

**Collaborative procedure between the World Health Organization
Prequalification of Medicines Programme (WHO/PQP) and national
medicines regulatory authorities (NMRAs) in the assessment and
accelerated national registration of WHO-prequalified pharmaceutical
products and vaccines**

Revision 1, draft for comments

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1. Definitions

Collaborative procedure (Procedure)

Procedure for collaboration between the WHO Prequalification Programme (WHO/PQP) and interested national medicines regulatory authorities (NMRAs) in the assessment and accelerated national registration of WHO prequalified pharmaceutical products and vaccines.

Participating authorities or participating NMRAs

NMRAs that voluntarily agree to implement this collaborative procedure and accept the task of processing applications for registration of WHO-prequalified pharmaceutical products and vaccines in accordance with the terms of the Procedure. A list of participating authorities is posted on the WHO/PQP web site (<http://www.who.int/prequal/>).

Pharmaceutical product

Any substance or combination of substances marketed or manufactured to be marketed for treating or preventing disease in human beings, or with a view to making a medical diagnosis in human beings, or to restoring, correcting or modifying physiological functions in human beings.

Vaccine

A vaccine is a biological preparation that improves immunity to a particular disease. A vaccine typically contains an agent that resembles a disease-causing microorganism, and is often made from weakened or killed forms of the microbe, its toxins or one of its surface proteins. The agent stimulates the body's immune system to recognize the agent as foreign, destroy it, and "remember" it, so that the immune system can more easily recognize and destroy any of these microorganisms that it later encounters.

2. Background information

National assessment of applications for registration of pharmaceutical products and vaccines (marketing authorization) is the key regulatory process that enables NMRAs to evaluate and monitor the quality, safety and efficacy of pharmaceutical products and vaccines.

For most countries the approach to registration of pharmaceutical products and vaccines is a combination of two components:

- the NMRA's own assessment of application documentation combined with verification of compliance with relevant good practices by inspections (mostly focusing on good manufacturing

practices (GMP) and inspections of manufacturing sites) and testing of product characteristics when applicable;

- consideration by the NMRA of decisions and outcomes of assessments and inspections made by NMRAs in other countries.

Consideration of the outcomes of assessments and inspections by trusted authorities substantially contributes to savings in regulatory resources and improvements in the quality of regulatory decisions, while retaining the prerogative of NMRAs to conclude their assessment by sovereign decisions, which reflect their own judgement of the benefit–risk balance as it relates to their specific country situation and the legislation in place. Taking into consideration the regulatory decisions of other NMRAs requires setting up a system that will permit:

- identification of reference authorities whose regulatory decisions are based on acceptable standards and identification of documents associated with such regulatory decisions, which are relevant to the regulatory environment in the country wishing to rely on such decisions;
- assurance that the product for which the decision has been taken by the reference NMRA is identical to the product being assessed, or, if it is not identical, that a clear understanding exists of the differences between the products subjected to assessment in the two regulatory environments;
- efficient use of available scientific expertise and human and financial resources to decide, with reasonable certainty, on the benefit–risk profile of an evaluated product when used in a given country;
- the choice by each NMRA of the approaches that will make best use of the resources, workload and competence of individual NMRAs.

Approaches could range from completely independent data reviews and inspections to adoption of regulatory decisions of trusted authorities without any further scientific review. A pragmatic approach is to verify product identity and assess only those areas which relate to use of the product in the country concerned and where failure to comply with regulatory standards could pose health risks. In the other areas, the outcomes of trusted authorities may be adopted.

This Procedure is based on the above-mentioned considerations. In line with the *Procedure for prequalification of pharmaceutical products*¹, and the *Procedure for assessing the acceptability in*

¹ *Procedure for prequalification of pharmaceutical products*. In: WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-fifth report. Geneva, World Health Organization, 2011 (WHO Technical Report Series, No. 961), Annex 10.

*principle of vaccines for purchase by United Nations Agencies*² it aims to provide a convenient tool for NMRAs wishing to enhance their pre-marketing evaluation and registration system by taking advantage of the scientific assessment work conducted by WHO/PQP. The present procedure is complementary to the WHO/PQP collaboration procedure with NMRAs in inspection activities (<http://www.who.int/prequal>, “Inspections”).

The Collaborative Procedure has been piloted from June 2012 and is currently in use for pharmaceutical products (<http://www.who.int/prequal>, “Collaborative Registration”). For vaccines, another Procedure for expedited review of imported prequalified vaccines for use in national immunization programmes was published already in 2007 and has been implemented for national registrations as from 2011, however the procedure did not include collaborative arrangements with the NMRAs.

Enhanced collaboration and information exchange between NMRAs and WHO/PQP benefits both partners. Subject to the agreement of the WHO prequalification holders concerned, NMRAs have access to assessment outcomes that are not in the public domain and that have been prepared in conformity with the WHO recommended standards on which the *Procedure for prequalification of pharmaceutical products* and the *Procedure for assessing the acceptability in principle of vaccines for purchase by United Nations Agencies* are based. Such reports and other documents help NMRAs to make their decisions and also assist in educating national regulatory staff. At the same time, feedback from NMRAs on the information and documentation received from WHO/PQP under the Procedure allows WHO/PQP to improve its work and ensures that the outcomes of prequalification assessments are relevant to NMRAs. As a consequence patients and vaccinees benefit from this collaboration by gaining faster access to medicines which have been found acceptable in principle for procurement by United Nations agencies. Depending on available resources, participating authorities have the opportunity to participate in the assessment process and in inspections organized by WHO/PQP.

This collaborative procedure also benefits manufacturers of prequalified pharmaceutical products and vaccines through faster and better harmonized regulatory approvals in participating countries. This Procedure, when combined with the *Collaboration Procedure with NMRAs in inspection activities*, alleviates the burden of additional national inspections on manufacturers.

² *Procedure for assessing the acceptability, in principle, of vaccines, for purchase by United Nations agencies*. In: WHO Expert Committee on Biological Standardization. Sixty-first report. Geneva, World Health Organization, 2013 (WHO Technical Report Series No. 978), Annex 6.

Due to positive experience with use of the Collaborative Procedure for pharmaceutical products, the Procedure is now extended also to vaccines. Experience obtained during practicing the Procedure so far has led to minor clarifications and amendments to make the Procedure less administratively demanding.

3. Principles of collaboration

3.1 This collaborative procedure is limited to those pharmaceutical products and vaccines that have been assessed and inspected by WHO/PQP in line with the procedures and standards available at www.who.int/prequal (“Information for applicants”) and have been found to be acceptable in principle for procurement by United Nations agencies as listed in the *List of WHO prequalified medicines and List of WHO prequalified vaccines*, available at www.who.int/prequal and <http://www.who.int/immunizationstandards/vaccinequality/PQvaccinelist>, respectively. For the time-being, the Procedure is not applicable to pharmaceutical products (medicines) which have been listed as prequalified on the basis of approval by stringent regulatory authorities.³

Although the Procedure mostly serves to accelerate the assessment and registration of multisource (generic) pharmaceutical products that completed the WHO/PQP prequalification process successfully⁴, it is applicable to vaccines and any pharmaceutical product for which the safety and efficacy has been documented to WHO/PQP by the submission of preclinical and clinical data. The Procedure has three major stakeholders: WHO/PQP, interested NMRAs and those WHO prequalification holders/applicants⁵ who agree that this procedure is used for applications for national registration of their WHO-prequalified product submitted to an NMRA.

3.2 WHO/PQP and participating authorities receive applications for the same pharmaceutical product or vaccine. Within the context of this Procedure, the same pharmaceutical product/same vaccine is characterized by:

- the same product dossier;⁶

³ Products listed as prequalified according to the procedure described in the Guidelines on submission of documentation for prequalification of finished pharmaceutical products approved by stringent regulatory authorities. In: WHO Technical Report Series, No. 986. Geneva: World Health Organization; 2014:Annex 5.

⁴ See footnote 1.

⁵ If the applicant for national registration is not the same as the WHO prequalification holder, the WHO prequalification holder must confirm to the NMRA and WHO/PQP by an authorization letter (as per the template annexed to Appendix 3, Part A) that the applicant is acting for, or pursuant to rights derived from, the WHO prequalification holder and that the prequalification holder agrees with the application of the procedure in the country concerned.

