

Coordination between WHO Living Guidelines and WHO EUL and PQ processes for Therapeutics in the context of COVID-19

Ensuring access to quality assured, safe and effective therapies is a core part of WHO's mission as the United Nations agency for human health. Both guidelines recommendations and WHO's EUL/PQ processes are relevant determinations for procurement agencies and member states.

Background on WHO Living Guidelines: "living guidelines", uses a combination of continuous literature surveillance, rapid updating of prioritized systematic reviews and virtual consultations with "living guideline" panels to update and develop new WHO recommendations. This approach has been applied by WHO to ensure that the latest evidence on covid-19 therapies and updated recommendations can reach health workers worldwide as quickly as possible.

Background on WHO EUL: The WHO Emergency Use Listing Procedure (EUL) is a risk-based procedure for assessing and listing unlicensed vaccines, therapeutics and in vitro diagnostics with the ultimate aim of expediting the availability of these products to people affected by a public health emergency. This will assist interested UN procurement agencies and Member States in determining the acceptability of using specific products, based on an essential set of available quality, safety, and efficacy and performance data.

In order to streamline and align WHO's living guidelines and EUL/PQ processes, EUL and PQ assessment processes may begin before recommendation for use via the guidelines process in the following context and steps:

1. The WHO technical department will assess clinical data that exists or is likely to be generated within 2-4 months, which may (depending on the results) support a positive WHO recommendation on the use of the product.
 - ⇒ Such clinical data will preferably be generated from randomized, controlled clinical trials and will be able to inform high quality evidence synthesis. For example, such data should ensure that large enough numbers of subjects/patients are enrolled in trials, sufficient numbers of events will be available and endpoints are sufficiently important for public health/clinical practice guideline decisions¹, and, where available, informed by alignment between the ongoing specific product trials and relevant WHO TPPs².
2. Where the WHO technical department makes the assessment that data exists that may support a positive WHO recommendation, evidence synthesis and critical appraisal for the guidelines process and assessment procedures for WHO EUL or prequalification may proceed in parallel.
3. Where such parallel assessment occurs, the outcomes will be announced in a coordinated fashion. Going forwards neither PQ nor EUL will be granted until a guidelines recommendation for use has been made.

¹ This would require sufficient numbers when combined (totality of evidence) (i.e. at least 2000 enrolled into) and sufficient end points (i.e. at least 50 events in treated arms). These are not absolute numbers, but rather illustrative. Note, end points that are patient-important outcomes and/or public health impact will be considered. Ph III data is preferred but WHO will look at Ph II and consider if sufficient numbers and patient-relevant outcomes (e.g., decline in hospitalization, decline in time to symptom resolution) and if full visibility on methodology, randomization techniques, etc.

² <https://www.who.int/publications/m/item/covid-19-therapeutics-target-product-profile-for-hospitalized-patients>
<https://www.who.int/publications/m/item/who-target-product-profiles-for-covid-19-therapeutics-for-non-hospitalized-patients>

By avoiding sequential guidelines and EUL/PQ procedures, it may be possible to bring forward access timelines by several weeks.

Although this procedure was developed in the context of covid-19, the possibility for parallel guidelines and PQ assessment processes extends beyond covid-19 to any medical product in advanced development potentially considered to align with a priority unmet need by the relevant WHO technical department.