WHO Global NCL Network

WHO-National Control Laboratory Network for Biologicals:
Impact of sharing testing practices
WHO-NCL Network for Biologicals

Outline

• Background
• Creation of the Network
• Objectives of the Network
• Structure
• Sharing of information
• Impact of sharing testing practices
Background: Global access Sustainable Development Goal 3.8

How to reach global access to needed vaccines in a timely manner?
Background - Global challenges to meet SDG goal 3.8

Globalization of vaccine industry – increasing number of production sites

More and more complex regulation

Regulatory authorities' capacities are limited (developed and developing countries)

Delay of vaccine supply – shortages

Duplication of efforts e.g. redundant testing, approval of variations
Background - WHO's vaccines testing – Challenges

WHO laboratories are testing vaccines of various manufacturers who may apply differing methods

Occurrence of out-of-specification – not related to quality

Increasing number of complex vaccines – test- and cost- intensive

Increasing number of applications for PQ – increased number of prequalified vaccines

Limited resources
Background WHO's vaccines testing – Developments

- Independent testing through qualified laboratories for:
  - new vaccines
  - monitoring of PQ’d vaccines /other incidents

- **Sharing of lot release data** by WHO contract laboratories with WHO – consent of manufacturers (19 agreements in place)

- **Harmonization** of test methods

- Performance of **collaborative studies**

- **Hands-on training courses** facilitated by WHO laboratories
Background WHO's vaccines testing – Directions

Immunization has huge **public health impact:**

- Quality issues can affect public trust in vaccination
- PQ processes further improvement – **Utilisation of resources**
  - WHO: Expert hub of members of NCL’s
  - Sharing of quality information with recipient countries
- Effective global regulation is only possible through collaboration and information-sharing
  - Creation of an infrastructure
WHO's response to global challenges: Creation of a global control laboratory network

- WHO called for stakeholder meeting in Bilthoven, The Netherlands, 30 August - 2 September 2016

- Representatives from:
  - 21 NCLs involved in testing WHO-prequalified vaccines
  - Manufacturers’ associations
  - DCVMN & IFPMA
  - European Directorate for the Quality of Medicines

- agreed on the creation of a WHO national control laboratories network

The art of partnerships, DCVMN 19th AGM, Kunming, 31 October 2018
WHO-National Control Laboratory Network for Biologicals launched with its 1st General meeting in 2017

WHO – global mandate (194 Member States), established ToR

Responsible NRAs/NCLs in producing countries have:
- Best oversight of PQ’d vaccines and testing methods
- Functional vaccine regulation and laboratories

Reliance on responsible national laboratories’ release testing

Impact on recipient countries:

- Reduce redundant testing
- Save costs
- Reduce the risk of inaccurate results
- Accelerated access to vaccines

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Structure of the Network for Biologicals

- WHO serves as secretariat of the Network

- Network membership:
  - Full Members: NCLs from countries producing WHO-prequalified vaccines (or other biological medicinal products), and WHO-contracted NCLs ➔ provide and share vaccine information
  - Associate Members: NCLs or NRAs in countries that are recipients of UN-procured vaccines (or direct purchases) ➔ receive information – Reliance and Recognition

Observers (UN procurement agencies, manufacturer associations and other stakeholders)
Objectives of the WHO NCL Network for Biologicals

- Share quality and technical information
- Facilitate recognition of lot release of the responsible NRA & NCL (as defined in WHO TRS, No. 978, annex 2) by recipient countries
- Promote the development of harmonized common standards and best practices, including the use of the 3R principles
- Contribute to and support test harmonisation, and to provide input to future development/ revisions of WHO guidelines
- Support strengthening of the NCL’s Network through technical assistance/ training
- Make information available to strengthen the recognition of WHO prequalification globally
Eligible and current members

- Eligible members: 194
- Eligible associate members: 170
- Eligible full members: 24
- Full members: 19
- Associate members: 6

<table>
<thead>
<tr>
<th>Associate members</th>
<th>Full members</th>
<th>Eligible full members</th>
<th>Eligible associate members</th>
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<td>Series1</td>
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<td>19</td>
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The art of partnerships, DCVMN 19th AGM, Kunming, 31 October 2018
Achievement - Full memberships: 19 signed agreements to date

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<th>Australia</th>
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<tbody>
<tr>
<td>Belgium</td>
<td>Germany</td>
<td>South Africa</td>
</tr>
<tr>
<td><strong>Brazil</strong></td>
<td>India</td>
<td><strong>Sweden (in process)</strong></td>
</tr>
<tr>
<td>Bulgaria</td>
<td>Indonesia</td>
<td>Switzerland</td>
</tr>
<tr>
<td>Canada</td>
<td>Italy</td>
<td>Thailand</td>
</tr>
<tr>
<td><strong>China</strong></td>
<td><strong>Japan</strong></td>
<td>The Netherlands</td>
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<tr>
<td>Cuba</td>
<td>Republic of Korea</td>
<td><strong>United States</strong></td>
</tr>
<tr>
<td>Denmark</td>
<td>Russia</td>
<td>United Kingdom</td>
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</table>

