Vaccines Testing: initial evaluation and post-prequalification monitoring

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Dr Ute Rosskopf
WHO - Constitution in 1948

"The enjoyment of the highest attainable standard of health is one of the fundamental rights of every human being without distinction of race, religion, political belief, economic or social condition."
WHO Report on Health 2015

"Almost all the **Sustainable Development Goals (SDGs)** are directly related to health or will contribute to health indirectly. One goal (SDG3) specifically sets out to “Ensure healthy lives and promote well-being for all at all ages.”

**Within goal 3 the target 3.8 is significant and directly linked to vaccines:**

"Achieve universal health coverage, including financial risk protection, access to quality essential health-care services and access to safe, effective, quality and affordable essential medicines and vaccines for all".
Background Prequalification - Vaccines

"Procedure for assessing the acceptability, in principle, of vaccines for purchase by United Nations agencies"

- Created in 1987
- Service provided to purchasing and procuring UN agencies/international procurement
Prequalification of vaccines - Provisions

- Vaccine on the priority list for prequalification
- Functionality of the national regulatory agency (NRA): Producing country must meet WHO vaccine regulation indicators
- Three pillars of vaccine evaluation:
  - WHO reviews the vaccine dossier (quality & clinical data)
  - WHO inspects the manufacturing site
  - WHO tests the final product
Background Prequalification

Prequalification of vaccines - Listing

- Issuance of acceptability letter
- Vaccine published on the WHO website: https://extranet.who.int/gavi/PQ_Web/
- Listed vaccines (more than 100) not only purchased by UN agencies, but also directly by countries & non governmental organizations

22 producing countries
>100 receiving countries
## Laboratory testing by WHO

### Pre- and post prequalification (PQ) testing

<table>
<thead>
<tr>
<th>Initial evaluation of a new product – Pre PQ</th>
<th>Annually performed targeted testing – Post PQ</th>
<th>Testing through contracted laboratories</th>
</tr>
</thead>
<tbody>
<tr>
<td>(WHO TRS no. 978, Annex 6, chapter 3.4)</td>
<td>(WHO TRS no. 978, Annex 6, chapter 10)</td>
<td>• Based on a forecast — in total 12 contracts have been issued to cover &gt; 300 tests for the current biennium 2018-2019</td>
</tr>
<tr>
<td>• Three final lots tested for consistency of final product characteristics</td>
<td>• Lots selected by WHO – risk based approach</td>
<td>➔ Paid service - Identical fees for each test parameter</td>
</tr>
<tr>
<td>• Testing by two laboratories (plus NCL)</td>
<td>• Two to three lots close to expiry dates</td>
<td></td>
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<tr>
<td>➔ WHO test report shared with the manufacturer</td>
<td>• Testing by one laboratory</td>
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<td></td>
<td>➔ WHO testing outcome reported to donors</td>
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</table>

The independent testing of vaccines is part of the procedure for evaluation of the acceptability, in principle, of vaccines for purchase by United Nations agencies (Technical report series 978).
Initial evaluation for PQ

- Three to five final lots are tested for consistency of final product characteristics
- Lots need to be formulated from consecutive bulk lots
- Additional information e.g. validation documents may be requested
- Usually potency is tested. On occasions other relevant tests can be performed
- Reference reagents are requested if applicable (HepB vaccine, Influenza vaccine)
- Lots are tested in parallel by two WHO laboratories
- (in case of inconsistent results: results of the national control laboratory are requested)

→ WHO test report shared with the manufacturer
Post pre-qualification monitoring

Targeted testing of prequalified vaccines

- Annually performed
- At the beginning of each year WHO approaches manufacturers to provide an overview of vaccine lots supplied to countries through UN agencies, but also direct purchases
- Lots for testing are selected by WHO
- Usually two to three lots close to their expiry dates are chosen
- Selection on a risk based approach
- Testing by one contract laboratory

→ WHO testing outcome reported to donors
Post pre-qualification monitoring

Reporting of lot release data

Annual review of national lot release reports by WHO provided by responsible national authorities

By > 10 laboratories based on currently 19 agreements

- WHO request to report in the beginning of the year
- Templates provided
- Reports evaluated by WHO
- Data anonymized for WHO report to donors
- Reporting of lot release data is a contract parameter - paid service by WHO
WHO report on vaccine testing-related activities

Information on:
● WHO-contracted testing (initial and post-PQ)
● National lot release data reported to WHO
● Related activities (lab audits, test method optimization, training, NCL network …)
● Annex 1: Results in table format.
Procedure of drafting Annex of the report

- Results of targeted testing/initial evaluation testing reported to WHO
- Annually WHO sends out xls template to NCLs for national release data
- NCLs provide batch release data:
  - lot numbers
  - potencies (NCL+man.)
  - etc.
- Information is reviewed
- Summary in annual report
### Challenges to meet SDG 3.8

