

WHO Global NCL Network



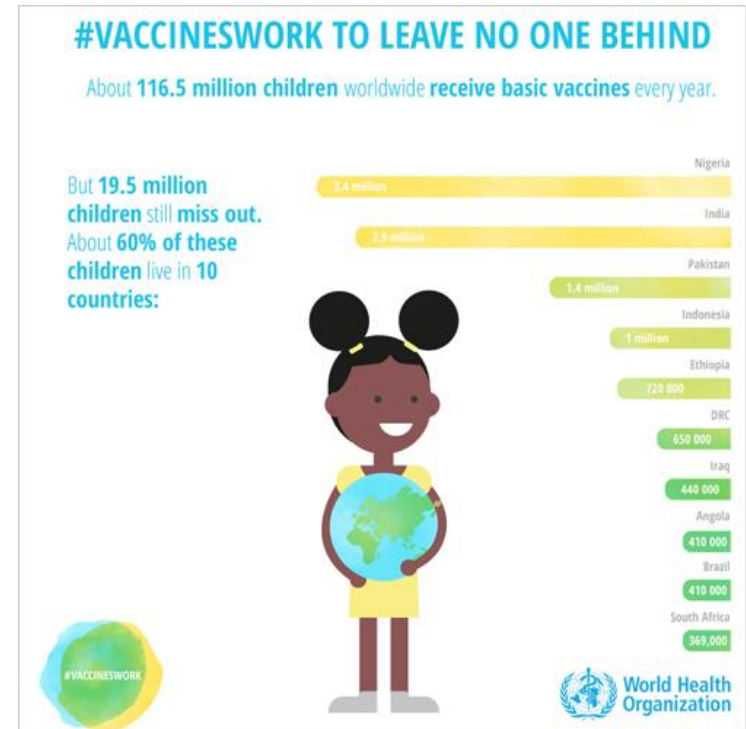
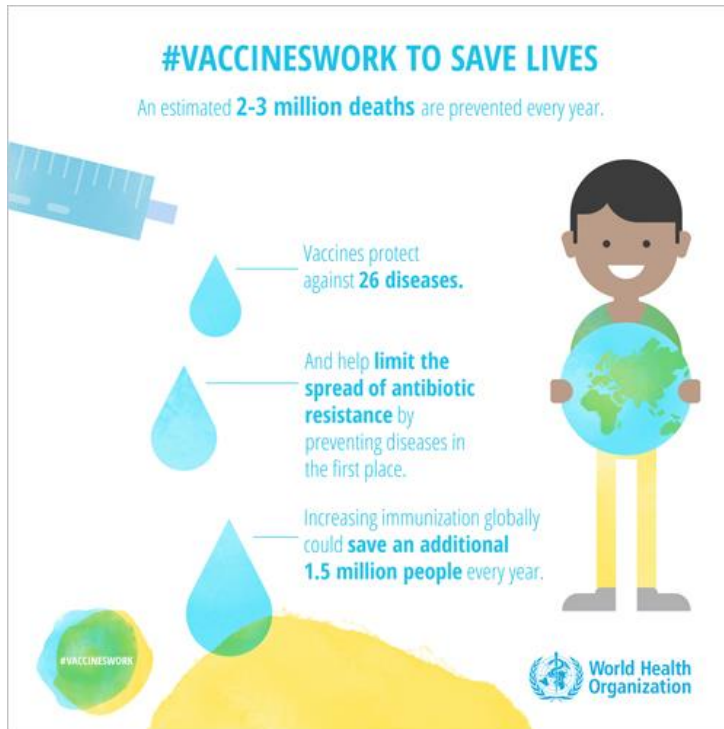
WHO-National Control Laboratory Network for Biologicals: Impact of sharing testing practices

