

FAQ: WHO Collaborative Procedure between WHO and National Medicines Regulatory Authorities in Assessment and Accelerated National Registration

The FAQ below relate to technical questions that national medicines regulatory authorities (NMRAs) and manufacturers may have with respect to the collaborative procedure implemented by the World Health Organization (WHO) Prequalification Team and NMRAs for the assessment and accelerated national registration of WHO-prequalified finished pharmaceutical products (FPPs). The procedure is described in the WHO Technical Series Report No. 996¹ and the related templates are as follows:

- [Appendix 1A](#) NMRA participation agreement
- [Appendix 1B](#) NMRA focal points' confidentiality undertakings
- [Appendix 2](#) Prequalification holder's consent to information-sharing
- [Appendix 3 Part A](#) Applicant's expression of interest in application of the procedure
- [Appendix 3 Part B](#) Acceptance by the NMRA to apply the procedure
- [Appendix 3 Part C](#) Notification of outcomes of national registration procedure
- [Appendix 4](#) Report on post-registration actions

GENERAL FAQ

1. For what products and in which countries can the procedure be used?

The procedure can be used to support applications for national registration of any FPP that has been assessed for WHO prequalification and prequalified.

2. Why might an NMRA decline to apply the procedure to registration of a specific WHO-prequalified FPP?

It is the prerogative of any NMRA to decide whether or not the procedure can be applied to an application. Reasons for declining to apply the procedure include non-compliance of the FPP with specific national treatment recommendations, or that the FPP was submitted for registration some time ago, its evaluation is already well advanced, and the NMRA prefers to complete registration through the normal route. It is rare, however, for an NMRA to decline to apply the procedure.

3. How are variations to the prequalified and the nationally-registered product managed?

To ensure that the quality, safety and efficacy of the prequalified FPP and nationally-registered FPP remain the same, the applicant must submit to the relevant NMRAs those variations that require NMRA approval before implementation, and no later than 30 calendar days after they have been approved by WHO.

A variation classified by WHO as for immediate notification is considered as approved if an objection is not issued by the WHO Prequalification Team: medicines (PQTm) within 30 calendar days of the date of acknowledgement of receipt of the variation application. PQTm will inform the relevant NMRAs, via the restricted-access website (see Q&A no. 4 below), about any variation to the prequalification status of a product when regulatory action is deemed to be justified. As with their initial registration of the prequalified FPP, the participating NMRAs are encouraged to base their decision regarding the variation on the WHO prequalification outcome.

¹ WHO Technical Report Series, No. 996. Annex 8, 2016. Collaborative procedure between the World Health Organization (WHO) Prequalification Team and national regulatory authorities in the assessment and accelerated national registration of WHO-prequalified pharmaceutical products and vaccines.

Variations classified by PQTm as for annual notification can be implemented immediately and should be submitted in parallel to PQTm and participating NMRAs.

If, as a result of a national variation procedure, the nationally-registered FPP is no longer the same in all respects as the WHO-prequalified FPP, or if a variation to a WHO-prequalified FPP is not also applied to the nationally-registered FPP (for a variation that is subject to national regulatory requirements), the participating NMRA informs PQTm, clearly specifying the deviation(s) involved.

NMRAs and holders of prequalified FPPs are requested to inform PQTm about any variation to a nationally-registered FPP that results in the prequalified product differing from the nationally-registered product. When the registration conditions of a nationally-registered product differs from those of the WHO-prequalified product, the two products can no longer be considered equivalent and WHO will remove the product from its list of prequalified FPPs registered under the collaborative registration procedure.

4. How reliable is the information-sharing website?

A MedNet website used for sharing information about prequalified FPPs has been developed for use by UN and partner organizations. Only designated PQTm staff and designated NMRA focal persons can access the site, which contains data on prequalified medicines submitted for registration in individual countries. MedNet has passed WHO Internet vulnerability testing, uses encrypted data communication and requires user authentication based on a valid unique email address.

5. PQTm already posts comprehensive information on prequalification on its website. What additional information will it provide to NMRAs participating in the procedure?

Information on the PQTm website is in the public domain and includes lists of prequalified products, WHO public assessment reports (WHOPARs) and WHO public inspection reports (WHOPIRs). WHOPARs and WHOPIRs exclude confidential information. In other words, PQTm's complete assessment reports and inspection reports are not made public. Since, however, regulators participating in the procedure need to be assured about the quality characteristics of individual medicines and the results of inspections, the complete reports are shared with NMRAs through the secure MedNet website (see Q&A no. 4 above). This enables them to take decisions on registration promptly, thereby accelerating the national registration procedure.

6. Does WHO charge for collaborative registration?

No. PQTm support for collaborative registration is free of charge for all applicants and NMRAs. Within countries, NMRAs' usual registration fees will normally apply to products registered under the collaborative procedure, although some NMRAs may waive these and others may apply additional fees for an accelerated process.

