WHO–RIVM
GLOBAL VACCINE QUALITY CONTROL LABORATORIES
NETWORKING MEETING

Lage Vuursche (Bilthoven), The Netherlands
30 August – 2 September 2016

Meeting report

Table of content

Executive summary .................................................................................................................. 2
1 Background and meeting objectives ................................................................................. 3
2 Meeting opening .................................................................................................................. 4
3 Presentations ....................................................................................................................... 4
   3.1 WHO prequalification of vaccines ............................................................................ 4
   3.2 Country presentations ............................................................................................... 4
   3.3 Manufacturers’ perspective ...................................................................................... 5
4 Discussions and outcomes ............................................................................................... 7
   4.1 Basic principles: best practice for lot release (Working Group 1) ......................... 7
   4.2 Increasing the acceptance of producing countries’ lot release certificate
       (Working group 2) ....................................................................................................... 8
   4.3 Design and mechanisms for information-sharing (Working Group 3) ............... 10
   4.4 The need for a network and its terms of reference (Working Group 4) ............ 11
5 Conclusions and way forward ......................................................................................... 12
6 References .......................................................................................................................... 13

ANNEXES ............................................................................................................................ 14
   Annex 1: List of participants .......................................................................................... 14
   Annex 2: Revised template for Lot release certificate .................................................. 17
   Annex 3: Draft TOR of the proposed network .............................................................. 19
Executive summary
The first Global Vaccine Quality Control Laboratories Networking Meeting was organized jointly by WHO and the Dutch National Institute for Public Health and the Environment (RIVM) in Lage Vuursche (Bilthoven), the Netherlands, from 30 August to 2 September 2016.

The meeting brought together experts from national control laboratories (NCLs) involved in testing of WHO-prequalified vaccines, manufacturer associations, the European Directorate for the Quality of Medicines (EDQM) and WHO.

WHO prequalification of vaccines includes a requirement for the functionality of vaccine regulation in the producing countries. These countries are responsible for lot release of prequalified vaccines, including laboratory testing. The latter is a demanding task and must be performed by adequately qualified and experienced laboratories. WHO has initiated a range of activities for information-sharing by NCLs and harmonization of testing amongst these laboratories.

The objectives of the meeting were to strengthen the network of laboratories involved in testing of WHO-prequalified vaccines, exchange information on vaccine control strategies applied by the NCLs and explore the potential for more extensive sharing of work and information. Four topics were discussed in working groups: 1) Basic principles and best practice for lot release; 2) the meaning and content of the lot release certificate; 3) design and mechanisms for information-sharing, and 4) the need for a network and its terms of reference. The outcomes of the group work were discussed in a plenary session and the following was agreed:

- To establish a network of national vaccine control laboratories responsible for the control and release of WHO-prequalified vaccines, with terms of reference as agreed during the meeting (Annex 3);
- To prepare an inventory of laboratory information and procedures, as a basis for collaboration and convergence;
- To task an interim steering committee, established on the last day of the meeting, with defining a roadmap for the network, and exploring financing options; and
- To organize the next network meeting in the second half of 2017 at a venue to be confirmed.

A strengthened network of NCLs responsible for release of WHO-prequalified vaccines is expected to increase efficiency of lot release processes, promote convergence, and encourage reliance on the outcomes by recipient countries, thus reducing redundant testing. This is expected to increase access to quality-assured vaccines in WHO Member States.

The organizers thank the Government of the Netherlands and the United States Agency for International Development (USAID) for their financial contributions towards this meeting.
1 Background and meeting objectives

Immunization is one of the most cost-effective public health interventions. Ensuring the consistent safety and efficacy of vaccines is critical for the success of immunization programmes and to maintain public confidence in these programmes so that adequate coverage is achieved and maintained.

To facilitate access to needed vaccines of assured quality, the WHO Prequalification Team (PQT) prequalifies vaccines for procurement by UN agencies, governments and other organizations according to a defined procedure [1].

Vaccine batches are subject to inherent variability caused by their biological origin. Lot release by the national regulatory authority (NRA) serves to confirm that each batch meets the specifications of its marketing authorization before it is released onto the market. A basis for WHO prequalification is the regulatory functionality of the producing country, which is responsible for regulatory oversight of the product, including lot release with independent laboratory testing as appropriate [2].

