

Annex 8

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

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1. Definitions

Collaborative procedure (Procedure)¹

Procedure for collaboration between the World Health Organization (WHO) Prequalification Team (WHO/PQT) and interested national regulatory authorities (NRAs) in the assessment and accelerated national registration of WHO-prequalified pharmaceutical products and vaccines.

Participating authorities or participating NRAs

NRAs 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/PQT website (for pharmaceutical products at <http://www.who.int/prequal/>, and for vaccines at http://www.who.int/immunization_standards/vaccine_quality/expedited_review/en/).

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, one of its surface proteins or genetically-engineered material. 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.

¹ Collaborative procedure between the World Health Organization (WHO) Prequalification of Medicines Programme and national medicines regulatory authorities in the assessment and accelerated national registration of WHO-prequalified pharmaceutical products appeared as Annex 4 (WHO Technical Report Series, No. 981, 2013).

2. Background information

National assessment of applications for registration of pharmaceutical products and vaccines (marketing authorization) is the key regulatory process that enables NRAs 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 NRA'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 NRA of decisions and outcomes of assessments and inspections made by NRAs in other countries, and for vaccines also official batch release by the national control laboratory performing the oversight of the vaccines.

Consideration of the outcomes of assessments and inspections by authorities, whose regulatory decisions are based on acceptable standards, substantially contributes to savings in regulatory resources and improvements in the quality of regulatory decisions, while retaining the prerogative of NRAs 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 NRAs 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 NRA is the same (see section 3.2) as the product being assessed or, if it is not the same, 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 NRA of the approaches that will make best use of the resources, workload and competence of individual NRAs.

Approaches could range from completely independent data reviews and inspections to adoption of regulatory decisions of reference authorities without any further scientific review. A pragmatic approach is to verify whether the product submitted for registration is the same (see section 3.2) as the product already prequalified 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 (e.g. stability data). In the other areas, the outcomes of reference authorities may be adopted.

To enhance timely access to prequalified products in countries, to ensure that the product in countries is the same as the one which is prequalified and to provide a model for regulatory information exchange among countries, this Procedure has been developed 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 principle of vaccines for purchase by United Nations agencies* (2) it aims to provide a convenient tool for NRAs wishing to enhance their premarketing evaluation and registration system by taking advantage of the scientific assessment work conducted by WHO/PQT. For pharmaceutical products the present procedure is complementary to the WHO/PQT collaborative procedure with NRAs in inspection activities (<http://www.who.int/prequal>, "Inspections").

The collaborative procedure was first piloted in 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 in 2007 and has been implemented for national registrations since 2010. However, this procedure did not include collaborative arrangements with the NRAs. In 2010 WHO/PQT piloted an expedited registration procedure that involved sharing of the WHO/PQT assessment reports with the NRAs.

Enhanced collaboration and information exchange between NRAs and WHO/PQT benefits all partners. Subject to the agreement of the WHO prequalification (PQ) holders concerned, NRAs 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* (1) and the *Procedure for assessing the acceptability in principle of vaccines for purchase by United Nations agencies* (2) are based. Such reports and relevant WHO documents help NRAs to make their decisions and also assist in training national regulatory staff. At the same time, feedback from NRAs on the information and documentation received from WHO/PQT under the Procedure allows WHO/PQT to improve its work and ensures that the outcomes of its assessments are relevant to NRAs. As a consequence patients and vaccinees benefit from this collaboration by gaining

faster access to pharmaceutical products and vaccines that have been found acceptable in principle for procurement by United Nations (UN) agencies. The collaborative registration procedure can be of particular relevance when implemented for pharmaceutical products and vaccines in emergency situations.

Depending on available resources, participating authorities have the opportunity to participate in the assessment process and in inspections organized by WHO/PQT.

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 WHO/PQT collaborative procedure with NRAs in inspection activities, alleviates the burden of additional national inspections on manufacturers.

3. Principles of collaboration

3.1 This collaborative procedure is applicable to:

- pharmaceutical products that have been assessed and inspected by WHO/PQT 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 UN agencies as listed in the *List of WHO prequalified medicines*, available at www.who.int/prequal. The Procedure is not applicable to pharmaceutical products that have been listed as prequalified on the basis of approval by stringent regulatory authorities (SRAs).² For such products the principal part of the assessment has been performed by SRAs and WHO/PQT is not in possession of assessment and inspection reports that can be shared;
- vaccines that have been assessed and inspected by WHO/PQT in line with the procedures and standards available at http://www.who.int/immunization_standards/vaccine_quality/pq_system/en/ and have been found to be acceptable in principle for procurement by UN agencies as listed in the *List of WHO prequalified vaccines*, available at http://www.who.int/immunization_standards/vaccine_quality/PQ_vaccine_list_en/en/. This Procedure is applicable to

² 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 Expert Committee on Specifications for Pharmaceutical Preparations: forty-eighth report. Geneva: World Health Organization; 2014: Annex 5 (WHO Technical Report Series, No. 986).

vaccines that successfully passed either the standard or streamlined prequalification process: http://www.who.int/immunization_standards/vaccine_quality/pq_revision2010/en/).

Although the Procedure mostly serves to accelerate the assessment and registration of prequalified multisource (generic) pharmaceutical products it is applicable to vaccines and any pharmaceutical product for which the safety and efficacy has been documented to WHO/PQT by the submission of preclinical and clinical data.