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

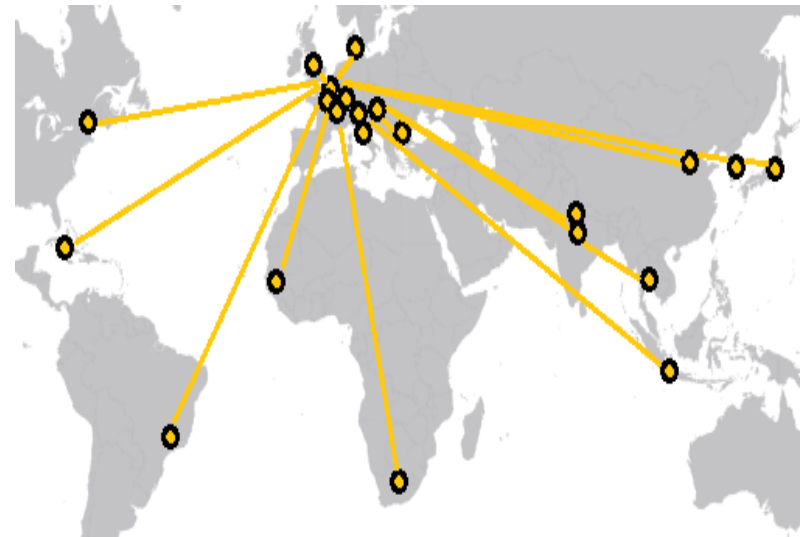
- Representatives from:

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**



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

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)