In a context of increasing globalization and scientific advances, quality assurance of vaccines is becoming more demanding. At a WHO/Health Canada consultation on vaccine lot release held in Ottawa in 2007 [3], regional networks were considered as an approach to help solve the resource limitations that affect many regulatory authorities especially in developing countries. In recent years, several WHO-contracted laboratories have expressed their wish for the establishment of a collaboration platform.

Existing collaborative networks on vaccines have a limited geographical scope. With 194 Member States worldwide, WHO has a mandate to coordinate a network at the global level. Such a network would have a wide impact, considering that WHO-prequalified vaccines are used to immunize approximately two thirds of infants worldwide [4].

The objectives of the meeting were:

- To strengthen the network of NCLs involved in testing of WHO-prequalified vaccines, build a common understanding of testing standards, and reduce redundant testing thus contributing to more cost-effective testing
- To exchange information on vaccine control strategies applied by NCLs and explore potential for more extensive sharing of work and information
- To bring together
  - experts from NCLs involved in testing of prequalified vaccines to facilitate future networking and communication
  - stakeholders such as WHO and other UN organizations, manufacturer associations, EDQM and donors to facilitate common understanding on vaccine quality assurance by WHO and vaccine producing countries
- To discuss the following topics in sessions and working groups:
  - Best practices for prequalified vaccine lot release process (including minimum technical testing to be performed annually by the releasing NCL)
  - Producing countries’ vaccine lot release certificate
  - Design and mechanisms for information-sharing
  - The need for a WHO Global Vaccines Quality Control Laboratories Network and its Terms of Reference

Representatives from national control laboratories of countries producing WHO-prequalified vaccines, WHO-contracted laboratories, manufacturers’ associations, EDQM and WHO were invited to attend the meeting. A list of participants is attached (Annex 1). Representatives of the NCLs of Australia, Sweden, Russia and the United States were unable to attend.
2 Meeting opening

Dr Ute Rosskopf welcomed participants and invited Dr Sue Hill, Director of the WHO Essential Medicines and Health Products Department, to make some introductory remarks. Dr Hill expressed her support for the move towards a global network of laboratories controlling WHO-prequalified vaccines, and emphasized that collaboration and work-sharing are indispensable in today’s regulatory environment.

Dr Martijn Bruysters of the Dutch National Institute for Public Health and the Environment (RIVM) then introduced the Director of the Institute, Drs Annemiek van Bolhuis, who welcomed participants and gave an overview of the RIVM’s work.

3 Presentations

3.1 WHO prequalification of vaccines

Dr Ute Rosskopf described the WHO prequalification process for vaccines [1]. A prerequisite for acceptance of applications is the functionality of the NRA of the producing country with regard to six critical functions as related to vaccines: 1) Marketing authorization and licensing activities, 2) post-marketing surveillance, 3) NRA lot release, 4) laboratory access, 5) regulatory inspections and 6) regulatory oversight of clinical trials.

WHO-PQT evaluates each candidate vaccine by reviewing its product dossier including quality and clinical data, inspecting the manufacturing site, and performing initial testing of the final product [1, Section 3.4] of the prequalification procedure. In 2012 WHO-PQT introduced a “streamlined” prequalification procedure, allowing for case-by-case reliance on assessment reports, testing results and/or inspection reports shared by NRAs under specific collaboration agreements [1, Section 4.2].

After prequalification, vaccines are monitored for continuous compliance with their specifications through release of each batch by the responsible NRA, and through an annual targeted testing programme [1, Chapter 10]. WHO PQT coordinates this testing, which is performed by contracted NCLs, listed on the WHO website [5].

In recent years, WHO-PQT has initiated a range of activities to increase the efficiency of testing through harmonization of test methodologies [6], hands-on training [7] and information-exchange. Since 2014 a number of agreements have been signed with manufacturers of prequalified vaccines, allowing the releasing NCLs to include the data gathered during independent lot release in their annual reports to WHO. The joint WHO/RIVM meeting was called with a view to extend these activities by creating a platform for collaboration and information-sharing by NCLs.

3.2 Country presentations

Presentations about their laboratories and lot release procedures were given by NCL representatives from 21 countries: Belgium, Bulgaria, Denmark, France, Germany, Hungary, Italy, the Netherlands, and the United Kingdom (all using the Official Control Authority Batch Release (OCABR) guidelines [8]), Canada [9] and Switzerland (making partial use of the OCABR guidelines), Brazil, Cuba, Senegal, South Africa, China, India, Indonesia, Japan, the Republic of Korea and Thailand. An overview is given below.

