

Post EUL submissions procedure

30 March 2022

The WHO Emergency Use Listing (EUL) is a procedure for assessing unlicensed vaccines during public health emergencies to expedite the availability of these products to the affected population. These assessed vaccines are expected to continue their development. New quality, safety and efficacy data should be submitted for evaluation and the risk benefit assessment updated accordingly.

During the public health emergency, manufacturers may experience supply chain/manufacturing disruptions due to manufacturing, distribution and trade restrictions. Ensuring continuity of supplies for vaccines to address the outbreak remains crucial. The addition of new manufacturing sites for part or all the manufacturing process, as well as changes in the site(s) responsible for quality control and the continued submission of these changes to WHO is part of the EUL process.

The recommendation of a vaccine under Emergency Use Listing is accompanied by a series of recommendations or conditions that must be addressed by the EUL holder within the timelines discussed and agreed at the time of the EUL recommendation. These conditions are referred to as Post EUL Commitments and included in the EUL process.

1) Post EUL variations

The vaccine applicant/EUL holder must promptly inform WHO of all changes to the vaccine regarding formulation, manufacturing process, testing methods, specifications, update on the labelling information, facilities and any other aspects that might (a) result in a change of the safety and/or efficacy and/or performance of the product or (b) change the basis for the listing recommendation.

WHO accepts rolling submission of the dossier pre-EUL (in line with the document [Emergency Use Listing procedure](#) and [Rolling review of COVID-19 vaccines](#)). However, rolling submissions Post EUL are no longer feasible per 1st of January 2022 and retro-actively for all vaccines recommended since 1 November 2021.

As part of the WHO EUL process for vaccines, variations can be classified in 2 groups:

1) Update of EUL recommendation: major variations that require WHO approval before vaccines can be made available via UN supply and/or COVAX. These include changes in the manufacturing and/or control sites that are necessary to prevent/mitigate shortages of supplies, additions of manufacturing sites for manufacturing antigen or finished EUL vaccine, changes in suppliers of starting materials, reagents, intermediates or active substances (DS), changes to the summary of product characteristics or WHO Product Information (SmPC/product insert-product leaflet). Manufacturers are requested to submit these variations once (and as soon as) the corresponding WHO regulatory authority of record approved the variation

2) For notification purposes: The WHO EUL Secretariat must be notified within one month of approval by the WHO regulatory authority of record of the vaccine under EUL recommendation on minor and moderate variations.

The submission of documents for all variations should include the following:

- a) Covering letter indicating the reason/scope of the submission
- b) NRA approval evidence including assessment reports
- c) List of changes
- d) High level overview of all documents supporting the proposed changes listed in the relevant section of Appendix 2 (Manufacturing and Quality Control) or Appendix 3 (Efficacy and Safety) of [Guidance on Variations to a Prequalified Vaccine](#), as appropriate.
- e) Indicate the CTD section that is being updated / impacted due to the submitted changes
- f) A separate Table of Content – hyperlinked – also remains important, especially if the submission contains several documents and different folders.
- g) Copy of the most recent revised label (if applicable) both the annotated and clean version
- h) Commit to ensure that the quality of the product is and will not be compromised (e.g., compliance with GMP is maintained)

2) Post EUL commitments

Once a vaccine is recommended for emergency use under the EUL, a list of Post EUL commitments is communicated to the WHO EUL holder. Tentative timelines for the submission of relevant documents in response to these set of conditions are requested. However, WHO EUL secretariat may agree or disagree with the proposed timelines. Failure to meet these commitments, could result in a de-listing of the vaccine.

In addition, the applicant should provide tentative timelines for the submission of additional/supplementary information based on the expected dates of completion/planned interim analyses of studies currently ongoing/or being initiated. Unexpected changes in agreed timelines should be communicated to the WHO EUL Secretariat.

Submission of responses to Post EUL commitments should clearly indicated the CTD section that is being updated.

The submission of Post EUL commitments should include the following:

- a) Covering letter indicating the reason/scope of the submission (e.g.: reference to the WHO recommendation or commitment).
- b) List of relevant documents supporting the update
- c) High level overview of the documents submitted (as per item b)
- d) Copy of the most recent revised label (if applicable).

The documentation should be submitted to the following email address WHOEU@who.int