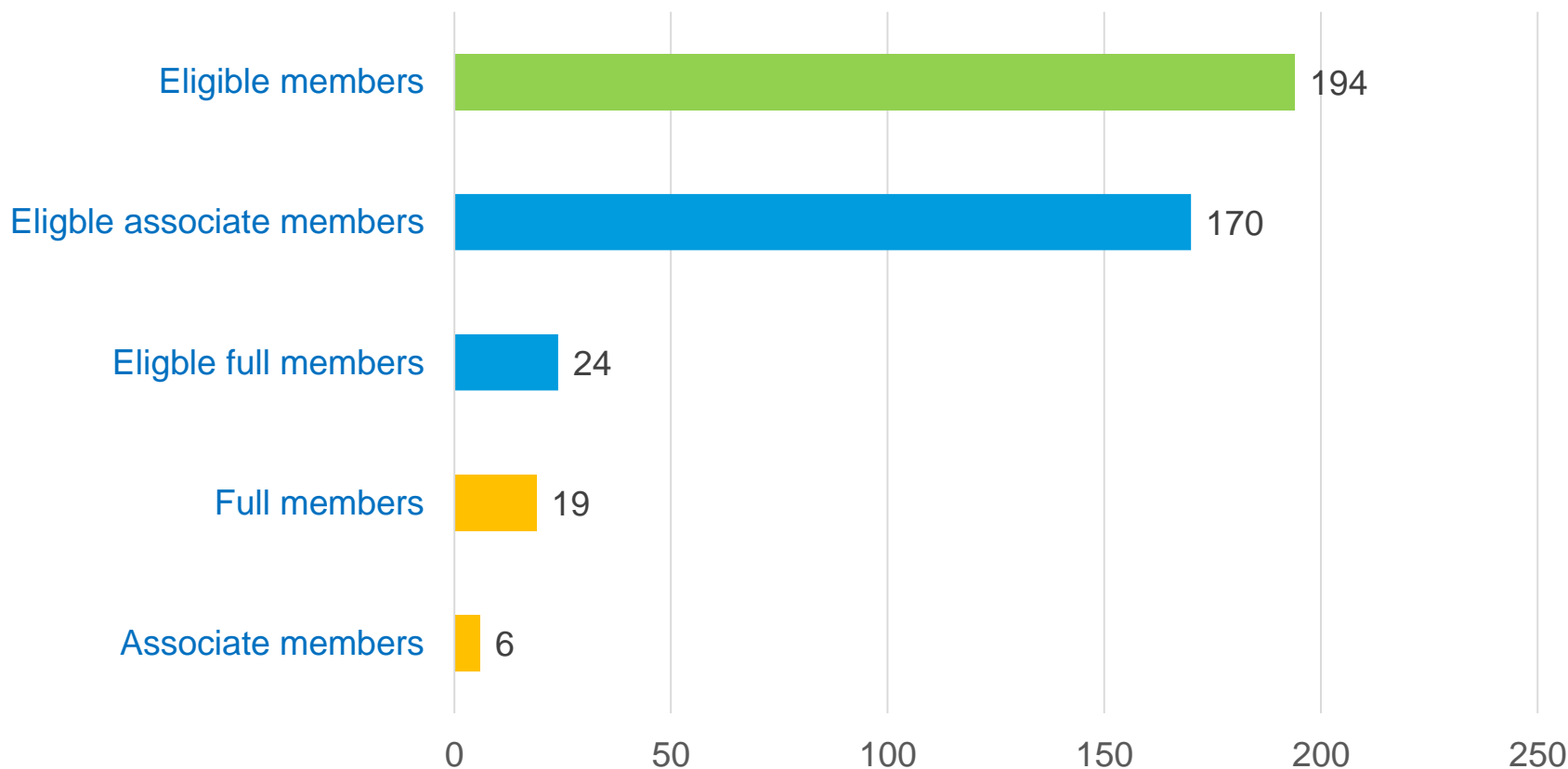


Objectives of the WHO NCL Network for Biologicals

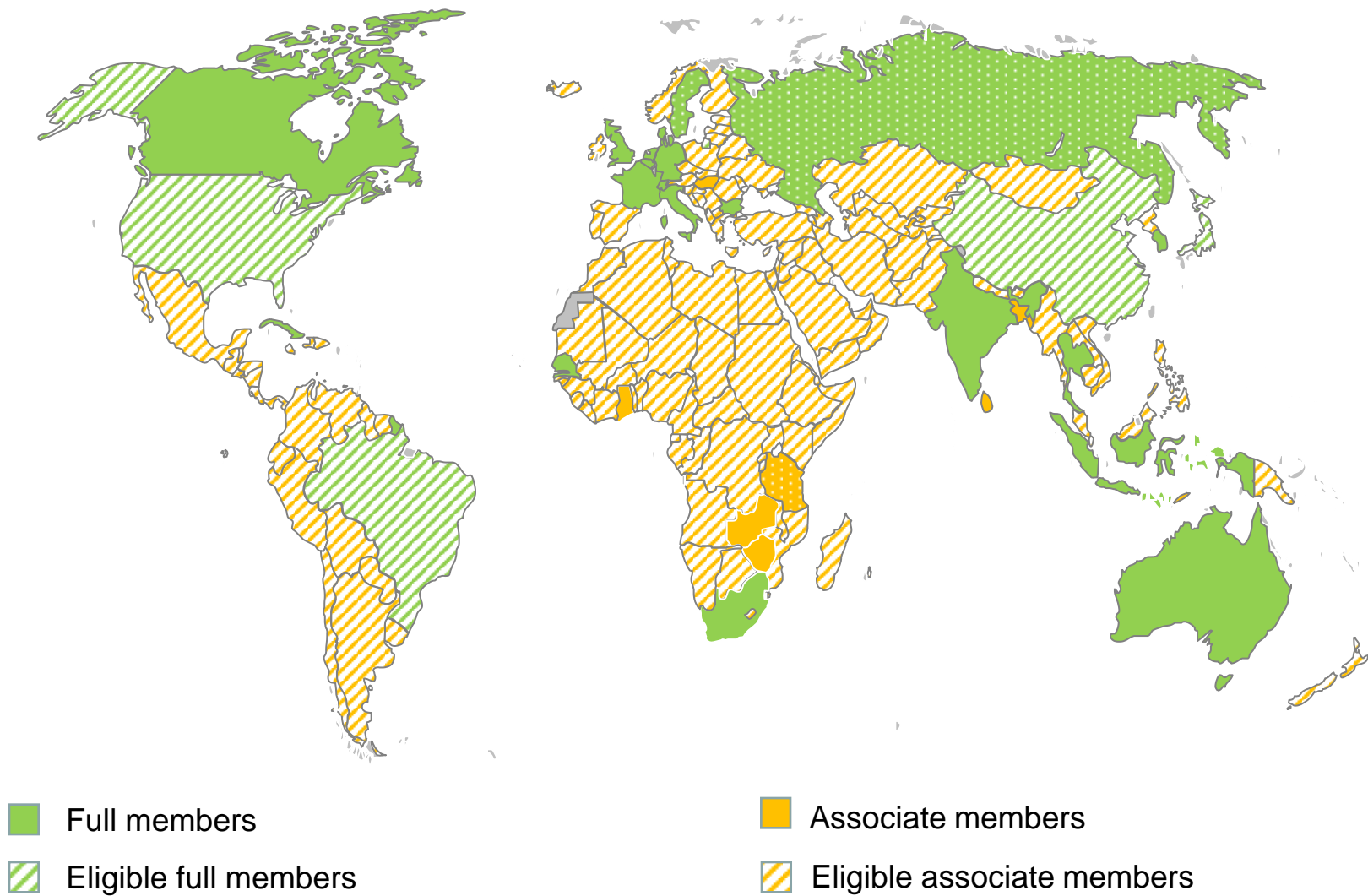


- Share quality and technical information
- Facilitate recognition of lot release of the responsible NRA & NCL (as defined in WHO TRS, No. 978, annex 2) by recipient countries
-  ➤ Promote the development of harmonized common standards and best practices, including the use of the 3R principles
- Contribute 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