Laboratories

- All laboratories reported that they work according to ISO/IEC 17025 standards. Most were accredited, one had an audit-based system and one was working towards accreditation.
All laboratories reported being engaged in several international and regional collaboration initiatives. Collaborative studies and joint audits were highlighted as being particularly useful.

Lot release practices applied in countries

- The number of batches released per year varied from just over 100 to several thousand batches, with an increasing tendency reported from several countries.
- For imported vaccines, there was some reliance on the lot release of producing countries with stringent regulatory authorities (e.g. ICH members and associates).
- WHO guidelines were reported to be followed for vaccines procured by UN programmes, with lot release performed by the designated responsible NRA. Prequalified vaccines for non-UN may be released in other countries under the respective national guidelines.
- Review of the lot summary protocol (LSP) was part of lot release in all countries.
- The decision to test was risk-based in most countries, even where regulations require testing of all batches, as in the EU and South Africa. The selection of lots for testing, was based on the nature of the product and factors such as consistency of production, product history (inspection findings, complaints, AEFI) and change control. In the UK, all batches of finished product and of drug substance are tested. In the Republic of Korea a risk-based system was introduced in April 2016. In Japan all batches are tested in line with public expectations; efforts are under way towards introducing a risk-based approach.
- The frequencies of testing varied between countries. Some laboratories reported that they do not perform any testing for specific products which have been categorized as low-risk according to risk-based factors as mentioned above. Where testing was performed, the frequency ranged from 10% (or at least 3 lots per year) to 100% of batches released.
- Apart from the testing frequencies, also the parameters tested varied between countries, ranging from full repeat of all licensed/pharmacopeia tests to selections of critical parameters. The establishment of criticality was based on the nature of the product as well as on the lab’s technical capabilities.
- Release certificates for the domestic market and for export were reported to differ in some countries. On the other hand, several laboratories reported using the same testing schedules for all samples, as they do not know which samples are for export.

3.3 Manufacturers’ perspective

Dr Thierry Pronce on behalf of IFPMA presented the manufacturers’ perspective. He expressed that manufacturers recognize the public health benefits of Independent Lot Release process and share the same common goal to ensure timely availability of safe, efficacious and high quality vaccines.

From a global perspective, while there is clear WHO guidance on lot release of WHO-prequalified vaccines, diverse national regulatory requirements complicate their delivery to end users. Some prequalified vaccines are supplied to over 100 countries, many of which have requirements for full testing. Re-testing of the same batch in four or more recipient countries is not uncommon. Often the testing provides no added value to the one from the NRA and moreover poses a risk of incorrect results and conclusions, potentially delaying the supply of vaccines to end users.

In light of current regulatory developments, including the move towards risk management and quality by design concepts, manufacturers support risk-based testing as recommended in WHO guidelines [2], taking into account the variability of the manufacturing method and consistency of production, and relying on the testing results of other competent authorities. Industry further supports a move away from in vivo testing methods, which introduce variability, and welcomes the
promotion of the 3R principles. The need for convergence of lot release requirements as a basis for information- and work-sharing was emphasized.
4 Discussions and outcomes

4.1 Basic principles: best practice for lot release (Working Group 1)
Chairperson: Dr Maria Baca-Estrada

Topics

- Acceptance and reliance:
  - How can we build trust in each other’s lot release processes?
  - Reliable results of technical testing performed by releasing country’s NCL
  - Transparency regarding established release processes, methods applied and frequency of testing
- How to maintain competence in testing
- Agreement on best practices towards a harmonized release process: Best practice guide; procedure for prequalified vaccine(s) lot release process and need to amend existing WHO guidance.

As all participants had expressed their interest to be part of this group, the topics were discussed in a plenary session on Day 2.

Discussion

1. Some best practices were identified from the country presentations, including recognition on the batch release of the producing country, risk-based testing, and performance of certain tests in parallel with the manufacturer’s tests to save time.

2. Lot release is only one element of a more comprehensive oversight throughout the product life-cycle that includes a range of regulatory mechanisms such as licensing activities, market surveillance, post-approval changes and GMP inspections. Collaboration among all NRAs/NCLs responsible for controlling WHO-prequalified vaccines, from within and outside the ICH region, has the potential to increase the trust of recipient countries in the quality of the vaccines regulated and released by these NRAs/NCLs.

