Application of parallel, coordinated, and independent evaluation procedures for health products that are eligible for prequalification[1] and require WHO recommendations[2] on their use

Scope

The objective of this review is to ensure high quality, efficiency, predictability, trust and alignment between the WHO Norms, Standards and Guidelines and the Prequalification of health products processes. This review aims at creating synergies between WHO departments responsible for issuing recommendations on health products, avoiding dissonant recommendations and ensuring consistency, quality and predictability of WHO's systems and hence facilitating evidence-based and timely decision-making by member states and procurement agencies who rely on WHO's specifications and guidance. The aim is also to ensure effective, safe products, innovations and recommendations reach people as fast as possible.

This interim report covers evaluation procedures for health products (medicines, vaccines, medical devices including diagnostics, vector control products and other health products) that:

- are eligible for WHO prequalification; and
- require a new dossier for prequalification assessment by the WHO Regulation and Prequalification Department (RPQ); and
- require a new or amended recommendation on their use from the responsible WHO department(s) and with the oversight of the Chief Scientist and Science Division (SCI) as part of WHO's Quality Norms and Standards work.

Background

In September 2023, WHO identified this review as a priority and established a cross-cutting working group to do an in-depth review of the WHO Guidelines and the Prequalification processes for health products and come up with a list of main findings and proposed actional recommendations on how to better align, streamline and improve these processes.

One of WHO's core functions is to facilitate timely access to quality-assured, safe and effective health products. This involves the development of recommendations for the use of these health products by the WHO departments responsible for issuing recommendations on health products responsible to do so as part of the WHO's normative work and the listing of prequalified products by RPQ.

[1] In this document, the term "prequalification" is considered to include Emergency Use Listing (EUL)

[2] In this document "recommendations" refers to guidelines and other recommendations developed in a group procedure or other appropriate expert/advisory group including those by SAGE, MPAG and other relevant committees that issue WHO recommendations related to health products.

The COVID-19 pandemic demonstrated that alignment of recommendation development and prequalification for COVID-19 related health products is possible and results in more timely access to these products saving lives. For example, access to the first oral antivirals was accelerated because the prequalification and guideline process was done in parallel.

Currently, the process of recommendation development typically takes between 6-24 months but, in some circumstances, can be much longer. Typically, prequalification assessment of health products for which a recommendation is being developed only starts once that recommendation is issued. This may delay access to important health products that require recommendations in countries that rely on these, resulting in an increase in health inequities. To address this, WHO applies the following guiding principles:

1. Clear, streamlined, predictable, timely and quality-assured WHO procedures for normative functions and pre-qualification
2. Independence of the normative and prequalification processes
3. Coherent and coordinated organizational positions on health products
4. Building on WHO's experience with SAGE immunization and therapeutics during the COVID-19 pandemic.

Parallel, coordinated although independent processes

To accelerate access to appropriate, quality-assured, safe and efficacious products in countries that rely on these normative procedures, WHO should move towards a coordinated and aligned evaluation approach for all health products that meet the criteria mentioned in the scope of this document. For this, WHO should apply parallel rather than the current sequential processes in its prequalification and development of recommendations under these guiding principles:

The parallel process will be initiated once the scientific relevance and need are agreed between the WHO departments responsible for issuing recommendations on health products, SCI and RPQ:

(a) a product is deemed eligible for prequalification pursuant to and in accordance with the relevant prequalification procedure; and

(b) the director of the WHO department responsible for issuing recommendations on use issues a formal memo to request a parallel process, and the RPQ and QNS Directors accept.

The parallel assessment process and timeline commences once:

(a) RPQ has received and formally accepted a complete dossier for assessment from the manufacturer, and

(b) The WHO department responsible for issuing recommendations on use has received (access to) the data package and decided, based on its completeness, to proceed with recommendation development (including interim recommendations and the principle of living guidelines).

The parallel process will be completed once the assessments result in a decision on publishing the recommendation and/or a prequalification decision. A flow chart of the proposed parallel processes is provided as an Annex.

Whilst these processes run in parallel, they will remain independent from each other in reaching their conclusion(s).