⁶ Submission of dossiers in CTD format as required by WHO/PQP is considered a standard. In exceptional situations data can be organized differently in line with specific national or WHO requirements, however the technical data included in the dossier must be the same. There may be country-specific differences in administrative data, or if required by NMRAs under exceptional circumstances, additional technical data can be provided (e.g. bioequivalence with a country-specific comparator).

- the same manufacturing chain, processes, control of materials and final product, and in case of vaccines also by the same batch release scheme;
- the same active pharmaceutical ingredient (API) and finished pharmaceutical product (FPP) specifications;
- the same essential elements of product information, in case of vaccines by the same product information, packaging presentation and labelling.⁷

3.3 WHO/PQP, with the agreement of the WHO prequalification holder, shares the full outcome, of prequalification assessments, inspections and if relevant, also results of laboratory testing, including final assessment and inspection reports, with participating authorities, under appropriate obligations of confidentiality and restrictions on use (see below).

As regards sharing the outcomes of assessments, inspections and results of laboratory testing, only data owned by the WHO prequalification holder and WHO are shared. Sharing of any other data is subject to additional agreement of the data owners concerned.

3.4 For the purpose of this collaborative procedure, participating authorities accept the product documentation and reports, in the format in which they are routinely prepared by WHO in accordance with the *Procedure for prequalification of pharmaceutical products*⁸ and the *Procedure for assessing the acceptability in principle of vaccines for purchase by United Nations Agencies*⁹, respectively. It should be noted, however, that participating authorities may require applicants to comply with specific requirements for local regulatory review. Each participating authority should make such specific requirements public.

3.5 Fees to be paid by the applicants to participating authorities will continue to follow standard national procedures. Similarly, the submission by manufacturers of samples for laboratory testing – if required – will continue to follow standard procedures as defined in national legislation and/or as defined by national regulatory authorities. Unless necessary, participating authorities are advised to refrain from pre-registration laboratory testing. Results from the laboratory testing organized in

⁷ The essential elements of product information include in particular the indications, contraindications, posology (dosing), special warnings and precautions for use, adverse reactions, storage conditions, primary packaging and shelf-life. For pharmaceutical products differences in brand name, the name of applicant or prequalification holder, language, format and degree of detail of the product information, labelling of internal and external packaging, among others, are not considered essential for the purposes of this procedure. The language of the product information may be different as long as the information content is the same as that approved by WHO/PQP.

⁸ See footnote 1.

⁹ See footnote 2.

the course of prequalification assessment or inspections will be included in the information package available to each participating authority.

3.6 Consistent with the terms of Appendix 1A and Appendix 3, Part B, each participating authority commits itself:

- to treat any information and documentation provided to it by WHO/PQP pursuant to this Procedure as confidential in accordance with the terms of Appendix 1A, and to allow access to such information and documentation only to persons:¹⁰
 - who have a need to know for the purpose of the assessment and accelerated registration of the product in question in the country and any post-registration processes that may be required;
 - who are bound by confidentiality undertakings in respect of such information and documentation which are no less stringent than those reproduced in Appendix 1A; and
- to issue its national regulatory decision on registration of a given prequalified product (whether positive or negative) within 90 calendar days after being given access to the confidential information and documentation concerning each product or receiving the submission, whichever is the later.¹¹

These commitments are provided by each participating authority to WHO/PQP in writing by entering into the agreement for participation in this Procedure as reproduced in Appendix 1A and are reconfirmed for each pharmaceutical or vaccine for which collaboration is sought (see Appendix 3, Part B).

Each participating NMRA nominates a maximum of three focal points (1 - inspections, 2 - assessment of pharmaceutical products, 3 - assessment of vaccines) who will access the restricted-access web site, through which WHO/PQP will communicate all confidential information and documentation. Focal points designated by the NMRA must sign the undertaking reproduced in Appendix 1B before they will be granted access to the restricted-access web site. Any change in

¹⁰ This includes the focal point(s) and all other persons in the NMRA who have access to any information and documentation provided by WHO/PQP.

¹¹ Participating authorities should issue their national regulatory decisions at the earliest opportunity after being given access to the confidential information and documentation on a given prequalified product. Although a time limit of 90 days is defined in the Procedure, the decision should normally be taken within 60 days. This deadline can be extended to a maximum of 90 days if predefined dates of technical or decision-making meetings do not allow a participating authority to issue its decision within 60 days. If a participating authority does not issue its decision within 90 days and does not communicate valid reasons for the delay to WHO/PQP, WHO/PQP will follow up with the head of the NMRA to clarify the situation.

designated focal points must be communicated to WHO/PQP in writing without delay and must be accompanied by an undertaking (Appendix 1B) signed by the new focal point(s).

- 3.7 The decision whether or not to register a given product in a particular country remains the prerogative and responsibility of each participating authority. Accordingly, a participating authority may come to a different conclusion from that reached by WHO/PQP. Within 30 calendar days of having taken its decision, the participating authority reports this decision, together with the dates of submission and registration and, if applicable, any deviations from the WHO/PQP's decision on prequalification and the reasons for such deviations,¹² to WHO/PQP. It does so through the restricted access web site by completing the form in Part C of Appendix 3. The NMRA provides a copy of the completed form to the applicant.
- 3.8 Participation by WHO prequalification holders/applicants is voluntary, through the submission to a participating NMRA of the expression of interest reproduced in Part A of Appendix 3. For each product, such participation will be subject to the WHO prequalification holder/applicant accepting the terms of this Procedure, including the confidential exchange of information and documentation between WHO/PQP and the NMRA (see Appendix 2).

The WHO prequalification holder/applicant can cease participation in this Procedure at any time provided that he or she informs WHO/PQP and the participating NMRAs in writing of his or her decision. In such a case the NMRA shall cease all use of the information disclosed to it for the respective product(s) as per the terms of the participation agreement (see Appendix 1).

- 3.9 The requirements and procedures in case of a variation (as defined in WHO guidelines¹³) may differ between NMRAs and WHO/PQP. The present collaborative procedure includes a variation

¹² This refers to a decision not to approve the marketing authorization of a WHO-prequalified product and to a decision to approve the marketing authorization, but with deviations in indications, contraindications, posology (dosing), special warnings and precautions for use, adverse drug reactions, storage conditions and shelf-life. For pharmaceutical products differences in brand name, name of applicant or prequalification holder, format of product information, level of detail of product information, labelling of internal and external packaging and language of product information are not considered to be deviations from the prequalification conclusions.

¹³ For pharmaceutical products: *WHO guidelines on variations to a prequalified product*. In: WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-seventh report. Geneva, World Health Organization, 2013 (WHO Technical Report Series, No. 981), Annex 3 (and any updates thereto).
For vaccines: Draft guidance on reporting variations to a prequalified vaccine
(http://www.who.int/immunization_standards/vaccine_quality/variations_pq_vaccine/en/)

procedure (see below under “Mechanisms for post-qualification and/or post-registration variations”) which is aimed at promoting consistency between variations accepted by WHO/PQP and variations accepted by participating authorities. There could be situations in which a manufacturer of a WHO-prequalified product submits a variation application to a participating authority and not to WHO/PQP, or vice versa. In such a case, the conditions of the national registration, which were initially “harmonized” with the WHO prequalification decision, may become essentially different through the product life-cycle. In such a case a product registered and procured in a participating country would no longer be the same as the “WHO-prequalified” product because the specifications, manufacturing sites and/or other essential parameters would no longer be the ones accepted by WHO/PQP. The WHO prequalification holders/Applicants and NMRAs are expected to inform WHO/PQP of the differences and their reasons, if a national variation procedure results in the nationally-registered product being no longer the same as the WHO-prequalified Product.

As a result, applicants are required to submit the variations which are submitted to WHO/PQP without delay to participating authorities, and participating authorities are encouraged to follow the outcomes of the WHO variation procedures for nationally-approved WHO-prequalified products. WHO/PQP will inform the NMRAs which have registered individual prequalified products, through the restricted-access web site, about variations to the prequalification status of such products, if and when regulatory action is deemed to be justified. The variation approved by PQP will be considered by WHO/PQP as accepted by the NMRA on a non-objection basis 30 days after information-sharing, unless and until the NMRA informs WHO/PQP otherwise as described in the paragraph below.

If a national variation procedure results in the nationally registered product being no longer the same¹⁴ as the WHO-prequalified product, or in the event that a variation of a WHO-prequalified product is not followed by the same variation of the nationally registered product, the participating authority informs WHO/PQP of the situation by submitting the form in Appendix 4, clearly specifying the deviations. The respective deadline for informing WHO is 30 days after the NMRA

(and any updates thereto).

