

WHO Operational Tool for efficient and effective lot release of SARS-CoV-2 (Covid-19) vaccines

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World Health
Organization

Scope of the tool

This operational tool was developed to assist national regulatory authorities in all countries to apply principles described in WHO Technical Guidelines to implement efficient and effective lot release of COVID-19 vaccines, including those granted WHO Prequalification or Emergency Use Listing, to mitigate potential bottlenecks and unnecessary wastage of these urgently needed products under the public health emergency of international concern.

Introduction

Vaccine lot release by a National Regulatory Authority (NRA) or National Control Laboratory (NCL) is a fundamental component of the post-licensing regulatory oversight of vaccines and is generally backed by national legislation. WHO Guidelines strongly emphasize the need to establish regulatory decision-making processes which minimize duplication and thereby make much-needed vaccines available for use with minimal delay during public health emergencies¹.

For WHO prequalified (PQ) vaccines supplied through UN agencies, or independently procured, WHO Guidelines² recommend vaccine receiving countries to apply the regulatory reliance concept for lot release, i.e., rely on, or recognize, each lot certificate issued by the responsible NRA/NCL³ that has been designated as well-functioning, stable authority operating at maturity level 3 or 4 following benchmarking of their regulatory systems by WHO^{4,5}.

The WHO National Control Laboratory Network for Biologicals (WHO-NNB) facilitates access to prequalified vaccines through recipient countries' reliance on and/or recognition of the lot release decisions of the responsible NRA. As a result of the efforts to encourage implementation of WHO guidance, many countries rely on the lot release certificates from the responsible NRA that are provided with each batch of non-COVID-19 PQ vaccines⁶.

Lot release of COVID-19 vaccines for WHO PQ/EUL by the responsible NRA/NCL designated by WHO

COVID-19 vaccines that are WHO emergency use listed (EUL) or prequalified (PQ) will become available for use following their lot release by the responsible NRA/NCL designated by WHO.

WHO recommends the responsible NCLs to perform independent lot release of vaccines by review of the manufacturers' summary lot protocol which may be supplemented by performance of testing of the vaccine. Independent lot release testing is expected to be a key element in the regulation and control of COVID 19 vaccines to support confidence in their use in urgently needed national and global immunization programmes.

Product-specific Official Control Authority Batch Release (OCABR) guidelines for independent lot

¹ Guidelines on regulatory preparedness for provision of marketing authorization of human pandemic influenza vaccines in non-vaccine producing countries, WHO Technical report series, 1004, Annex 7 <https://www.who.int/biologicals/vaccines/influenza/en/> (accessed 04 January 2021)

² Guidelines for independent lot release of vaccines by regulatory authorities, WHO Technical Report Series, 978, Annex 2 https://www.who.int/biologicals/areas/vaccines/lot_release_of_vaccines/en/ (accessed 04 January 2021)

³ The responsible NRA/NCL is defined as the NRA/NCL taking responsibility for regulatory oversight of a product with regard to the critical regulatory functions defined by WHO, including independent lot release, WHO Technical Report Series, 978, page 51, https://www.who.int/biologicals/areas/vaccines/lot_release_of_vaccines/en/ (accessed 04 January 2021)

⁴ https://www.who.int/medicines/regulation/benchmarking_tool_version_vi/en/ (accessed 04 January 2021)

⁵ also referred to as "Stringent Regulatory Authorities, SRAs, in this document

⁶ https://www.who.int/immunization_standards/vaccine_quality/who_nnb/en/ (accessed 04 January 2021)

release of pandemic COVID-19 vaccine platforms by the European network of Official Medicines Control Laboratories have been published.⁷ These NCLs, together with additional NCLs of the WHO-NNB, will release COVID-19 vaccine lots according to international standards and the product specifications set out in the EUL/PQ recommendation or the stringent regulatory authorities (SRA's) emergency use authorization, conditional marketing authorization or equivalent.

In addition to the lot-by-lot release, PQ/EUL requires the responsible NRA/NCLs to conduct post-release surveillance of vaccine quality-related issues (e.g., during their use) and ensure timely exchange of any information or findings with WHO on any issues related to product quality.

Expedited lot release of COVID-19 vaccines by countries receiving PQ/EUL vaccines or vaccines approved by Stringent Regulatory Authorities (SRAs)^{8,9}

During the COVID-19 pandemic, the allocated COVID-19 vaccines should be released to the immunization programme in the shortest possible time without compromising quality and safety. Testing of vaccines requires sophisticated and complex analytical methods and equipment that should be managed by trained staff. Additional in-country testing may severely delay access to vaccines; utilize the remaining shelf-life of the vaccine whilst testing is performed; quickly exhaust reference materials and standards, which could lead to delays in testing; and put an unreasonable burden on the vaccine manufacturers to undertake method transfer to numerous NCLs globally in a short time frame.