Achievement - Associate memberships: 6 signed agreements to date

<table>
<thead>
<tr>
<th>Bangladesh</th>
<th>Hungary</th>
<th>Zambia</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ghana</td>
<td>Sri Lanka</td>
<td>Zimbabwe</td>
</tr>
</tbody>
</table>
Network for Biologicals: operates and shares information via ....

- E-mails
- Network meetings
- Sharepoint
Sharing of Information

- Creation of SharePoint Site
- Restricted access: granted based on signed Confidentiality Agreement

- Main site with general information and Country site specific for every member: NCL/NRA
Sharing of Information: Main site

Background
The NRAs/NCLs responsible for testing and release of WHO-prequalified vaccines have the best oversight of products and testing methods. Each year they test thousands of lots against approved specifications. In 2016 WHO brought together representatives of NCLs involved in testing WHO-prequalified vaccines at a networking meeting. It was agreed to establish a Network providing a platform for exchange of quality and technical information on prequalified vaccines.

“Cooperation and networking can help ensure efficient testing, save costs and reduce the risk of inaccurate results. Access to vaccines can be greatly accelerated if recipient countries rely on the lot release done by the responsible NCL”

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 member states, thereby reducing redundant testing, and contributing to more cost-effective testing and more effective regulatory oversight.

Objectives
- Share quality and technical information related to prequalified products.
- Facilitate recognition of lot release of the responsible NRA&NCL (as defined in WHO Technical Report Series, No. 978, Annex 2) by recipient countries.
- Promote the development of harmonized common standards and best practice, including the use of the 3R principles.
- Contribute to and support test harmonization, and to provide input to future development / revisions of WHO guidelines.
- Support strengthening of the NCLs in Network through technical assistance / training.
- Make information available to strengthen the recognition of WHO prequalification globally.

Future Directions
In the future, the Network could also serve to share information on other biological medicinal products.
Sharing of Information: Country Sites

- 2 different country sites in content: giving information versus taking information,
- Full members provide information via their country sites about vaccine quality, testing of vaccines,...
- Associate members or NRA’s from recipient countries provide information about their NRA **BUT** have access to information of full member sites and by consequence access to vaccine quality information

→ Creates transparency and trust
Sharing of Information: Country Site

Sciensano

- Contact / Organogram
- Prequalified Vaccines
- Other Vaccines
- Laboratory Activities
- Vaccine Test Methods
- External Collaboration
- 3R Program
- Lot Release Procedure

Sciensano
Quality of Vaccines and Blood Products

Contracted by WHO for technical testing of vaccines
Contracted by WHO for sharing of lot release information
Lot release for Belgian and European market

Quality Assurance Standards: ISO/IEC 17025 and ISO/IEC 9001

Related national regulatory authority: Federal Agency for Medicines and Health Products
Sharing of Information: Country Site

Contact - Organogram

<table>
<thead>
<tr>
<th>Function</th>
<th>Name</th>
<th>E-mail address</th>
<th>Phone number</th>
</tr>
</thead>
<tbody>
<tr>
<td>NCL Focal Point</td>
<td>Geneviève Waeterloos</td>
<td>Geneviè<a href="mailto:ve.Waeterloos@sciensano.be">ve.Waeterloos@sciensano.be</a></td>
<td>+32 2 642 53 39</td>
</tr>
<tr>
<td>QA Manager</td>
<td>Patricia Cliquet</td>
<td><a href="mailto:Patricia.Cliquet@sciensano.be">Patricia.Cliquet@sciensano.be</a></td>
<td>(to follow)</td>
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# Sharing of Information: Country Site