It is important to note that each of RPQ, SCI/RFH and WHO departments responsible for issuing recommendations must continue to respect and use "only as permitted" any confidential information obtained by such department from manufacturers and other third parties. By way of example, under the terms and conditions of the established prequalification procedures and agreements signed with manufacturers in connection with these procedures, any confidential information obtained by WHO in connection with a prequalification process:

(a) may be used solely for WHO's prequalification assessment process;

(b) may not be used by WHO for any normative process or other purposes; and

(c) may not be shared or used by WHO/RPQ with any other persons (within or outside WHO) for any normative process or other purposes for which authorization has not been given. It is critical that WHO respects the confidential information that external organizations share.

Manufacturers will be requested to submit their health product-specific dossier to each of:

(a) RPQ, for the purposes of conducting WHO's prequalification process; and

(b) the WHO department(s) responsible for issuing recommendations on use, for the purposes of conducting WHO's recommendation process.

Any changes to the above must be justified in the form of efficiency and feasibility and preceded by appropriate changes in the prequalification procedures and letters of agreement with manufacturers.

Information to be shared across the prequalification and recommendation processes is only for coordination purposes like updates on process status to enable smooth planning. For the avoidance of doubt, WHO departments that are involved in the prequalification process, on the one hand, and the recommendation process, on the other hand, shall not share with each other any information on any potential outcomes of each other's processes at any time unless and until the processes have been independently and fully completed. It is important that the two processes proceed in parallel yet independently of each other so that they do not become rate-limiting steps for or exert undue influence on the outcome of each other.

Once the parallel process has commenced, the WHO department(s) responsible for issuing recommendations on use and RPQ are committed to proceed with their independent evaluation in a timely manner until the assessment's outcome is reached. Throughout the parallel process, any procedural matters are discussed and coordinated between the WHO department(s) responsible for issuing recommendations on use and RPQ.

Timeframe

Subject to resource availability, the parallel assessment process should take no more than twelve months from commencement (as defined above) to completion (decisions on publication and/or prequalification). This twelve-month timeframe aligns with the timeframes agreed by NRAs and other relevant competent authorities worldwide on the assessment pathways of health products. Notwithstanding this, RPQ will

continue to adhere to its procedural timeframes for each product stream, which are all under twelve months.

Should the assessment of RPQ or the WHO department responsible for issuing recommendations on the use of the health product identify that additional data are required, the clock stops for that WHO department until these data have been provided by the manufacturer. The clock does not necessarily also stop for other WHO department(s) involved, as the parallel process includes a coordinated communication of outcomes. Therefore, if there are delays in receiving additional data, the total time for the parallel processes may exceed twelve months.

The topic of developing measurable targets on processing times and their monitoring has not been part of this initial review. RPQ has data available on prequalification processing time, focusing on completing WHO's part of the dossier assessment up to a decision. For most product types, targets are set at 270 calendar days. However, these targets do not include the time the manufacturer needs to provide additional data requested during the assessment. Performance reports are published on the prequalification website. The time to produce evidence-based guidelines and/or recommendations varies with respect to the nature and requirements of the subject, although the proposed period of 12 months has been endorsed by the WHO departments responsible for issuing recommendations on health products subject to the conditions explained in the text.

WHO will publish data on the timelines for both processes and set measurable targets for meeting this 12-month timetable.

Coordination on internal and external communication

Once the parallel processes for recommendation development and prequalification have been independently completed, the department(s) responsible for issuing recommendations on the use of health products and RPQ will coordinate internal and external communication(s). Possible scenarios include:

- If both recommendations and prequalification assessments of a health product are positive (i.e., the health product or product class in question has received at least conditional recommendation for use for at least one indication and has been found by RPQ to meet all requirements for prequalification under the relevant procedure), a coordinated external communication of these positive outcomes will occur. If one process completes well before the other, the coordinated decision may be to issue these communications separately.
- If the outcome from one of the processes is positive and the other negative, the departments involved will liaise to determine a coordinated and risk-based way forward.

Annex: Graphic reflection of process flow