¹⁴ Within the context of this Procedure, the same pharmaceutical product is characterized by the same product dossier, the same manufacturing chain, processes and control of materials, the same API and FPP specifications and the same essential elements of product information, as further described in paragraph 3.2 above.

has been informed by WHO/PQP about variation outcome. Other participating NMRAs, which have registered the WHO-prequalified product in question pursuant to this Procedure, will be made aware of such deviations through the restricted access web site. In addition, if the fact that a WHO-prequalified product has been registered in a particular country pursuant to this Procedure has been made public, any subsequent deviations should also be made public.

- 3.10 If a prequalified product is withdrawn by the WHO prequalification holder, or is suspended or delisted by WHO/PQP, WHO/PQP will inform each participating authority which has approved, or is in the process of reviewing, the product pursuant to this collaborative procedure, of the withdrawal, suspension or delisting and the reasons for taking this action, through the restricted-access web site and subject to the obligations of confidentiality contained in Appendix 1A. Similarly, when an NMRA deregisters or suspends the registration of a prequalified pharmaceutical product or vaccine for any reason, it will inform WHO/PQP of this decision and of its reasons through the restricted-access web site. Other participating NMRAs which have registered the WHO-prequalified product in question pursuant to this Procedure will be made aware of such national deregistration or suspension through the restricted-access web site. In addition, if the fact that a WHO-prequalified product has been registered in a country pursuant to this Procedure has been made public, any subsequent deregistration or suspension should also be made public.
- 3.11 Participation in this Procedure does not exempt applicants for national registration and holders of national registration from the respective national regulatory requirements. Participating authorities retain the right to assess submitted data and organize site inspections to the extent they deem appropriate. WHO encourages NMRAs not to perform repetitive assessment of thoroughly assessed data, but rather to focus on data verification to be assured that the same product is submitted for registration as is prequalified. It is highly recommended not to re-inspect the sites that were already inspected by WHO-PQP inspection teams or by National Regulatory Authorities recognized by WHO as stringent or – with respect to inspections of vaccine manufacturing sites - as functional.
- 3.12 Sharing of information related to the Procedure between WHO/PQP, WHO prequalification holders/applicants and NMRAs is governed by Appendices 1, 2, 3 and 4. Completed Appendices 1 and 2 must be submitted to WHO/PQP without any change in the content of the Appendices. Provision of Appendices 3 and 4 can be substituted by provision of the same information by other means.

4. Steps in the collaboration for national registration of a pharmaceutical product or a vaccine¹⁵

4.1 The applicant submits the product dossier for a WHO-prequalified pharmaceutical product or a vaccine to a participating NMRA. The technical part of the dossier is updated to reflect the data as approved by WHO/PQP during the initial prequalification procedure, and consecutive variation procedures and requalification (where applicable). The applicant must provide the participating authority with:

- an application dossier complying with established national requirements, including the same technical information as that approved by WHO/PQP. To the extent that national regulatory requirements allow, the technical part of the dossier will be identical to the current version of the WHO/PQP dossier¹⁶. In specific cases the NMRA may agree to accept an abbreviated dossier.
- an expression of interest reproduced in Part A of Appendix 3;
- country-specific data;
- any fees that may be payable to the NMRA pursuant to national requirements.

Wherever possible, to minimize the workload of the NMRA and facilitate the process, applicants should ensure that they express their interest to use the Procedure (Appendix 3, Part A) to the NMRA and to WHO/PQP before submitting a national application for registration. If acceptable to NMRAs, not only should the technical content of the dossiers be the same, but also the format in which data are presented should closely follow the format in which dossiers are submitted to WHO/PQP, i.e. the common technical document (CTD) format in the case of pharmaceutical products and the Product Summary File format in the case of vaccines.

In situations where the applicant wishes to apply the Procedure to an application which is already pending within the NMRA, the applicant should first update the dossier to ensure that the technical part of the information is the same as that approved by WHO/PQP.

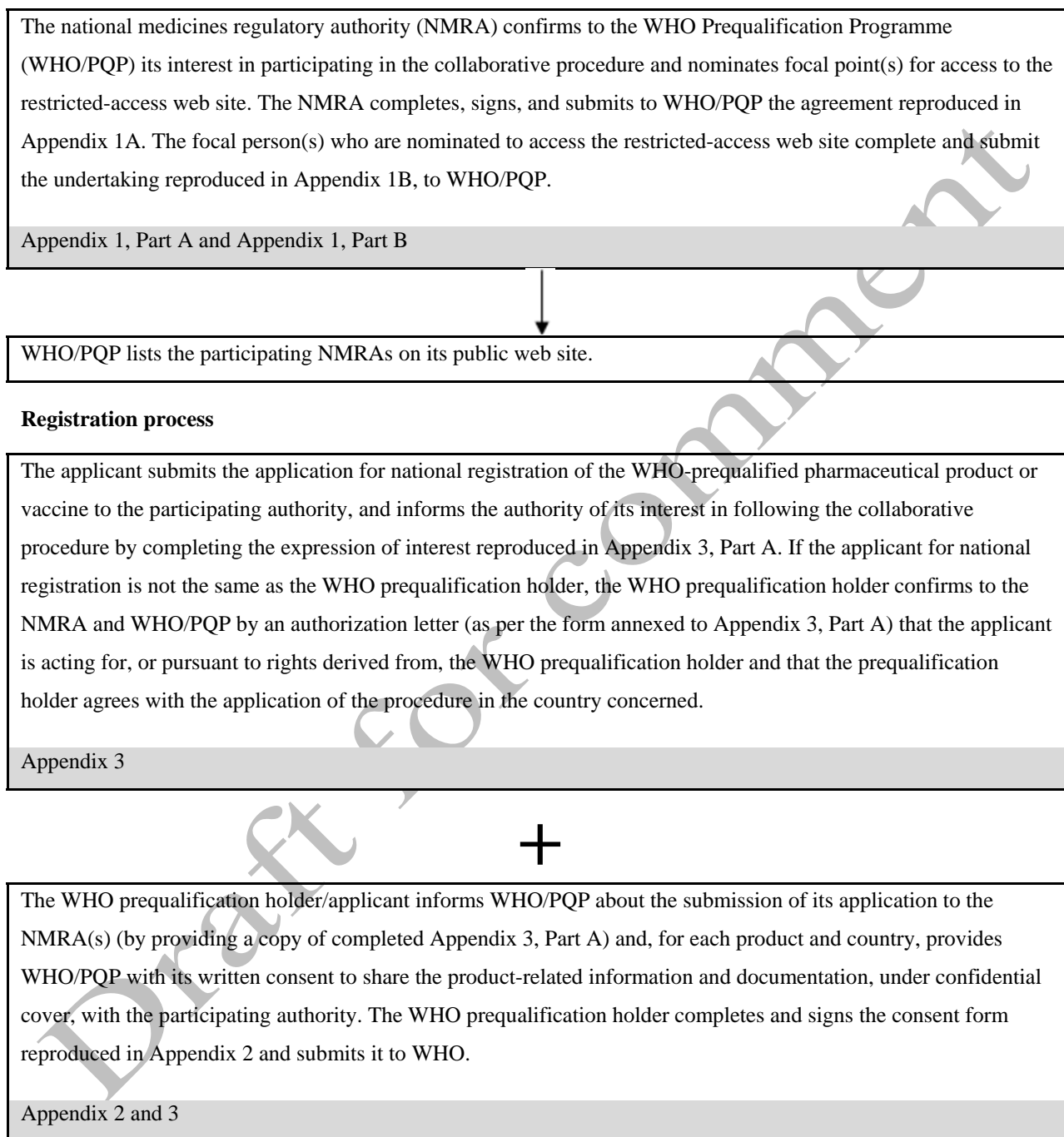
¹⁵ In addition, to complement the steps of this collaborative procedure, joint inspections may be arranged under the collaborative procedure for joint inspections posted on the WHO/PQP web site (www.who.int/prequal, "Inspections").

¹⁶ In the case of vaccines that are prequalified by the 'Streamlined procedure for vaccines with marketing authorization/licensing granted by eligible NRAs' (as defined in the *Procedure for assessing the acceptability, in principle, of vaccines, for purchase by United Nations agencies*. In: WHO Expert Committee on Biological Standardization. Sixty-first report. Geneva, World Health Organization, 2013 (WHO Technical Report Series No. 978), Annex 6.) the submitted data should reflect essential data submitted to the respective NRA that granted the authorisation/licence and additional documents as provided to WHO.