7. Will the public know whether an FPP has been registered through this collaborative procedure?

Yes. PQTm maintains an up-to-date list on its website (see: <https://extranet.who.int/prequal/>) of prequalified products that have been registered through this procedure.

FOR NMRAS

8. What data should be submitted by the applicant to an NMRA for an FPP that is to be registered through the collaborative procedure?

The administrative data must be submitted in line with national requirements. Technical data has to be the same — and the applicant must attest to this — as that currently approved by WHO for the prequalified FPP concerned. Any deviation should be communicated and explained to the respective NMRAs (using Appendix 3A). It is recommended that NMRAs accept the technical data in CTD format (as submitted to and approved by PQTm). If the NMRA requires any additional specific technical data, this should be explained to the applicant.

9. How should participating NMRAs use the information about the FPP that is shared by PQTm?

In principle, NMRAs are free to decide how to use any information provided by PQTm in their own registration process. NMRA verification of essential data is recommended, to ensure that the FPP for national registration is the same as the prequalified product. If this is not the case, the applicant should be requested to provide an explanation of any differences observed. If an NMRA has sufficient capacity, the NMRA's own independent conclusions, based on the applicants' dossier, can be compared, for training purposes, with the WHO prequalification outcomes (as described in the assessment and inspection reports). Alternatively, the NMRA may focus on selected aspects of the product that are most relevant to its national context, or rely fully on PQTm's assessment. In whichever case, the NMRA will have continued access to the prequalification information after registration and can seek additional advice from PQTm.

10. What happens if an NMRA does not issue a decision within 90 days?

It may not be possible for the NMRA to issue its decision regarding registration within 90 days. If this is the case, the NMRA must communicate to PQTm its justification for its delayed decision. If the NMRA fails to do so, PQTm will follow up with the NMRA, to investigate the situation and to agree on remedial actions.

11. What happens if the NMRA reaches a conclusion that differs from PQT's prequalification decision?

Although generally not expected to be the case, an NMRA may conclude independently and differently from PQTm, and decide not to register a prequalified product or to approve additional, different regulatory conditions. In such cases, the NMRA should explain and justify any deviations in its information to PQTm (using Appendix 3C). PQTm should be always informed:

- about a decision not to register a product
- any deviations with respect to the manufacturing chain, manufacturing processes, specifications, control methods, package size, indications, contraindications, dosing, special warnings and precautions for use, adverse drug reactions, storage conditions and/or shelf-life
- any deviations occurring post-registration.

Such deviations will mean that the product submitted for national registration cannot be considered to be the same as the prequalified product. In the case of a product already under the procedure, PQTm will remove the product from the list of prequalified products that have been registered through the collaborative procedure.

Conversely, differences in brand name, in the names of the applicant/registration holder, in data format, language or level of detail of product information, or in labelling of internal and external packaging, are acceptable deviations given that they do not affect the quality of the product for which compliance with good manufacturing practices continues to apply.

12. Can NMRAs change their nominated focal persons?

The legal representative of the NMRA can request PQTm for a change with respect to one or more focal persons. A signed confidentiality undertaking must be attached for each new focal point.

In the interest of smooth and safe information exchange PQTm encourages NMRAs to minimize changes of focal point.

FOR APPLICANTS

13. Which data should be submitted to NMRAs when registration will be carried out via the collaborative procedure?

The administrative data must be submitted in line with national requirements. PQTm recommends that technical data is submitted in CTD format, as submitted to PQTm, and that the dossier submitted to the NMRA is updated in line with any changes implemented during the prequalification process and/or variations. Data in CTD format are normally accepted for the purpose of the collaborative procedure, including by those NMRAs that request different organization of data for products that are submitted for national registration only (i.e. are not prequalified).

14. Must the FPP to be registered be identical with the prequalified FPP, or can it be adapted to suit country requirements?

The prequalified FPP and the product to be registered by participating NMRAs should essentially be the same. This means that they should have

- the same manufacturing chain, processes and controls of materials and final product
- the same specifications of active pharmaceutical ingredient and finished product
- the same essential elements of product information (including indications, contra-indications, dosing, special warnings and precautions for use, adverse drug reactions, storage conditions and shelf-life).

Conversely, differences in brand name, applicant name (provided the applicant has the right to represent the prequalification holder), the language, format and degree of detail of the product information, labelling of internal and external packaging, etc., are permitted. See also [Contents and Structure of a WHOPAR](#).

15. Can a product be considered to be the same as the WHO-prequalified product if it is packaged in different packs or pack sizes?