WHO advises that receiving countries do not conduct lot release test again on vaccines procured from assured sources, e.g., vaccines that are WHO prequalified, listed under WHO EUL, or approved by SRAs, as they have been tested and released already by NRAs with stable, formal approaches for vaccine approval. In other words, in order to expedite the deployment of the EUL listed vaccines as rapidly as possible, WHO's recommended lot release strategy is to rely on the lot release certificates issued by the responsible NCL that are provided with each batch of PQ/EUL vaccines. This will mitigate the bottleneck of in-country independent testing and is already the case in many countries for non-COVID-19 vaccines.

The NCL lot release certificate will be provided to recipient countries by the manufacturer of the vaccine lot. The certificates may be either in the form of a WHO model certificate¹⁰, national release certificate or an EU OCABR certificate which, as well as being the basis for lot release reliance within Europe, is recognized in many countries outside Europe. Countries are strongly encouraged to either continue with, or to newly implement specifically for COVID-19 vaccines, this practical example of regulatory reliance.

If countries are required by law to review the summary lot protocols, vaccine release should be done quickly and through the review of the minimum documents. The overall release time should not be more than 2 working days¹¹. Countries may also want to explore if there can be any law or exception granted in the case of emergency use of a vaccine with existing SRA approval. For further reading please see the WHO Guidelines for independent lot release of vaccines by regulatory authorities¹².

⁷ <https://www.edqm.eu/en/ocabr-activities-related-covid-19-vaccines> (accessed 04 January 2021)

⁸ Guidance on developing a national deployment and vaccination plan for COVID-19 vaccines, INTERIM GUIDANCE 16 November 2020 https://www.who.int/publications/i/item/WHO-2019-nCoV-Vaccine_deployment-2020.1 (accessed 04 January 2021)

⁹ "Product eligibility under the COVAX Facility" https://extranet.who.int/pgweb/sites/default/files/documents/Product-Eligibility_COVAX-Facility_Dec2020_0.pdf (accessed 04 January 2021)

¹⁰ WHO Model NRA/NCL Lot Release Certificate for SARS-CoV-2 (Covid-19) vaccines is provided as Annex

¹¹ https://www.who.int/docs/default-source/coronaviruse/act-accelerator/virat-vraf2.0_final_3dec2020.xlsx?sfvrsn=37fd4fa8_1&download=true (accessed 04 January 2021)

¹² Guidelines for independent lot release of vaccines by regulatory authorities, WHO Technical Report Series, 978, Annex 2 https://www.who.int/biologicals/areas/vaccines/lot_release_of_vaccines/en/ (accessed 04 January 2021)

Lot release of self-procured or donated COVID-19 vaccines

For self-procured or donated COVID-19 vaccines, review of the summary lot protocol by the procuring/receiving NRA/NCL is essential for assuring the safety and quality of these products. This is additional to the lot release that should have been performed in the country of manufacture. Recognition/acceptance of lot release certificates from the NRA/NCL of the country where the vaccine is manufactured, or from another competent NRA/NCL, should be considered as a strategy.

Re-testing of COVID-19 vaccines performed by receiving countries may impact timely access to, and be associated with a disruption of, their vaccine supply. Several countries have indicated to WHO that, rather than retest, they will implement reliance on the release performed by the responsible NRA/NCL. WHO considers this to be a good model and countries considering repeat in-country laboratory testing for COVID-19 vaccines are strongly encouraged to consult with WHO on the challenges of doing so and on other strategies available prior to making any decision on lot release procedures.

Development history of the Document

The document was drafted by the WHO Department of Regulation and Prequalification with inputs from WHO Departments and technical units responsible for: developing and maintaining the WHO Guidelines (MHP/HPS/TSS¹³); coordinating global and regional workshops on the Guidelines (MHP/HPS/TSS); managing the WHO-NNB (MHP/RPQ/REG¹⁴); managing the WHO Prequalification of vaccines programme (MHP/RPQ/PQT¹⁵); and the COVID vaccines regulatory and safety preparedness and deployment coordination (MHP).

An initial draft was reviewed by the following stakeholders: WHO Departments: IVB¹⁶, UHC¹⁷, Science Division and WHE¹⁸; WHO Regional Advisors for access to medicines and COVID task force members; WHO EPI managers; UNICEF, CEPI and GAVI with their technical advisors.

Version 1.0 (this document) was prepared by RPQ taking into account the comments received.

¹³ MHP: Division of Access to Medicines and Health Products; HPS: Department of Health Product Policy and Standards; TSS: Unit of Technical Standards and Specifications

¹⁴ RPQ: Department of Regulation and Prequalification; REG: Unit of Regulation and Safety

¹⁵ PQT: Unit of Prequalification

¹⁶ IVB: Department of Immunization, Vaccines and Biologicals

¹⁷ UHC: Division of Universal Health Coverage

¹⁸ WHE: Division of Health Emergency Preparedness