- 4.2 For each application under this Procedure, WHO/PQP is informed by the WHO prequalification holder/applicant about the submission to the participating NMRA by providing a copy of completed Appendix 3, Part A. The WHO prequalification holder provides WHO at this time with its written consent for WHO/PQP to provide the product-related information in compliance with the applicable confidentiality requirements to the NMRA of the country concerned (see Appendix 2).
- 4.3 The participating NMRA informs WHO/PQP and the respective applicant of each application which it accepts or declines to include in this Procedure. It is the decision of individual NMRAs whether to apply the Procedure for individual submissions. If accepting to initiate the procedure, NMRA requests WHO/PQP to provide it with the necessary information and documentation (Appendix 3, Part B). The Procedure applies only to applications that the NMRA has accepted as complete.
- 4.4 Within 30 calendar days of receipt of the WHO prequalification holder request WHO/PQP shares the most recent product-related information and assessment, inspection and laboratory testing outcomes through the restricted-access web site with the participating authority. This information is subject to the obligations of confidentiality and restrictions on use and may include assessment report(s), variation assessment report(s) if applicable, inspection report(s) of the most recent inspection(s), the letter of prequalification or requalification and results of laboratory testing, if applicable. At the request of the participating authority, WHO/PQP provides explanations and/or more detailed information.
- 4.5 After receiving the information and documentation from WHO/PQP, the participating authority undertakes an accelerated assessment of the product in question. For each application, the participating authority is required to issue the relevant national decision within 90 calendar days from the day it received access to the complete prequalification documentation. Within 30 days of having taken its decision, the participating authority reports this decision, together with an indication of the dates of submission and registration, and, if applicable, any deviations from the WHO prequalification conclusion and the reasons for such deviations, to WHO/PQP through the restricted-access web site. This report is provided to WHO/PQP using Part C of Appendix 3 and is copied to the applicant. WHO/PQP lists pharmaceutical products and vaccines registered according to this Procedure by participating NMRAs on its public web site. The steps in the collaboration for national registrations of a pharmaceutical product or vaccine are summarized in Figure 1.

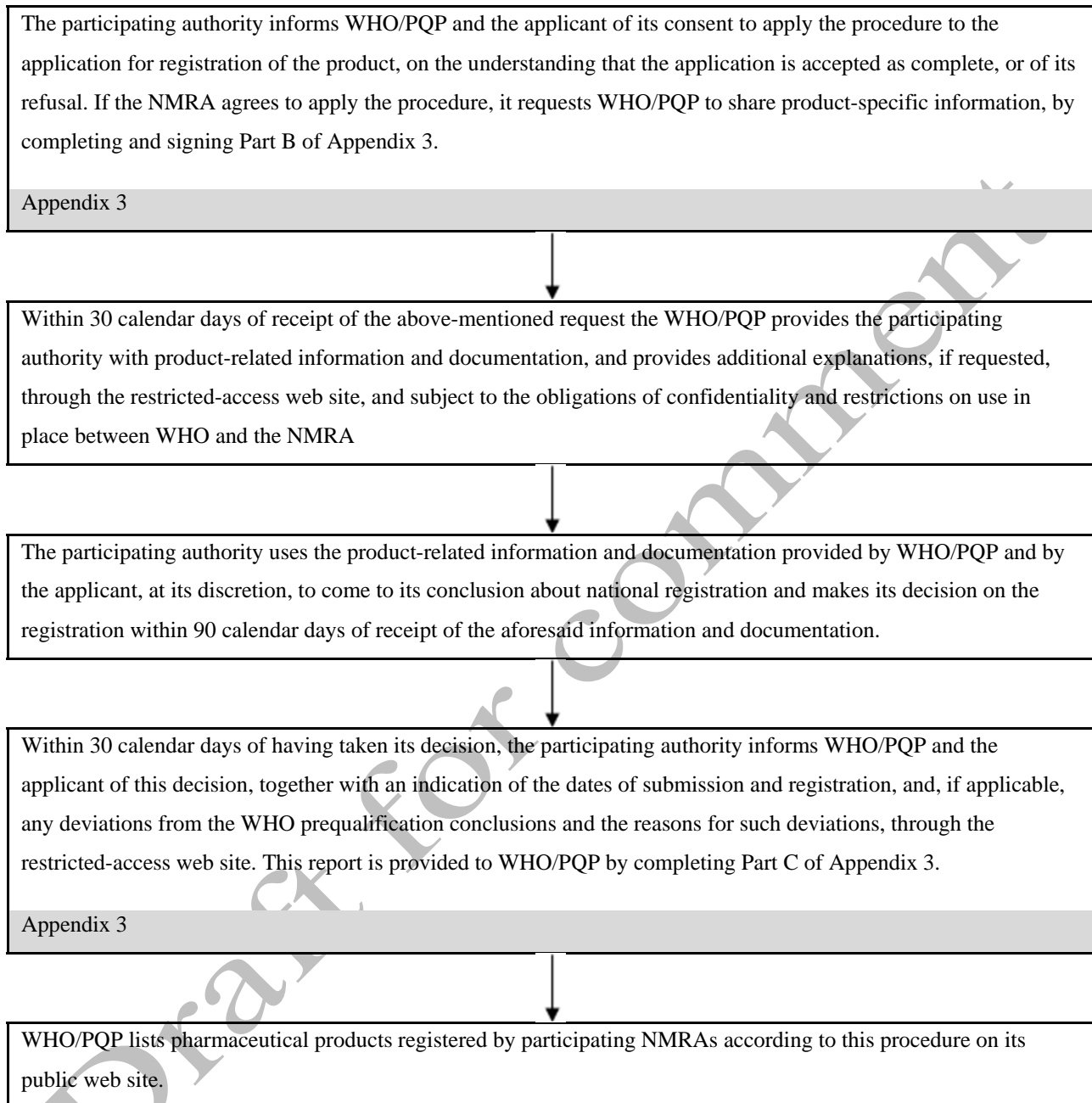
Figure 1

Flowchart showing the principal steps of the collaborative procedure



Continues

Figure 1 continued



Continues

Figure 1 *continued*

Post-registration processes

The WHO prequalification holder/applicant submits variations simultaneously to WHO/PQP and relevant participating authorities. If regulatory action is deemed to be justified, WHO/PQP promptly provides the participating authorities concerned, through the restricted-access web site, and subject to the above-mentioned obligations of confidentiality and restrictions on use, with outcomes of its assessment and post-prequalification inspection, and any related information it considers relevant. If a national variation procedure results in the nationally-registered product being no longer the same¹⁷ as the WHO-prequalified product, or in the event that a variation of a WHO-prequalified product is not followed by the same variation of the nationally-registered product, the participating authority informs WHO of the situation within 30 calendar days of obtaining access to the information and documentation provided by WHO/PQP, by submitting the form reproduced in Appendix 4, clearly specifying the deviations. Other participating NMRAs which have registered the WHO-prequalified product in question pursuant to this procedure will be made aware of such deviations through the restricted-access web site.

Appendix 4

WHO/PQP informs the participating authority, through the restricted-access web site, and subject to the above-mentioned obligations of confidentiality and restrictions on use, about withdrawals, suspensions or delistings of prequalified pharmaceutical products or vaccines. The participating authority informs WHO/PQP, through the restricted-access web site, of national deregistration or suspension (for any reason) of a prequalified pharmaceutical product or vaccine and the reasons for doing so.

Other participating NMRAs which have registered the WHO-prequalified product in question pursuant to this procedure will be made aware of such national deregistration or suspension, through the restricted-access web site.

Appendix 4

WHO/PQP removes a product from the list published in line with this procedure:

- if the nationally-registered product is no longer the same¹⁸ as the WHO-prequalified product, or
- if the NMRA deregisters a WHO-prequalified product, or
- if WHO/PQP delists a WHO-prequalified product.

WHO/PQP will also publish the reasons for the removal from the list.

¹⁷ See footnote 14.

¹⁸ See footnote 14.