<table>
<thead>
<tr>
<th>General</th>
<th>WHO</th>
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<tr>
<td>• <strong>Globalization</strong> of vaccine industry: increasing number of production sites</td>
<td>• WHO contracted laboratories test vaccines of various manufacturers (differences in used methods)</td>
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<tr>
<td>• Increased <strong>complex regulation</strong></td>
<td>• Increasing number of <strong>complex vaccines</strong> (test and cost intensive)</td>
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<tr>
<td>• <strong>Limited resources</strong> of regulatory authorities (developed and developing countries)</td>
<td>• <strong>Increasing</strong> number of <strong>applications</strong> for prequalification</td>
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<tr>
<td>• <strong>Duplication of efforts</strong> through redundant testing and approval of variations</td>
<td>• <strong>Increased</strong> number of <strong>prequalified vaccines</strong> to be monitored</td>
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<td>• <strong>Non-compliances</strong> in test outcomes by importing countries: delay in vaccine access, disruption of vaccine delivery</td>
<td>• <strong>Limited resources</strong> (laboratories, WHO)</td>
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</table>
WHO response to challenges: 

WHO test programme

- Harmonization of test methodologies (performance of feasibility studies, collaborative studies and hands-on training courses)

- Change in PQ procedure section 3.4 (endorsed by ECBS, meeting 2014):
  - Optimized logistics: Introduction direct shipments of vaccines to WHO test laboratories
  - Use of NCL of producing country (testing)
  - Use of resources: lot release data gathered by the official national control laboratory (on consent of manufacturers) and technical know-how
WHO response to challenges: 

→ WHO test programme

**WHO test programme** → Creation of a structure to make information available to others, namely – receiving = importing countries.

Established **WHO-National Control Laboratory Network for Biologicals (WHO-NNB)** with the mission

“…to facilitate access to and availability of prequalified vaccines (or other biological medicinal products) through reliance on the batch release of the respective Network Members by recipient countries, thereby reducing redundant testing, and contributing to more cost-effective testing and more effective regulatory oversight.”
WHO-National Control Laboratory Network for Biologicals

... aiming to

- share quality and technical information about prequalified products
- facilitate recognition of national lot release by recipient countries
- promote development of harmonized common standards and best practice, including use of the 3R principles
- contribute to and support: test harmonization & future development / revisions of WHO guidelines
- support strengthening of the NRAs and NCLs in the Network through technical assistance.
- promote recognition globally of WHO prequalified vaccines.
What each partner brings to the Network

Responsible NRAs/NCLs in producing countries have

- Best oversight of PQ’d vaccines and testing methods
- Functional vaccine regulation and laboratories

WHO:

- acknowledged body with an international mandate of 194 Member States and WHA resolution 67.20 concerning networks
- existing expert hub of qualified NCLs testing for WHO
- reports on vaccine quality data = WHO test outcome (pre- and post-PQ)
- Reports on vaccine quality data through sharing of lot release data
- established Terms of Reference & Participation Agreement
- electronic platform in a secured, confidential setting
WHO-NNB: Expert hub / Service centre

20 full members
WHO-NNB

> 33 members in total

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<td>Australia</td>
<td>Lesotho (AM) signature imminent</td>
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<td>Austria (AM)</td>
<td>Mexico (AM)</td>
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<td>Bangladesh (AM)</td>
<td>Morocco (AM)</td>
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<tr>
<td>Belgium</td>
<td>Namibia (AM) (signature imminent)</td>
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<td>Bulgaria</td>
<td>Republic of Korea</td>
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<td>Bhutan (AM)</td>
<td>Russian Federation</td>
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<td>Botswana (AM)</td>
<td>Senegal</td>
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<tr>
<td>Brazil – signature imminent</td>
<td>South Africa</td>
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<td>Canada</td>
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New associate member since 26/11/2019: Botswana
Newly interested members: Egypt, Lebanon, Lesotho, Saudi Arabia
WHO response to challenges: ➔ Electronic platform = SharePoint

To date 12 requests sent out to:
BB-NCIPD (via BDA); Bilthoven Biologicals B. V.; Eubiologics Co. Ltd.; Green Cross corp.; GSK Vaccines; Janssen Vaccines Corp.; LG Chem Ltd.; Merck Sharp & Dohme Corp.; Pfizer; PT Bio Farma; Sanofi Pasteur; Valneva Sweden AB

Total formerly signed agreements: 5 for sharing information with WHO and the Network members

Annual Quality Reports
Letters have been sent to several vaccine manufacturers regarding the permission to their lot release data. Up to date five manufacturers agreed to extend their agreements of data sharing with the Network members. Below you will find a link to the annual quality reports which were submitted by the responsible NCLs. Please contact the WHO secretariat if you wish to access information from a manufacturer which has not signed the agreement yet.
Conclusion: Network serves as...

- an information and service center which collects, contributes and distributes quality information in a secure and confidential setting

- an expert hub which assures quality and safety of vaccines
Conclusion: Network facilitates and...

by consequence it facilitates and accelerates access to quality vaccines (….and other biological medicinal products)
- reach SDG 3.8:

"Achieve universal health coverage, including financial risk protection, access to quality essential health-care services and access to safe, effective, quality and affordable essential medicines and vaccines for all".
Thank you
for listening,
for your collaboration!