## Prequalified Vaccines

<table>
<thead>
<tr>
<th>Vaccine type</th>
<th>Country of production</th>
<th>NRA of regulatory oversight</th>
<th>NCL responsibility</th>
<th>Samples received from</th>
<th>Testing Upstream &amp; Final Product</th>
<th>Risk based approach applied?</th>
<th>Nr of released batches: 2016</th>
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<tbody>
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<td>PEI</td>
<td>Sciensano</td>
<td>manufacturer</td>
<td>UP + FP</td>
<td>yes (DTaP in vivo)</td>
<td>57</td>
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<tr>
<td>Diphtheria-Tetanus-Pertussis (acellular)-Polio (Inactivated)-Hepatitis-B-Haemophilus influenzae type b-Polio (Inactivated)</td>
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<td>PEI/Sciensano</td>
<td>Sciensano</td>
<td>manufacturer</td>
<td>UP + FP</td>
<td>yes (DTaP in vivo)</td>
<td>119</td>
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<tr>
<td>Hepatitis A (inactivated)</td>
<td>Belgium</td>
<td>FAMHP</td>
<td>Sciensano</td>
<td>manufacturer</td>
<td>UP + FP</td>
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<tr>
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<td>FAMHP</td>
<td>Sciensano</td>
<td>manufacturer</td>
<td>UP + FP</td>
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<tr>
<td>Hepatitis A + Hepatitis B</td>
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<td>FAMHP</td>
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<td>UP + FP</td>
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<td>manufacturer</td>
<td>UP + FP</td>
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<td>Measles, Mumps and Rubella</td>
<td>Belgium</td>
<td>FAMHP</td>
<td>Sciensano</td>
<td>manufacturer</td>
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<td>Meningococcal ACYW-135 (conjugate vaccine)</td>
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<td>EMA</td>
<td>Sciensano</td>
<td>manufacturer</td>
<td>UP + FP</td>
<td>no</td>
<td>27 (EU and non EU)</td>
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<tr>
<td>Pneumococcal (conjugate)</td>
<td>Belgium &amp; Singapore</td>
<td>EMA</td>
<td>Sciensano</td>
<td>manufacturer</td>
<td>UP</td>
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</table>
Sharing of Information: Country Site

Laboratory Activities

- DT-DTwP vaccine combinations
- DTaP vaccine combinations
- Haemophilus Influenzae type b vaccine
- Hepatitis A vaccine
- Hepatitis B vaccine
- Human Papillomavirus vaccine
- Inactivated Poliomyelitis vaccine
- Measles, Mumps, Rubella and Varicella vaccine
- Meningococcal vaccine
- Oral Poliomyelitis vaccine
- Pneumococcal vaccine
- Rotavirus vaccine

More information appears when clicking on the link
### Sharing of Information: Country Site

#### Laboratory Activities - DT DTwP vaccine combinations

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<td>n. a.</td>
<td>n. a.</td>
<td>n. a.</td>
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<td>n. a.</td>
<td>n. a.</td>
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<td>n. a.</td>
<td>n. a.</td>
<td>1</td>
<td>see DTaP</td>
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<tr>
<td>T potency assay</td>
<td>yes</td>
<td>n. a.</td>
<td>n. a.</td>
<td>1</td>
<td>see DTaP</td>
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<tr>
<td>Specific toxicity DT</td>
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<td>n. a.</td>
<td>n. a.</td>
<td></td>
<td></td>
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<tr>
<td>HepB potency assay in vivo</td>
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<td>WHO (2016)</td>
<td>n. a.</td>
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<td>WHO (2016)</td>
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<tr>
<td>Hib: total saccharide content</td>
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<td>BSP135 (2014)</td>
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<tr>
<td>Hib: free saccharide content</td>
<td>?</td>
<td>n. a.</td>
<td></td>
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</table>
Vaccine Test Methods

- Biological Test Methods
- Immunochemical Methods
- Physicochemical Test Methods
Sharing of Information: Country Site

Lot Release Procedure

SOP Management of samples
- Dispatching
- Test plan (StarLIMS)
- Planification
- Testing
- Data Encoding
- Test Validation

SOP Testing & assay report

Analytical SOPs

SOP Lot release
- Documentation
- Reception
- Log in
- Data Encoding
- Protocol review
- Batch release or certificate of non compliance

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WHO’s shares quality information on its SharePoint: Reports testing outcome

- **Pre PQ testing**: Initial evaluation of a new product ➔ (WHO test report shared with the manufacturer)
- **Post PQ testing**: Annually performed targeted testing ➔ (WHO testing outcome reported to donors)
- Annual evaluation of lot release information – report
Impact of Network: WHO 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
... 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".
Next steps

● WHO
  – Continue seeking agreements for information-sharing including all manufacturers
  – Promote membership in the Network and disseminate information

● Role/responsibility of manufacturers associations and NRAs/NCLs:
  – Intense exchange
  – Identify and respond to needs of recipient countries
  – Promote membership in the WHO-Network

Target: Access to SharePoint for all 194 member states!
Feedback from stakeholders after the 2nd General Network meeting...

“The progresses done since last year are impressive and the vision you gave to the network should contribute to significant public health improvements!”

“We hope that a fully operational network will facilitate a harmonized and mutually recognized lot release process that will ultimately help to promote increased immunizations and save lives.”
Acknowledgements

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Thank you

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Regulation of Medicines and Other Health Technologies
Essential Medicines and Health Products
World Health Organization (Geneva, Switzerland)

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