5. Collaboration mechanisms for post-prequalification and/or post-registration variations

- 5.1 Post-prequalification variations submitted to WHO/PQP are expected to be submitted simultaneously to any relevant participating authorities, and vice versa. Submission of variations to NMRAs should respect national regulatory requirements. Applicants for national variations should inform participating authorities about the fact that the same application for a variation is being processed by WHO/PQP.
- 5.2 WHO/PQP promptly shares the outcomes of variation assessment and of related post-prequalification inspection reports (if applicable) and any other information that it considers relevant, through the restricted-access web site, and subject to the above-mentioned obligations of confidentiality and restrictions on use, with the relevant participating authorities, in all cases in which a variation (including “notification” according to WHO/PQP’s variation procedures¹⁹) requires regulatory action (e.g. where product quality, safety, efficacy or patient information materials are concerned).
Within 30 days of obtaining access to the information and documentation from WHO/PQP, each participating authority informs WHO/PQP through the restricted access web site if and to what extent a variation of a WHO-prequalified product is not followed by the same approved variation of the nationally-registered product and, as a consequence, the nationally-registered product is no longer the same²⁰ as the WHO-prequalified product.
- 5.3 If a national variation procedure occurs independently of a variation submitted to WHO-PQP and results in the nationally-registered product being no longer the same²¹ as the WHO-prequalified product, the participating authority informs WHO/PQP within 30 days about the subject and outcome of this national variation procedure.
- 5.4 Deviations under 5.2 and 5.3 above may include change of source of active ingredients or starting materials, manufacturing sites, manufacturing process, product specifications, testing methods, storage conditions, shelf-life, packaging material, indications, contraindications, posology (dosing), special warnings and precautions for use, adverse reactions and other changes specified in WHO/PQP guidelines²². Differences in brand name, name of applicant or WHO prequalification holder, format of product information, level of detail of product information, labelling of internal

¹⁹ See footnote 13.

²⁰ See footnote 14.

²¹ See footnote 14.

²² See footnote 13

and external packaging and language of product information are not considered to be deviations from the prequalification conclusions for pharmaceutical products. For vaccines such changes must be reported to WHO/PQP, which provides opinion to which extent the difference represents deviation from prequalification conclusions.

- 5.5 If a national variation procedure results in the nationally-registered product being no longer the same²³ as the WHO-prequalified Product, or if a variation of the WHO-prequalified Product is not followed by a variation of the nationally-registered product and, as a consequence, the nationally-registered product is no longer the same, the WHO prequalification holder will inform WHO/PQP of the differences and their reasons.
- 5.6 WHO/PQP removes a product from the list published in line with this Procedure if the nationally-registered product is no longer the same²⁴ as the WHO-prequalified product.

6. Withdrawals, suspensions or delistings of prequalified pharmaceutical products or vaccines and national deregistrations

- 6.1 If a WHO-prequalified product is withdrawn from prequalification by the WHO prequalification holder, or if a product is suspended or delisted by WHO/PQP, WHO/PQP will promptly, through the restricted-access web site, and subject to the above-mentioned obligations of confidentiality and restrictions on use, inform relevant participating authorities accordingly, providing the reasons whenever needed.
- 6.2 In the case that a participating NMRA deregisters or suspends the registration of a prequalified pharmaceutical product or vaccine for any reason, the participating authority informs WHO/PQP of the decision (together with an indication of the reasons), through the restricted-access web site. The information should be provided promptly whenever product quality, safety or efficacy are concerned and in all other cases within 30 working days. A participating authority is encouraged to consult WHO/PQP before adopting a decision about deregistration or suspension of registration of a WHO-prequalified product.
- 6.3 In case a WHO-prequalified product is deregistered at the national level, or in case WHO/PQP delists a prequalified product, WHO/PQP adjusts the information about this product on its web site accordingly.

²³ See footnote 14.

²⁴ See footnote 14.

Appendix 1:

NMRA participation agreement and undertaking for NMRA focal point(s)

Appendix 1, Part A

Agreement to participate in the collaborative procedure between the World Health Organization Prequalification Programme and national medicines regulatory authorities (NMRAs) in the assessment and accelerated national registration of WHO-prequalified pharmaceutical products and vaccines

Details of national medicines regulatory authority (NMRA)

Name of NMRA (“the NMRA”)

Postal address: _____

Country: (“the Country”) _____

Telephone number (please include codes): _____

E-mail (Please indicate contact details as appropriate for inclusion in the list of participating NMRAs maintained on the WHO web site): _____

Scope of agreement

Applicants for national registration of a WHO-prequalified pharmaceutical product or vaccine (hereafter referred to as “Applicants”) may express their interest to the NMRA for the assessment and accelerated registration of this product (“the Product”) in the Country under the “Collaborative procedure between the World Health Organization Prequalification Programme (WHO/PQP) and national medicines regulatory authorities in the assessment and accelerated national registration of WHO-prequalified pharmaceutical products or vaccines ” (hereafter referred to as “the Procedure”).¹

Subject to the NMRA agreeing to conduct such assessment and consider such accelerated registration of the Product under the Procedure (by submitting the form reproduced in Part B of Appendix 3 attached to the Procedure to WHO PQP through the restricted-access web site), the NMRA hereby confirms for each such Product that it will adhere to, and collaborate with the WHO/PQP and the applicant of the Product in accordance with, the terms of the Procedure.

¹ If the applicant for national registration is not the same as the WHO prequalification holder, the WHO prequalification holder must confirm to the NMRA and to WHO/PQP by an authorization letter (as per the template annexed to Appendix 3, Part A) that the applicant is acting for, or pursuant to rights derived from, the WHO prequalification holder, and that the WHO prequalification holder agrees with the application of the Procedure in the country concerned.

Confidentiality of information

Any information and documentation relating to the Product and provided by WHO/PQP to the NMRA under the Procedure may include but shall not necessarily be limited to:

- the full WHO/PQP assessment and inspection outcomes (reports) and if relevant, also results of laboratory testing;
- information and documentation on variations (as defined in WHO guidelines²), as well as information and documentation on any actions taken by WHO/PQP or NMRAs post-prequalification of the Product;
- all such data, reports, information and documentation being hereinafter referred to as “the Information”.

As regards sharing the outcomes of assessments, inspections and laboratory testing, only data owned by the WHO prequalification holder and WHO are shared. Sharing of any other data is subject to additional agreement of the data owners concerned.

WHO/PQP agrees to make such Information available to the NMRA through a restricted-access web site exclusively for the purpose of the assessment and accelerated registration of the Product in the Country and any post-registration processes that may be required, in accordance with and subject to the terms of the Procedure (“the Purpose”). The NMRA agrees to treat any Information provided by WHO/PQP as aforesaid as strictly confidential and proprietary to WHO/PQP, the WHO prequalification holder/applicant and/or parties collaborating with WHO/PQP and/or the WHO prequalification holder/applicant. In this regard, the NMRA agrees to use such Information only for the Purpose and to make no other use thereof. Thus, the NMRA undertakes to maintain the Information received from WHO/PQP in strict confidence, and to take all reasonable measures to ensure that:

² For pharmaceutical products: *WHO guidelines on variations to a prequalified product*. In: WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-seventh report. Geneva, World Health Organization, 2013 (WHO Technical Report Series, No. 981), Annex 3 (and any updates thereto).

For vaccines: Draft guidance on reporting variations to a prequalified vaccine

(http://www.who.int/immunization_standards/vaccine_quality/variations_pq_vaccine/en/)

(and any updates thereto).

- the Information received from WHO/PQP shall not be used for any purpose other than the Purpose;
- the Information shall only be disclosed to persons who have a need to know for the aforesaid Purpose and are bound by confidentiality undertakings in respect of such information and documentation which are no less stringent than those contained herein.

The NMRA warrants and represents that it has adequate procedures in place to ensure compliance with its aforesaid obligations.

The obligations of confidentiality and restrictions on use contained herein shall not cease on completion of the Purpose.

The obligations of confidentiality and restrictions on use contained herein shall not apply to any part of the Information which the NMRA is clearly able to demonstrate:

- was in the public domain or the subject of public knowledge at the time of disclosure by WHO/PQP to the NMRA under the Procedure; or
- becomes part of the public domain or the subject of public knowledge through no fault of the NMRA; or
- is required to be disclosed by law, provided that the NMRA shall in such event immediately notify WHO/PQP and the applicant in writing of such obligation and shall provide adequate opportunity to WHO/PQP and/or the applicant to object to such disclosure or request confidential treatment thereof (provided always, however, that nothing contained herein shall be construed as a waiver of the privileges and immunities enjoyed by WHO/PQP and/or as submitting WHO/PQP to any national court jurisdiction).