	Associate members	Full members	Eligible full members	Eligible associate members	Eligible members
■ Series1	6	19	24	170	194



Achievement - Full memberships: 19 signed agreements to date



Australia	France	Senegal
Belgium	Germany	South Africa
<i>Brazil</i>	India	<i>Sweden (in process)</i>
Bulgaria	Indonesia	Switzerland
Canada	Italy	Thailand
<i>China</i>	<i>Japan</i>	The Netherlands
Cuba	Republic of Korea	<i>United States</i>
Denmark	Russia	United Kingdom

Achievement - Associate memberships: 6 signed agreements to date

Bangladesh	Hungary	Zambia
Ghana	Sri Lanka	Zimbabwe

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

News and Events

Role of WHO / UN

Where we are inside WHO

Quality Surveillance

Our members

Search NCL

Search Vaccine

Meeting Documents

Sharing Best Practices

Useful links



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

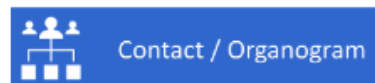


Sharing of Information: Country Site



Belgium

Sciensano



Contact / Organogram



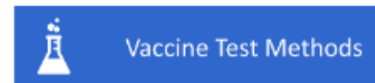
Prequalified Vaccines



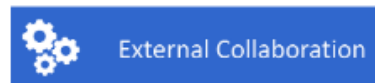
Other Vaccines



Laboratory Activities



Vaccine Test Methods



External Collaboration



3R Program



Lot Release Procedure



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

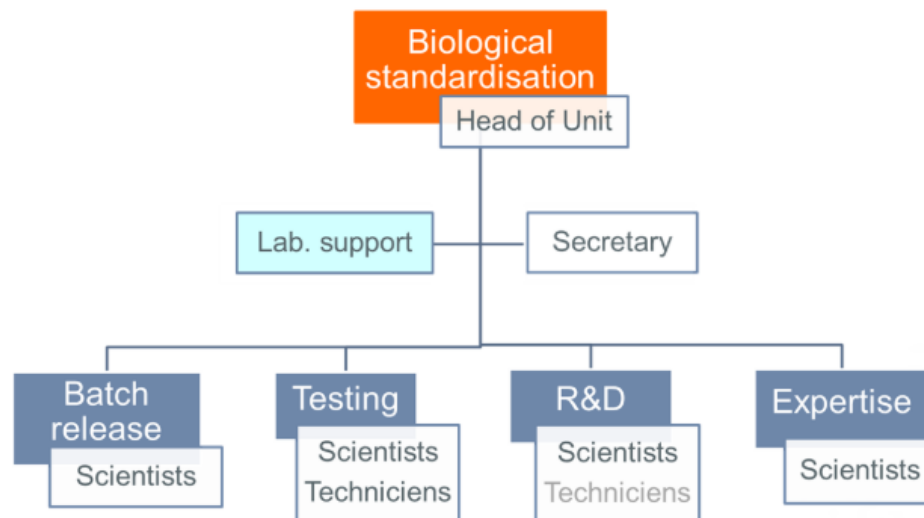
Quality Assurance Standard: ISO/IEC 17025 and ISO/IEC 9001

Related national regulatory authority: [Federal Agency for Medicines and Health Products](#)

Sharing of Information: Country Site

Contact - Organogram

Function	Name	E-mail address	Phone number
NCL Focal Point	Geneviève Waeterloos	Geneviève.Waeterloos@sciensano.be	+32 2 642 53 39
QA Manager	Patricia Cliquet	Patricia.Cliquet@sciensano.be	(to follow)