3. The same requirements should apply for vaccines released onto the local market and those for export. This will increase confidence of recipient countries in the lot release process of the responsible NRA.

4. Agreement on harmonized practices with minimum criteria for lot release of WHO-prequalified vaccines was felt to be too ambitious in the short term. Harmonization will occur gradually through incorporation of best practices into national guidelines.

5. Activities to maintain competence despite reduced testing schedules were described by several NCL representatives. Maintaining competency is a requirement of the Quality Management System (e.g. ISO/IEC 17025) and is supported in part by participation in proficiency studies. Information-sharing among NCLs may help to identify opportunities for collaboration in this regard.

Outcomes

The meeting participants supported a move towards transparency around each other’s lot release practices as a first step towards convergence. More transparency among the wider circle of countries receiving WHO-prequalified vaccines can create additional trust, fostering reliance and reduction of redundant testing.

Next steps

Building on laboratory information available at WHO and on the presentations made at the meeting, a “mapping” exercise will be conducted by questionnaire, covering aspects such as: Mandate and reporting structure of the NCL relative to the NRA, mechanisms to maintain competence, sampling procedures, and approaches to implement risk-based decisions on testing. Parts of the questionnaire may need to be product-specific.
4.2 Increasing the acceptance of producing countries’ lot release certificate (Working group 2)
Chairperson: Dr Geneviève Waeterloos; Co-chair: Dr Barbara Bolgiano

Topics

- What kind of information should be included in the NRA release certificate in the country of production?
- Minimum information required?
- Distinguishing between vaccine release certificates of country of production and those of procuring countries

Meeting document: Model certificate for the release of DT-based combined vaccines by NRAs [10]

Discussion

The working group discussed updates to WHO model format for lot release certificates [10] and proposed a revised template, which was discussed in the plenary report-back session on Day 3. The following revisions were agreed:

- Reference to paragraph 7.3 of WHO guidance on lot release¹, defining on what basis the lot was released. This paragraph was thought to adequately reflect the fact that testing may or may not have been conducted in accordance with a risk-based schedule, and that the lot release is supported by the wider regulatory oversight of the NRA of the country of production.
- Mention of ISO/IEC 17025 as the common standard adhered to by all participating laboratories.
- Addition of fields for the marketing authorization number, manufacturing details, diluents and their expiry dates, and the releasing institution’s name.

Furthermore, some revisions to the format and presentation of references were proposed for ease of use and maintenance.

Outcomes

The agreed revised template for release of compliant lots is shown in Annex 2. It is intended for use by NCLs when releasing WHO-prequalified vaccines. NCLs have the right to delete any statements on the template that are not in line with their legal and regulatory set-up.

A similar template will apply for non-compliant lots, with the mention “non-compliant” in the concluding statement.

¹ From: WHO lot release guidelines [2], Paragraph 7.3:
“The responsible NRAs/NCLs are required to issue a certificate of release for vaccines that are distributed through United Nations agencies (16). Vaccines distributed through United Nations agencies are prequalified by WHO, to ensure that the products comply with the quality and safety standards established by the Organization. This release certificate is issued on the basis of, as a minimum, a review of the lot summary protocol for the relevant lot.
The responsible NRA/NCL plays a key role in ensuring that products meet the specifications outlined in the marketing authorization and WHO recommendations. This is achieved by maintaining regulatory oversight, assessing and approving changes to manufacturing processes – including testing and specifications, compliance with GMP – and PMS of AEFI. The release certificate issued by the responsible NRA/NCL should be forwarded by the United Nations agencies to the NRA/NCL of the receiving country, and the summary protocol will be provided upon request.”
Next steps
Current WHO guidance makes provision for product-specific templates. The use of a common template for lot release of prequalified vaccines in line with relevant guidance [2] will be proposed for consideration by the WHO Expert Committee for Biological Standards at its next meeting.
4.3 Design and mechanisms for information-sharing (Working Group 3)

Chairperson: Dr Surinder Singh

**Topics**

- Sharing of data gathered through national lot release (inclusion of all NCLs of PQ vaccine-producing countries – if, what and how?)
- What data / information, in addition to the vaccine quality data gathered through national lot release process, could be shared:
  - among NCLs (network members) and WHO
  - with NCLs of other recipient countries (associate members)?
- Mechanism for information-sharing
- Confidentiality undertakings
- Sharing of data about quality of vaccines with stakeholders (if, what and how? for stakeholders: UN agencies, manufacturers?)