Upon completion of the Purpose, the NMRA shall cease all use and make no further use of the Information disclosed to it under the Procedure, and shall promptly destroy all of the Information received from WHO/PQP which is in tangible or other form, except that the NMRA may retain copies of the Information in accordance with its established archival procedures, subject always, however, to the above-mentioned obligations of confidentiality and restrictions on use.

The Purpose for each product shall be deemed completed as soon as:

- the WHO prequalification holder/Applicant discontinues participation in the Procedure for the particular product;
- the Product is deregistered by the NMRA and/or delisted by WHO/PQP.

The access right of the NMRA's focal person(s) to the restricted-access web site will cease automatically upon the NMRA ceasing to participate in the Procedure. If and as soon as an NMRA focal point is replaced by a new focal point or ceases to be an employee of the NMRA, such focal point's access to the restricted-access web site shall automatically terminate.

The NMRA agrees that it has no right in or to the Information and that nothing contained herein shall be construed, by implication or otherwise, as the grant of a licence to the NMRA to use the Information other than for the Purpose.

Timelines

In respect of each Product which the NMRA accepts to assess and consider for accelerated registration under the Procedure, the NMRA undertakes to abide by the terms of the Procedure, including but not limited to the following timelines for processing each application:

- within 90 calendar days of obtaining access (through the restricted access web site) to:
 - the data submitted to WHO/PQP for prequalification of the Product and owned by the WHO prequalification holder,
 - the full WHO/PQP assessment and inspection outcomes (reports), the NMRA undertakes to take a decision on the national registration of the Product;
- within 30 working days of the NMRA's decision on national registration of the Product, the NMRA undertakes to inform WHO/PQP of this decision and of any deviations from the WHO prequalification conclusions (with an indication of the reasons for such deviations) by completing and submitting the form attached as Appendix 3, Part C to the Procedure to WHO/PQP through the restricted-access web site;
- if a national variation procedure results in the nationally registered product being no longer the same³ as the WHO-prequalified product, or if and to the extent a variation of a WHO-prequalified product is not followed by a variation of the nationally-registered product and as a consequence, the nationally-registered product is no longer the same² as the WHO-prequalified product, the NMRA undertakes to inform WHO/PQP thereof (together with an indication of the reasons for such deviations) within 30 days of the conclusion of the national variation procedure or within 30 days of having received access to the information and documentation provided by WHO/PQP, as

³ Within the context of this Procedure, the same pharmaceutical product is characterized by the same product dossier, the same manufacturing chain, processes and control of materials, the same API and FPP specifications and the same essential elements of product information, as further described in paragraph 3.2 of the Procedure

the case may be (i.e. by completing and submitting the form attached to the Procedure as Appendix 4 to WHO/PQP through the restricted-access web site);⁴

- the NMRA undertakes to inform WHO/PQP in case the NMRA deregisters or suspends the registration of the Product in the Country, by completing and submitting the form attached to the Procedure as an Appendix 4 to WHO/PQP through the restricted access web site, and to do so promptly if this decision is based on quality, safety of efficacy concerns, and within 30 working days if this decision is based on other reasons.

Focal points for access to restricted-access web site

The NMRA has designated the person(s) listed below to act as focal point(s) for access to WHO/PQP's restricted-access web site. The undertaking(s) completed and signed by the focal point(s) is(are) attached hereto as an Appendix to this agreement.

Any change in designated focal points must be communicated to WHO/PQP without delay in writing and will be subject to the new focal point having signed and submitted to WHO the undertaking reproduced in Appendix 1B to the Procedure. The NMRA also undertakes to inform WHO/PQP if and as soon as a designated focal point ceases to be an employee of the NMRA.

Focal point for inspections

If applicable, this should be the same focal point as for the “WHO/PQP collaborative procedure between WHO/PQP and selected NMRAs in inspection activities” (<http://who.int/prequal>). The same person should be designated for inspections of pharmaceutical products and vaccines.

1.

Mr/Ms/Dr:

First name (and initials): _____

Surname/family name: _____

Title in NMRA: _____

E-mail: _____

Phone: _____

⁴ If the fact that a WHO-prequalified product has been registered in a country pursuant to this Procedure has been made public any subsequent deviations should be made public also.

A signed undertaking is attached

Focal point(s) for dossier assessment

For dossier assessment, different persons can be nominated for pharmaceutical products and vaccines. The same person may be nominated to be the focal point for inspections and dossiers assessment. If additional person(s) are nominated for dossier assessment, please complete details below.

2.

Mr/Ms/Dr as a focal point for dossier assessment of

pharmaceutical products only

pharmaceutical products and vaccines

First name (and initials): _____

Surname/family name: _____

Title in NMRA: _____

E-mail: _____

Phone: _____

A signed undertaking is attached

3.

Mr/Ms/Dr as a focal point for dossier assessment of vaccines

First name (and initials): _____

Surname/family name: _____

Title in NMRA: _____

E-mail: _____

Phone: _____

A signed undertaking is attached

Miscellaneous

The NMRA agrees that WHO/PQP may list its name on the WHO/PQP web site as a participant in the Procedure. Except as provided herein before, neither party shall, without the prior written consent of the

other party, refer to the relationship of the parties under this Agreement and/or to the relationship of the other party to the Product, the Information and/or the Purpose, in any statement or material of an advertising or promotional nature.

This Agreement shall not be modified except by mutual agreement of WHO and the NMRA in writing. The NMRA furthermore undertakes to promptly inform WHO/PQP of any circumstances or change in circumstances that may affect the implementation of this Agreement.

The parties shall use their best efforts to settle amicably any dispute relating to the interpretation or execution of this Agreement. In the event of failure of the latter, the dispute shall be settled by arbitration. The arbitration shall be conducted in accordance with the modalities to be agreed upon by the parties or in the absence of agreement, with the UNCITRAL Arbitration Rules in effect on the date of this Agreement. The parties shall accept the arbitral award as final.

It is agreed furthermore that nothing contained in this Agreement shall be construed as a waiver of any of the privileges and immunities enjoyed by WHO under national and international law, and/or as submitting WHO to any national court jurisdiction.

Agreed and accepted for pharmaceutical products and vaccines

For the NMRA

Signature: _____

Name: _____

Title: _____

Place and date: _____

Attachments:

1. Signed undertaking(s) of NMRA focal point(s) (Appendix 1, Part B)

Appendix 1, Part B

Undertaking for NMRA focal point(s)

The undersigned:

Mr/Ms/Dr: _____

First name (and initials): _____

Surname/family name: _____

Title in NMRA: _____

Name of NMRA (“the NMRA”) _____

Country: (“the Country”) _____

E-mail: _____

Phone: _____

Applicants for national registration of WHO-prequalified pharmaceutical products or vaccines (hereafter referred to as “Applicants”) may express their interest to the NMRA for the assessment and accelerated national registration of such products under the “Collaborative procedure between the World Health Organization Prequalification Programme (WHO/PQP) and national medicines regulatory authorities (NMRAs) in the assessment and accelerated national registration of WHO-prequalified pharmaceutical products and vaccines” (hereafter referred to as “the Procedure”).¹

Subject to the NMRA agreeing to conduct such assessment and consider such accelerated registration of a WHO-prequalified product under the Procedure, WHO/PQP will communicate confidential Information (as hereinafter defined) relating to each such product to the NMRA, and the NMRA will communicate outcomes of the national registration procedure and post-registration actions in respect of such products to WHO/PQP, through a restricted-access web site, which can be accessed only by the focal points designated by the NMRA, including the undersigned. For the purpose of accessing the restricted-access web site and downloading Information and uploading reports in accordance with and subject to the terms of the Procedure, WHO/PQP will provide the undersigned with a secret access code. The undersigned

¹ If the applicant for national registration is not the same as the WHO prequalification holder, the WHO prequalification holder must confirm to the NMRA and to WHO/PQP by an authorization letter (as per the template annexed to Appendix 3, Part A) that the applicant is acting for, or pursuant to rights derived from, the WHO prequalification holder, and that the prequalification holder agrees with the application of the Procedure in the country concerned.

undertakes to treat this access code as strictly confidential and not to disclose it to any other person whatsoever. The undersigned furthermore undertakes to take all precautionary measures that may be needed to prevent any other person whatsoever from obtaining the aforesaid secret access code and from accessing the restricted-access web site (i.e. except for the other designated focal points who have signed this undertaking).