Sharing of Information: Country Site

Prequalified Vaccines

<input type="checkbox"/> Vaccine type	Country of production	NRA of regulatory oversight	NCL responsibility	Samples received from	Testing Upstream & Final Product	Risk based approach applied?	Nr of released batches: 2016
Diphtheria-Tetanus-aP (reduced antigen content)	Belgium	PEI	Sciensano	manufacturer	UP + FP	yes (DTaP in vivo)	57
Diphtheria-Tetanus-Pertussis (acellular)-Polio (Inactivated)-Hepatitis-B-Haemophilus influenzae type b-Polio (Inactivated)	France	PEI/Sciensano	Sciensano	manufacturer	UP + FP	yes (DTaP in vivo)	119
Hepatitis A (inactivated)	Belgium	FAMHP	Sciensano	manufacturer	FP	no	46
Hepatitis B	Belgium	FAMHP	Sciensano	manufacturer	UP + FP	no	75
Hepatitis A- Hepatitis B	Belgium	FAMHP	Sciensano	manufacturer	UP + FP	no	31
HPV	Belgium	FAMHP	Sciensano	manufacturer	UP + FP	no	28
Measles, Mumps and Rubella	Belgium	FAMHP	Sciensano	manufacturer	FP	no	113 EU + 204 non EU
Meningococcal ACYW-135 (conjugate vaccine)	Belgium	EMA	Sciensano	manufacturer	UP + FP	no	27 (EU and non EU)
Pneumococcal (conjugate)	Belgium & Singapore	EMA	Sciensano	manufacturer	UP	no	73 (conjugated bulks)
Polio Vaccine - Inactivated (IPV)	Belgium	FAMHP	Sciensano	manufacturer	FP	no	8 (EU and non EU)
Polio Vaccine - Oral (OPV) Bivalent Types 1 and 3	Belgium	FAMHP	Sciensano	manufacturer	UP + FP	no	2 EU + 108 non EU

Sharing of Information: Country Site



Belgium

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



Belgium

Laboratory Activities - DT DTwP vaccine combinations

<input type="checkbox"/> Activity	Performed?	Accredited?	Participation in collaborative study?	Participation in proficiency testing?	No of lots - tests in 2016	Remark
Review of lot summary protocol	yes	n. a.	n. a.	n. a.	?	
Appearance	yes	yes		n. a.	80	nr of runs p tested
D potency assay	yes			n. a.	1	see DTaP
T potency assay	yes			n. a.	1	see DTaP
wP potency assay	yes	yes (2015)		n. a.	5 (2015)	need of rev. reference a
Specific toxicity DT	no		n. a.	n. a.		
Specific toxicity wP	yes	yes (2015)		n. a.	2 (2015)	
HepB potency assay in vitro	?	yes (2015)	WHO (2010)	n. a.	2	
HepB potency assay in vivo	yes			n. a.	1	WHO TSA c
Hib bulk: MSD	?	yes	WHO (2016)	n. a.	19	
Hib: total saccharide content	?		BSP135 (2014)	n. a.	62	
Hib: free saccharide content	?			n. a.	62	

