs Board Ghana</td>
<td>Cancelled by manufacturer</td>
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<tr>
<td>Diphtheria-Tetanus-Pertussis (whole cell)-Hepatitis B-Haemophilus influenza type b: Quinvaxem</td>
<td>Bema Biotech Korea Corp., Republic of Korea</td>
<td>Sudan: The Federal Ministry of Health</td>
<td>Accepted by NRA &amp; routed to WHO/HQ</td>
<td>Approved by WHO/HQ</td>
<td>Executed by NRA</td>
<td>1</td>
</tr>
<tr>
<td>Diphtheria-Tetanus-Pertussis (whole cell)-Hepatitis B-Haemophilus influenza type b: Quinvaxem</td>
<td>Bema Biotech Korea Corp., Republic of Korea</td>
<td>Congo: Ministère de la Santé et de la Population</td>
<td>Submitted by manufacturer</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Hepatitis B: Revac-B+</td>
<td>Bharat Biotech International Limited, India</td>
<td>Ghana: Food and Drugs Board Ghana</td>
<td>Submitted by manufacturer</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Hepatitis B: Hepavax</td>
<td>Bema Biotech Korea Corp., Republic of Korea</td>
<td>Sudan: National Medicines &amp; Poisons Board</td>
<td>Submitted by manufacturer</td>
<td></td>
<td></td>
<td>0</td>
</tr>
</tbody>
</table>
ASANTE SANA!