No. All parts of a WHO-prequalified FPP have undergone assessment by PQTm, including its different stages of manufacture, packaging in its final container and labelling. Nationally-registered packs or pack sizes therefore cannot be considered as WHO-prequalified unless a variation has been submitted to PQTm, in accordance with WHO guidelines on variations to a prequalified product,² and accepted by PQTm. In case of doubt please contact Dr Luther Gwaza: gwazal@who.int

16. The format of the FPP submitted for national registration differs from that of the prequalified FPP. How should applicants ensure that both submissions are the same?

Submission of dossiers in CTD format, as approved by PQTm, is highly recommended and NMRAs are encouraged to accept such dossiers. If NMRAs require that data be submitted in a different format, applicants should submit data in the format (i.e. the national format) requested. The technical part of the dossier, however,

² WHO guidelines on variations to a prequalified product http://apps.who.int/prequal/info_general/documents/TRS981/TRS981_annex3.pdf

must include the relevant data approved by PQTm during initial prequalification, details of any variations submitted and approved of re-qualification (where applicable). In addition, country-specific data should be submitted as required by NMRAs.

17. My company wishes to register a prequalified product, but is not the prequalification holder. Can the procedure be applied to that product?

Yes, provided your company has the right to act for and the authority to represent the prequalification holder for the purposes of the application for national registration. For example, a local agent may be acting on behalf of a company with respect to its prequalified product. In this instance, the prequalification holder must sign an authorization letter entitling the applicant to act on its behalf (see the proposed wording at the end of Appendix 3 Part A).

For the purposes of this procedure the prequalification holder is the entity listed as “applicant” on WHO's online list of prequalified FPPs, irrespective of whether it performs any manufacturing activities itself.

18. My product is still under assessment for prequalification. Can the procedure be applied to that product?

No. Prequalification assessment and related inspection information can be shared only after evaluation has been completed successfully and the product is listed as prequalified on the medicines prequalification website. However, PQTm recommends that potential applicants inform the WHO collaborative procedure focal persons about their interest in making use of the collaborative procedure, and to indicate in which countries registration will be sought. PQTm can then assist in preparations for application of the procedure.

19. A variation is pending with PQTm for my prequalified FPP. Can the procedure be applied?

Yes, but the applicant should inform the NMRA of the pending variation.

20. My product is already pending registration in a participating country. Can the procedure be applied to it?

Yes. In such a case, when completing Appendix 3 Part A (Applicant's expression of interest in application of the procedure) the applicant should indicate the date of application to the NMRA and the application file number, and clearly state any differences between the product of the pending submission and the prequalified product. The national dossier should be updated, or if the NMRA agrees, replaced by the WHO-approved dossier, to ensure that the technical data in the product to be registered are the same as those of the prequalified product. Each NMRA will decide how best to handle such applications, and inform applicants accordingly.

21. Prequalification assessment information can be commercially sensitive. How is data confidentiality ensured?

Participating NMRAs commit themselves in the Participation Agreement (Appendix 1, Part A) to keep any commercially-sensitive information confidential. PQTm shares its information with NMRAs on a secure website (see Q&A no. 4 above). Access is granted to a limited number (two or three) nominated focal points per NMRA (normally responsible for example, for pharmaceutical product assessment or inspection agendas), and subject to signed agreements and confidentiality undertakings (Appendix 1, Part B).

PQTm does not share with NMRAs the full extent of data as presented in FPP prequalification dossiers. But it does share the Quality Overall Summary (QOS) and the Bioequivalence Trial Information Files (BTIF), with any annotation and/or requests for additional information, responses to any requests, as well as inspection reports and corrective and preventive actions. The scope of information that is shared is limited to data owned by the

prequalification holder. It is assumed that — independently of the collaborative procedure — any sensitive data will be submitted to NMRAs by the applicants as part of the national product dossiers.

22. Some of the prequalification assessment information is owned by other parties (e.g. the API manufacturer). Will this information also be shared?

No. PQTm will share only data information owned by the prequalification holder. It will not share any information owned by third parties unless an agreement has been reached with the data owners concerned. When giving consent to information sharing the prequalification holder should specify any data that is being submitted that is owned by a third party.

23. Will any waivers, special fees or special conditions be granted for national submissions made using this procedure?

No. Unless NMRAs introduce specific mechanisms or exceptions, registration will follow all normal national requirements and procedures.

24. Our company's product is registered via the collaborative procedure in country X. We have submitted a variation to PQTm, but the NMRA of country X does not control this type of variation. What should we do?

Irrespective of whether or not a formal national variation process exists in a participating country, PQTm will share its assessment information on major variations that warrant post-registration regulatory action. With respect to positive decisions, unless the NMRA objects within 30 days of PQTm posted the decision on the password-protected website, it will be understood that the NMRA agrees with PQTm's decision and that the variation also applies to the nationally-registered product.

25. Our company's FPP is already registered in a country via the regular national process, and all its technical features are the same as those of the prequalified product. Can my FPP be included on the "collaborative registration" product list?

Yes, provided the country in question is willing to participate in the collaborative procedure.