Sharing of Information: Country Site



Belgium

Vaccine Test Methods

Biological Test Methods

Immunochemical Methods

Physicochemical Test Methods



Belgium

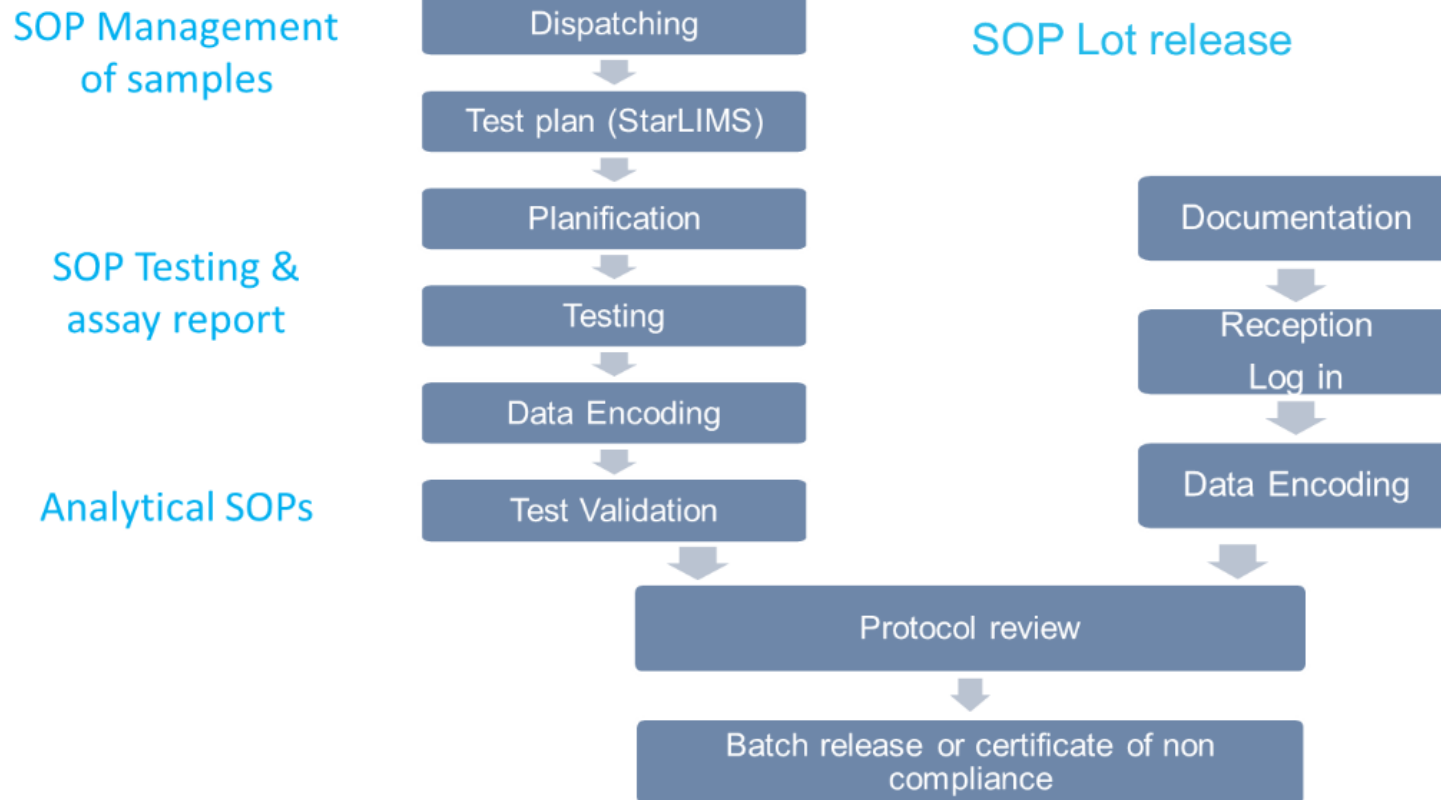
Biological Test Methods

[Back to Vaccine Test Method page](#)

<input type="checkbox"/> Parameter	Method	Performed?	Reference method?	Remark
Diphtheria potency assay	challenge (lethal / paralytical)	yes	Ph.Eur. 2.7.6	
Tetanus potency assays	challenge	yes	Ph. Eur. 2.7.8	
Acellular pertussis potency assay	serology	yes	Ph.Eur. 1356 (2013); Ph.Eur. 2067 (2013); Ph.Eur. 2071: 2.7.16; TRS 979	
Whole pertussis potency assay	ic challenge	yes	Marketing Authorisation; Ph. Eur. 2.7.7	needs to be n
Pertussis residual toxicity	Histamin Sensitisation Assay	yes	Marketing Authorisation; Ph.Eur. 2.6.33.	
Hep A potency assay - in vivo	Immunization and serology	yes	Ph.Eur. 2.7.15	for WHO only
HepB potency assay in vivo	Immunization and serology	yes	TRS 978	for WHO only
IPV potency assay in vivo	Immunization and serology	(yes)	Marketing Authorisation/ In house; PhEur -0214	last test in 20 manufacturer
Measles potency assay	cell culture / identity / vaccine titration	yes	Marketing Authorisation; Ph. Eur. 1057/2442; TRS 840	

Sharing of Information: Country Site

Lot Release Procedure

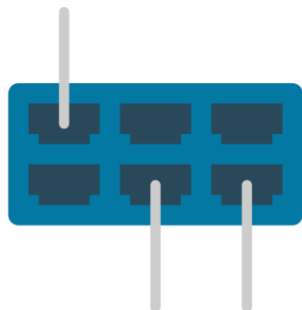


WHO's shares quality information on its SharePoint: Reports testing outcome



- **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

Impact of Network for Biologicals

- ... 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



Dr Ute Roskopf

Regulatory Systems Strengthening

Regulation of Medicines and Other Health Technologies

Essential Medicines and Health Products

World Health Organization (Geneva, Switzerland)

Office: +41 (0)22 791 2950

Email: rosskopfu@who.int