“Information” as aforesaid means any information and documentation relating to a WHO-prequalified product to be provided by WHO/PQP to the NMRA under the Procedure, including but not necessarily limited to:

- the full WHO/PQP assessment and inspection outcomes (reports) and if relevant, also results of laboratory testing;
- information and documentation on subsequent variations (as defined in WHO guidelines²), as well as information and documentation on any actions taken by WHO/PQP, or NMRAs post-prequalification of the Product.

As regards sharing the outcomes of assessments, inspections and results of laboratory testing, only data owned by the WHO prequalification holder and WHO are shared. Sharing of any other data is subject to additional agreement of the data owners concerned.

The undersigned confirms that:

1. the NMRA has bound him or her to obligations of confidentiality and restrictions on use no less stringent than those contained in Appendix 1A to the Procedure; and that
2. the aforesaid obligations of confidentiality and restrictions on use shall not cease on completion of the assessment and accelerated registration of any product in the Country, nor on completion of any post-registration processes that may be required, nor on the undersigned ceasing to be an employee of (or ceasing to have another relationship with) the NMRA.

² For pharmaceutical products: *WHO guidelines on variations to a prequalified product*. In: WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-seventh report. Geneva, World Health Organization, 2013 (WHO Technical Report Series, No. 981), Annex 3 (and any updates thereto).
For vaccines: Draft guidance on reporting variations to a prequalified vaccine
(http://www.who.int/immunization_standards/vaccine_quality/variations_pq_vaccine/en/)

The undersigned shall automatically cease having the right to access the restricted-access web site when the NMRA designates a new focal point to replace the undersigned or when the undersigned ceases to be an employee of the NMRA.

This Undertaking shall not be modified except by mutual agreement of WHO and the undersigned in writing. The undersigned furthermore undertakes to promptly inform WHO/PQP of any circumstances or change in circumstances that may affect the implementation of this Undertaking.

The parties shall use their best efforts to settle amicably any dispute relating to the interpretation or execution of this Undertaking. In the event of failure of the latter, the dispute shall be settled by arbitration. The arbitration shall be conducted in accordance with the modalities to be agreed upon by the parties or in the absence of agreement, with the UNCITRAL Arbitration Rules in effect on the date of this Undertaking. The parties shall accept the arbitral award as final.

It is agreed furthermore that nothing contained in this Undertaking shall be construed as a waiver of any of the privileges and immunities enjoyed by WHO under national and international law, and/or as submitting WHO to any national court jurisdiction.

Agreed and accepted by the Undersigned:

Signature: _____

Name: _____

Title in NMRA: _____

Place and date: _____

Appendix 2:

Consent of WHO prequalification holder for WHO to share information with NMRA confidentially under the Procedure

Reference is made to the attached expression of interest for the assessment and accelerated national registration under the Procedure of the following WHO prequalified pharmaceutical product or vaccine (hereafter referred to as "the Product") in [country].¹

pharmaceutical product

vaccine

WHO prequalification details:

WHO prequalification reference number: _____

Date of prequalification (dd/mm/yyyy): _____

Date of requalification (if applicable): _____

WHO prequalification holder:² _____

Application details:

Name of entity: ("the Applicant"): _____

Street: _____

City and country: _____

E-mail: _____

Phone: _____

The WHO prequalification holder hereby consents to WHO/PQP providing the following information and documentation to the NMRA of [country] ("the NMRA") for the assessment and accelerated registration of the Product in the country under the Procedure and to freely discuss the same with the aforesaid NMRA for this purpose:

- the full WHO/PQP assessment and inspection outcomes (reports), results of laboratory testing and if relevant, also assessment and inspections reports of other regulatory bodies, provided that these bodies gave their written consent to the use of such reports for the purpose of the Procedure;

¹ Please complete a separate form of this Annex for each country.

² If the applicant for national registration is not the same as the WHO prequalification holder, the WHO prequalification holder must confirm to the NMRA and to WHO/PQP by an authorization letter (as per the template annexed to Appendix 3, Part A) that the applicant is acting for, or pursuant to rights derived from, the WHO prequalification holder, and that the prequalification holder agrees with the application of the Procedure in the country concerned.

- information and documentation on subsequent variations (as defined in WHO guidelines³), as well as information and documentation on any actions taken by WHO/PQP post-prequalification of the Product.
- all such data, reports, information and documentation being hereinafter referred to as “the Information”.

As regards sharing the outcomes of assessments and inspections, only data owned by the WHO prequalification holder and WHO are shared. Sharing of any other data is subject to additional agreement of the data owners concerned.⁴

Such consent is subject to the NMRA having entered into an agreement with WHO/PQP as per Appendix 1A to the Procedure and having agreed to conduct the assessment and consider the accelerated registration of the Product under the Procedure, by having submitted the form reproduced in Part B of Appendix 3 to the Procedure to WHO.

The WHO prequalification holder/Applicant commits to submit post-prequalification variations simultaneously to WHO/PQP and any relevant participating authorities, and vice versa. Submission of variations to NMRAs should respect national regulatory requirements. If a national variation procedure results in the nationally-registered product being no longer the same⁵ as the WHO-prequalified Product, or if a variation of the WHO-prequalified Product is not followed by a variation of the nationally-registered

³ For pharmaceutical products: *WHO guidelines on variations to a prequalified product*. In: WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-seventh report. Geneva, World Health Organization, 2013 (WHO Technical Report Series, No. 981), Annex 3 (and any updates thereto).

For vaccines: Draft guidance on reporting variations to a prequalified vaccine (http://www.who.int/immunization_standards/vaccine_quality/variations_pq_vaccine/en/)

⁴ In case that certain data submitted to WHO/PQP by the WHO prequalification holder in relation to prequalification of the Product are not in his/her ownership, the WHO prequalification holder specifies such data in an annex to this declaration of consent.

⁵ Within the context of this Procedure, the same pharmaceutical product is characterized by the same product dossier, the same manufacturing chain, processes and control of materials, the same API and FPP specifications and the same essential elements of product information, as further described in paragraph 3.2 of the Procedure.

product and, as a consequence, the nationally-registered product is no longer the same, the WHO prequalification holder/Applicant will inform WHO/PQP of the differences and their reasons.

For the WHO prequalification holder

Signature: _____

Name: _____

Title: _____

Place: _____

Date (dd/mm/yyyy): _____

Draft for comment

Appendix 3:

Expression of interest to NMRA for the assessment and accelerated national registration, acceptance by NMRA and notification of Procedure outcomes

Appendix 3, Part A

Expression of interest to the national medicines regulatory authority (NMRAs) for the assessment and accelerated national registration of a WHO-prequalified pharmaceutical product or vaccine

In line with the Procedure, the undersigned Applicant¹ expresses its interest in the application of the above-mentioned Procedure by the NMRA of [country] (“the NMRA”) in respect of the following submission for national registration:

pharmaceutical product

vaccine

Application details:

Name of entity: (“the Applicant”) _____

Street: _____

City and country: _____

E-mail: _____

Phone: _____

Date of application (dd/mm/yyyy): _____

Product name in national system (if known): _____

National reference number (if known): _____

Product details for pharmaceutical products:

API(s) (INN): _____

Dosage form and strength: _____

Packaging: _____

Manufacturing site(s), including block(s)/unit(s) if appropriate: _____

Product details for vaccines:

Name of vaccine _____

Composition: _____

¹ If the applicant for national registration is not the same as the WHO prequalification holder, the WHO prequalification holder must confirm to the NMRA and to WHO/PQP by an authorization letter (as per the template annexed to Appendix 3, Part A) that the applicant is acting for, or pursuant to rights derived from, the WHO prequalification holder, and that the prequalification holder agrees with the application of the Procedure in the country concerned.

Packaging: _____

Manufacturing site(s), including block(s)/unit(s) if appropriate: _____

WHO prequalification details:

WHO prequalification reference number: _____

Date of prequalification (dd/mm/yyyy): _____

WHO prequalification holder: _____

The Applicant confirms that the information and documentation provided in support of the above-mentioned submission for national registration is true and correct, that the product submitted for national registration is the same² as the WHO-prequalified product and that the technical information in the registration dossier is the same³ as that submitted to the WHO Prequalification Programme (WHO/PQP).