**Discussion**

The working group discussed the above topics and proposed a structured, step-wise approach to information-sharing on an ‘as-needed’ basis:

- Immediately after the meeting, presentations and contact details were shared among the meeting participants.
- In the short term (i.e., the next year), shareable information could include numbers of vaccine lots released, and laboratory information collected through the ‘mapping’ exercise, e.g. the risk-based considerations underlying the testing schedules.
- In the longer term, sharing could be extended to lot release results and comparison with manufacturer’s results, lot release certificates, and information on testing methodologies. Manufacturers will be consulted before exchange of any information that may include proprietary or confidential elements.

Initial exchanges will be by e-mail. A future perspective is the establishment of a dedicated electronic platform with defined access rights for different user types. It was noted that this must be designed and maintained adequately to ensure that it is secure and user-friendly.

**Outcomes**

The meeting served to establish contacts among participants, enabling them to approach each other for scientific and technical exchanges.

There was general agreement to the principle of exchanging information on an “as-needed” basis, using a step-wise approach to gradually expand the type of information exchanged.

**Next steps**

NCL representatives will consult within their NRAs and with manufacturers and other stakeholders to explore what information can and should be shared. This builds on existing reporting to WHO, which includes sharing of lot release results by some of the contracted laboratories.

WHO will obtain advice from its legal department on establishing confidentiality agreements and undertakings, building on existing agreements.
4.4 The need for a network and its terms of reference (Working Group 4)
Chairperson: Professor Derek Litthauer

Topics

- How to promote convergence of services of NCLs – need for a network?
- How can the network contribute to facilitate access to and availability of quality assured vaccines?
- How can the network contribute to build regulatory reliance?
- Terms of reference and organization: Objectives, activities (including 3R initiatives), membership/participation, management, continuity.

Meeting document: Draft terms of reference for the proposed network

Discussion

The need for a network to promote gradual convergence of national regulations on vaccine lot release and regulatory reliance was confirmed in the discussions of Working Group 1. The discussions focused on the draft terms of reference, membership and management structure of the network, incorporating some of the outcomes of earlier discussions. The following was agreed:

1. The network is expected to communicate its experience and best practices “upward”, providing input to the development and revision of WHO guidance related to vaccines, and “outward”, raising awareness of its activities among recipient countries of WHO-prequalified vaccines and other stakeholders.
2. While adherence to the 3R principles cannot be enforced, the network may be used for promotion of these principles in the longer term as a means to make testing less variable and thus more efficient.
3. Full members should include the NCLs responsible for testing and releasing WHO-prequalified vaccines. A liaison officer from a regulatory body can be appointed to ensure inclusion of regulatory decision-makers. In addition to associate members from recipient countries, other stakeholders, such as UN Agencies and manufacturers, should have the possibility to be admitted as observers. The roles of the different types of members, e.g. in terms of access to shared information, would be determined on a case-by-case basis.
4. A steering committee with a balanced geographical representation will serve as a management structure for the network. Continuity will be ensured by replacing 50% of its members at each new election. The steering committee will be elected at the next network meeting. Until then, an interim steering committee, to be appointed at this meeting, will propose an organizational framework and a roadmap for the network, with prioritization of short-term and long-term activities.

Outcomes

The revised draft TOR are attached to this report (Annex 3).

Next steps:

Participation in the network as a full member is voluntary but strongly encouraged. NCL representatives, in consultation with their national authorities, will confirm that there is no legal or other obstacle to their participation in the proposed network.
5 Conclusions and way forward
The meeting outcomes as specified in the meeting terms of reference were the following:

- Established contacts between experts from NCLs involved in testing of prequalified vaccines for scientific and technical exchange on vaccine testing
- Overview of applied strategies of vaccine quality control by individual NCLs
- Meeting report (including outcome of the working groups and the way forward)
- Agreed position on the future collaboration within the WHO Global Vaccines Quality Control Laboratories Network and - if applicable - its Terms of Reference

In concluding the meeting, Dr Ute Roskopf said that she was very happy to see that all of the above meeting outcomes were achieved, and that the common position on future collaboration was to establish a WHO global vaccines control laboratories network.