Non-essential differences⁴ from the information submitted to WHO/PQP are following:

Subject to the NMRA agreeing to conduct the assessment and consider the accelerated registration of the Product under the Procedure, the Applicant:

1. undertakes to adhere to, and collaborate with the NMRA and WHO/PQP in accordance with the terms of the Procedure; and
2. will authorize WHO/PQP⁵ to provide the NMRA confidential access to the following information and documentation and to freely discuss the same with the aforesaid NMRA for the above-mentioned Purpose:
 - the full WHO/PQP assessment and inspection outcomes (reports), results of laboratory testing and if relevant, also assessment and inspections reports of other regulatory

² Within the context of this Procedure, the same pharmaceutical product is characterized by the same product dossier, the same manufacturing chain, processes and control of materials, the same API and FPP specifications and the same essential elements of product information, as further described in paragraph 3.2 of the Procedure.

³ Only the technical data included in the dossier must be the same. There may be country-specific differences in administrative data, or if required by NMRAs under exceptional circumstances, additional technical data can be provided (e.g. bioequivalence with a country-specific comparator).

⁴ As defined in Section 3.2 of the Procedure, for pharmaceutical products differences in administrative information, brand name, name of applicant/prequalification holder (provided that the applicant is acting for, and has the authority to represent the WHO prequalification holder), format of product information, level of detail of product information, labelling of internal and external packaging and language of product information are not considered to be essential differences.

⁵ If the applicant for national registration is not the same as the WHO prequalification holder, then the authorization to WHO/PQP must be provided by the WHO prequalification holder or their legal representative.

bodies, provided that these bodies gave their written consent to the use of such reports for the purpose of the Procedure;

- information and documentation on subsequent variations (as defined in WHO guidelines⁶), as well as information and documentation on any actions taken by WHO/PQP post-prequalification of the Product.

As regards sharing the outcomes of assessments and inspections, only data owned by the WHO prequalification holder and WHO are shared. Sharing of any other data is subject to additional agreement of the data owners concerned.

3. authorizes the NMRA to freely share and discuss all registration and the Product related information provided by the Applicant to the NMRA, with WHO/PQP, subject to the obligations of confidentiality and restrictions on use as contained in the NMRA's participation agreement and focal points' undertakings.

The application for national registration was submitted before the Applicant decided to apply the Procedure to the Product and therefore at the time of submission the registration dossier did not respect conditions of the Procedure. Steps taken to update the submission to the NMRA to make the dossier “the same” as required by the Procedure, are listed and referenced in the attached letter.

The applicant is not the WHO prequalification holder. An authorization letter from the WHO prequalification holder is attached.

For the Applicant

Signature: _____

Name: _____

Title: _____

Place: _____

⁶ For pharmaceutical products: WHO guidelines on variations to a prequalified product. In: WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-seventh report. Geneva, World Health Organization, 2013 (WHO Technical Report Series, No. 981), Annex 3 (and any updates thereto).

For vaccines: Draft guidance on reporting variations to a prequalified vaccine

(http://www.who.int/immunization_standards/vaccine_quality/variations_pq_vaccine/en/)

Date (dd/mm/yyyy): _____

Template for authorization letter

To be provided if the applicant is not the WHO prequalification holder. Please provide a separate letter for each NMRA concerned, with a copy to WHO/PQP.

This is to confirm that (*name of applicant*) seeking registration for prequalified product number (*WHO/PQ number*) in (*name country*) under the WHO collaborative procedure for accelerated registration of WHO prequalified products, is acting for, or pursuant to rights derived from (*name of WHO prequalification holder*) and that (*name of WHO prequalification holder*) agrees with the application of the Procedure in the country concerned.

For (*name of WHO Prequalification holder*) :

Signature _____

Name _____

Title _____

Date _____

Draft for comment

Appendix 3, Part B

Decision on acceptance by the NMRA to apply the Procedure to a specified WHO-prequalified pharmaceutical product and request for access to product-specific information and documentation

Please complete all fields marked *. For other fields, if there have been changes to the details as completed in Part A, please complete the relevant fields below. Where fields below are left blank, the data in Part A are considered to be valid.

Application details:

Name of entity: (“the Applicant”)

Street: _____

City and country: _____

E-mail: _____

Phone: _____

*Date of receipt of submission:(dd/mm/yyyy): _____

Product name in national system (if known): _____

*National reference number): _____

Product details for pharmaceutical products:

API(s) (INN): _____

Dosage form and strength: _____

Packaging: _____

Manufacturing site(s), including block(s)/unit(s) if appropriate: _____

Product details for vaccines:

Name of vaccine: _____

Composition: _____

Packaging: _____

Manufacturing site(s), including block(s)/unit(s) if appropriate: _____

WHO prequalification details:

*WHO prequalification reference number: _____

Date of prequalification (dd/mm/yyyy): _____

WHO prequalification holder _____

Please complete either section A or section B below:

Section A

The NMRA agrees to conduct the assessment and the accelerated registration of the above-mentioned product (“the Product”) under the Procedure and requests access to product-specific information, in accordance with and subject to the terms of the Procedure and the Agreement between WHO/PQP and the NMRA dated // (dd/mm/yyyy).

Section B

The NMRA has decided not to apply the Procedure to the above-mentioned Product for the following reasons:

*For the NMRA of (indicate country)

Signature: _____

Name: _____

Title: _____

Place: _____

*Date (dd/mm/yyyy): _____

Appendix 3, Part C

Notification of outcomes of national registration procedure by the NMRA

Product and application details as completed in Parts A and B above apply.

Please complete either Section A or B below:

Section A

Registration has been granted, and the above-mentioned product (“the Product”) is identified as follows in the national medicines register:

Name of the Product: _____

National registration number: _____

Date of registration (dd/mm/yyyy): _____

Product details (if different from those specified in Parts A and B):

Product details for pharmaceutical products:

API(s) (INN): _____

Dosage form and strength: _____

Packaging: _____

Manufacturing site(s), including block(s)/unit(s) if appropriate: _____

Product details for vaccines:

Name of vaccine: _____

Composition: _____

Packaging: _____

Manufacturing site(s), including block(s)/unit(s) if appropriate: _____

Registration holder (if different from the Applicant as specified in Parts A and B):

Name of entity: _____

Street: _____

City and country: _____

E-mail: _____

Phone: _____

Are the national registration conclusions different from prequalification outcomes?⁷ (Yes/No)

If you answered Yes to the above question:

Deviation	Reason

Please specify whether registration is subject to specific commitments, the registration is provisional or conditional, use of the Product is limited by specific prescribing restrictions, or additional clinical trials or additional data are required:

Section B

The application for registration of the Product was rejected for the following reasons:

For the NMRA

Signature: _____

Name: _____

Title: _____

Place: _____

Date: (dd/mm/yyyy) _____

⁷ This refers to deviations in indications, contraindications, posology (dosing), special warnings and precautions for use, adverse drug reactions, storage conditions and shelf-life. For pharmaceutical products differences in brand name, name of applicant/prequalification holder, format of a product information, level of detail of product information, labelling of internal and external packaging and language of product information are not considered to be a deviation from the prequalification conclusions.

Appendix 4:

Report on post-registration actions in respect of a product registered under the Procedure

Variation of the national registration resulting in the national registration conditions being inconsistent with the WHO/PQP prequalification conclusions

Deregistration or suspension of the registration of the product

Product details:

Product name in national system: ("the Product") _____

National registration number: _____

Date of registration (dd/mm/yyyy): _____

WHO prequalification details:

WHO prequalification reference number: _____

Date of prequalification (dd/mm/yyyy): _____

WHO prequalification holder: _____

The national variation procedure has resulted in the nationally-registered Product being no longer the same¹ as the WHO-prequalified product.

Deviation	Reason

¹ Within the context of this Procedure, the same pharmaceutical product is characterized by the same product dossier, the same manufacturing chain, processes and control of materials, the same API and FPP specifications and the same essential elements of product information, as further described in paragraph 3.2 of the Procedure.

The variation notified to NMRA by WHO/PQP has not been followed by a variation of the nationally-registered Product and, as a consequence, the nationally-registered product is no longer the same² as the WHO prequalified product.

Deviation	Reason

The Product has been deregistered or the registration of the Product has been suspended.

Deregistration (Yes/No): _____

Suspension of registration: (Yes/No): _____

Effective date (dd/mm/yyyy): ____ / ____ / ____

Reasons:

For the NMRA

Signature: _____

Name: _____

Title: _____

Place: _____

Date: (dd/mm/yyyy) _____

² See footnote 1.