It was proposed that the interim steering committee of the network should consist of the four chairpersons of the working groups (Dr Maria Baca-Estrada, Dr Geneviève Waeterloos, Dr Surinder Singh and Professor Derek Litthauer) together with the WHO/TAL secretariat (Dr Ute Roskopf) and with support by Dr Martijn Bruysters (RIVM) and Dr Olexandr Polishchuk (WHO). All the nominees agreed to serve on the interim steering committee.

The way forward will entail the following next steps as agreed in the meeting discussions.

1. The interim steering committee will exchange frequently by e-mail and teleconference until the next network meeting to:
   - Support the preparation of the meeting report,
   - Draft a road map for the network, including timelines,
   - Develop and circulate a questionnaire for mapping of NCL information and
   - Explore financing of the network, including the next meeting and e.g. a rotational post at WHO.

2. Meeting participants will:
   - Confirm their participation in the network in consultation with their NRA, including the types of information that can be shared; and
   - Complete the mapping questionnaire to be circulated by the interim steering committee.

3. WHO/TAL will approach additional laboratories releasing prequalified vaccines to share their lot release data with WHO (on the consent of respective manufacturers), including laboratories not currently contracted by WHO, and for posting of information about the existence and extent of such reporting on the WHO web site.

4. The next network meeting will be held in the second half of 2017 at the National Institute of Biologicals (NIB) in Noida, India (venue to be confirmed). The first regular steering committee will be elected at that meeting.
6 References


3 Meeting report. WHO/Health Canada Consultation on Vaccine Lot Release, Ottawa, Canada, 28 February to 1 March 2007. Available at: http://www.who.int/biologicals/publications/meetings/areas/vaccines/lot_release/Final%20Re p%20Mtg_lot%20release%20March%202007-2.pdf?ua=1


5 List of WHO contracted laboratories performing tests on behalf of the WHO vaccine prequalification programme. World Health Organization. 8 April 2015. Available at: www.who.int/immunization_standards/vaccine_quality/Laboratories_table_08April2015.pdf?ua=1


7 Supporting countries in quality assurance for pentavalent vaccines. First WHO-ISS hands-on laboratory training course held in Rome, Italy. World Health Organization. Available at: www.who.int/immunization_standards/vaccine_quality/vmc/en/


ANNEXES

Annex 1: List of participants

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<tr>
<th>Name</th>
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**Manufacturers’ representatives**

IFPMA: International Federation of Pharmaceutical Manufacturers & Association
DCVMN: Developing Countries Vaccine Manufacturers Network

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Annex 2: Revised template for Lot release certificate

Model certificate for the release of prequalified vaccines by NRAs

<table>
<thead>
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<tr>
<td>International non-proprietary Name / Common name:</td>
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</tr>
<tr>
<td>Batch numbers appearing on package and other identification numbers associated with this batch:</td>
<td></td>
</tr>
<tr>
<td>Type of container used:</td>
<td></td>
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<tr>
<td>Total number of containers or lot size:</td>
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<tr>
<td>Number of doses per container:</td>
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<tr>
<td>Date of start of period of validity (e.g. manufacturing date):</td>
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<tr>
<td>Date of expiry (DD/MON/YYYY):</td>
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<tr>
<td>Storage conditions:</td>
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</tr>
<tr>
<td>Diluent lot number(s) (if applicable):</td>
<td></td>
</tr>
<tr>
<td>Diluent expiry date(s) (if applicable):</td>
<td></td>
</tr>
<tr>
<td>Marketing authorisation number (member state) issued by:</td>
<td></td>
</tr>
<tr>
<td>Name and address of manufacturer:</td>
<td></td>
</tr>
<tr>
<td>Site(s) of manufacturing</td>
<td></td>
</tr>
<tr>
<td>Name and address of marketing authorisation holder if different:</td>
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</table>

The following lot(s) of __________________________________________ vaccine produced by ____________ (1) whose numbers appear on the labels of the final evaluated containers, complies with the relevant marketing authorization, the national specifications and provisions for the release of biological products(2) and Part A(3) of the WHO Recommendations to assure the quality, safety and efficacy of the concerned vaccines (yyyy), (4) and with corresponding WHO recommendations for each of the vaccine’s individual components, as well as with WHO good manufacturing practices: main principles for pharmaceutical products; (5) Good manufacturing practices for biological products; (6) and Guidelines for independent lot release of vaccines by regulatory authorities. (7)

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(1) Such as batch number of final bulk.
(2) Some product may also have approved extended controlled temperature conditions at the end of use.
Certificate no. ________

This batch has been examined using documented procedures which form part of a quality system which is in accordance with the ISO/IEC 17025 standard.

The release decision is based on the elements described in paragraph 7.3 of the Lot Release guideline\(^{(7)}\):

This batch has been found compliant with the above by the institute below, member of the WHO Network of National Vaccine Control Laboratories.

Name (typed) __________________________________________

Institute ______________________________________________

Position ______________________________________________

Signature ______________________________________________

Date ___________________________________________________

\(^{(1)}\) Name of manufacturer.

\(^{(2)}\) If any national requirements have not been met, specify which one(s) and indicate why the release of the lot(s) has nevertheless been authorized by the NRA.

\(^{(3)}\) With the exception of provisions on distribution and shipping, which the NRA may not be in a position to assess.

\(^{(4)}\) The relevant WHO Technical Report Series, No. XXX, Annex Y.


Annex 3: Draft TOR of the proposed network

Global Network of National Control Laboratories (NCLs) of countries producing vaccines or other biological medicinal products prequalified by WHO

Introduction
The network will form one part of a larger strategy to promote a risk-based approach to lot release testing, as recommended in WHO guidelines on Lot Release Testing of Vaccines (WHO Technical Report Series 978) for the lot release of prequalified vaccines. The network will serve as a platform for confidential exchange of quality and technical information on vaccines prequalified by WHO.

The foundation of the network responds to World Health Assembly Resolution no. 67.20, which calls for regulatory system strengthening for medical products through the following actions:
• Strengthen WHO’s prequalification programme, including its integration and coherence.
• Support the building-up of effective national and regional regulatory bodies and networks.

Objectives
1. To facilitate access to and availability of prequalified vaccines through reliance on the batch release of the respective network member states, thereby reducing redundant testing, and contributing to more cost-effective testing.
2. To share information on product-related quality and technical information on prequalified vaccines gathered through the national lot release processes within the network as well as the annual reports of WHO contracted laboratories and NRAs/NCLs of countries producing WHO-prequalified vaccines.
3. To facilitate mutual recognition by promoting the development of harmonized common standards and best practice, including the use of the 3R principles, for the release of prequalified batches.
4. To contribute to and support WHO in test harmonization –, and providing input to future revisions of WHO guidelines.
5. To support strengthening of the network through technical assistance / training to members of the network.
6. To pass information on to other countries to strengthen the recognition of WHO prequalification globally.

Activities
• To document the quality of released vaccine batches using a unified WHO batch release certificate.
• To establish information sharing mechanisms (e.g. sharing of annually reported batch release data\(^4\) and other relevant technical information\(^5\) and best practices, such as defining control strategies and promoting application of the 3R principles) and a framework for recognition of results by network members and NCLs/NRAs in countries that are recipients of UN procured vaccines.
• To initiate and facilitate information exchange on existing test methods to harmonize their use.

\(^4\) Or in future via an online database
\(^5\) For example, NCL data in comparison with data from manufacturers. The steering committee will determine, with legal advice and in consultation with manufacturers, what data can and should be shared.
• To submit experience gained with the possible refinement of WHO model protocols for the manufacturing and control of specific vaccines, and suggestions in this regard, for consideration by WHO.
• To disseminate information on activities to other stakeholders, e.g. regional offices.

Composition
Membership will include:

a) Full members: NCLs from countries producing WHO-prequalified vaccines, and WHO-contracted NCLs;

b) Associate members: NCLs/NRAs in countries that are recipients of UN-procured vaccines; and

c) Observers (e.g. UN procurement agencies, manufacturers).

The roles will be determined on a case-by-case basis.

Secretariat: WHO.

Steering committee: WHO and an elected group of members on a rotational basis, with representation from different geographic regions.

Confidentiality
Confidentiality undertakings between parties exchanging confidential information will need to be in place. Building consent into the PQ application process for the subsequent sharing of confidential lot release information could also be considered.

Financing
[To be discussed by the Interim Steering Committee]