The Procedure has three major stakeholders: WHO/PQT, interested NRAs and those WHO PQ holders or applicants³ who agree that this Procedure is used for applications for national registration of their WHO-prequalified product submitted to an NRA.

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

- the same product dossier;⁴
- the same manufacturing chain, processes, control of materials and finished product, and in the case of vaccines also by the same batch release scheme;
- the same active ingredient and finished product specifications;
- the same essential elements of product information for pharmaceutical products,⁵ in the case of vaccines by the same product information, packaging presentation and labelling.

³ If the applicant for national registration is not the same as the WHO PQ holder, the WHO PQ holder must confirm to the NRA and WHO/PQT 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 PQ holder and that the WHO PQ holder agrees with the application of the procedure in the country concerned.

⁴ Submission of dossiers in common technical document (CTD) format as required by WHO/PQT 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 NRAs under exceptional circumstances, additional technical data can be provided (e.g. bioequivalence with a country-specific comparator).

⁵ 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. Differences in brand name, the name of applicant or WHO PQ 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/PQT.

- 3.3 WHO/PQT, with the agreement of the WHO PQ 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 PQ holder and WHO are shared. Sharing of any other data (e.g. related to a closed part of the Active pharmaceutical ingredient master file) 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* (1) and the *Procedure for assessing the acceptability in principle of vaccines for purchase by United Nations agencies* (2). 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 continue to follow standard national procedures. Similarly, the submission by manufacturers of samples for laboratory testing – if required – continues to follow standard procedures as defined in national legislation and/or as defined by NRAs. Participating authorities are advised to refrain from preregistration laboratory testing. Results from the laboratory testing organized in 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 1, Part A and Appendix 3, Part B, each participating authority commits itself:
- to treat any information and documentation provided to it by WHO/PQT pursuant to this Procedure as confidential in accordance with the terms of Appendix 1, Part A, and to allow access to such information and documentation only to persons⁶

⁶ This includes the focal point(s) and all other persons in the NRA who have access to any information and documentation provided by WHO/PQT.

- 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 1, Part A;
- to issue its national regulatory decision on registration of a given prequalified product (whether positive or negative) within 90 calendar days⁷ of regulatory time.⁸ If the applicant takes a long time to complete missing parts of the documentation without any justification, to provide additional data or to respond to other queries raised by NRAs, or if the applicant fails to provide the NRA with necessary information and cooperation, the NRA is entitled to terminate the Procedure and switch to the normal registration process. Such termination is communicated to the applicant and to WHO/PQT using Appendix 3, Part C.

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

Each participating NRA nominates a maximum of three focal points and specifies their areas of responsibility (inspections, assessment of pharmaceutical products, assessment of vaccines). These focal points will access the restricted-access website through which WHO/PQT will communicate all confidential information and documentation. Upon

⁷ 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 of regulatory time 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 of regulatory time and does not communicate valid reasons for the delay to WHO/PQT, WHO/PQT can follow up with the head of the NRA to clarify the situation. The timeline should be reduced as much as possible to facilitate access to products needed in case of emergency situations.

⁸ Regulatory time starts after a valid application for the registration according to the Procedure has been received and access to the confidential information has been granted (whichever is the later) and continues until the date of decision on registration. The regulatory time does not include the time granted to the applicant to complete missing parts of the documentation, provide additional data or respond to queries raised by NRAs.

justified request of an NRA to WHO/PQT, the number of focal points can be increased.

Focal points designated by the NRA must sign the undertaking reproduced in Appendix 1, Part B before they will be granted access to the restricted-access website. Any change in designated focal points must be communicated to WHO/PQT in writing without delay and must be accompanied by an undertaking (Appendix 1, Part B) 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/PQT or can decide to discontinue the Procedure for a specific product. Within 30 calendar days of having taken its decision, the participating authority reports this decision to WHO/PQT, together with the dates of submission and registration and, if applicable, any deviations from the WHO/PQT's decision on prequalification and the reasons for such deviations⁹ and/or any decision to discontinue the Procedure for a specific product. It does so through the restricted-access website by completing the form in Part C of Appendix 3 or providing the same information in another format. The NRA provides a copy of the completed form or the information to the applicant.
- 3.8 Participation by WHO PQ holders/applicants is voluntary, through the submission to a participating NRA of the expression of interest reproduced in Part A of Appendix 3. For each product such participation will be subject to the WHO PQ holder/applicant accepting the terms of this Procedure, including the confidential exchange of information and documentation between WHO/PQT and the NRA (see Appendix 2).

The WHO PQ holder/applicant can cease participation in this Procedure at any time provided that he or she informs WHO/PQT and the participating NRAs in writing of his or her decision. In such a case the NRA 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).

⁹ This refers to a decision not to approve the registration of a WHO-prequalified product and to a decision to approve the registration, 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 WHO PQ 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 PQ conclusions.

- 3.9 The requirements and procedures in case of a variation (as defined in WHO guidelines (3)) may differ between NRAs and WHO/PQT. The present collaborative procedure includes a variation procedure (see section 5) which is aimed at promoting consistency between variations accepted by WHO/PQT 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/PQT or vice versa. In such a case the conditions of the national registration, which were initially “harmonized” with the WHO PQ 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/PQT. The WHO PQ holders/applicants and NRAs are expected to inform WHO/PQT of the differences and the reasons for them, if, due to inconsistencies in variations, the nationally-registered product is no longer the same as the WHO-prequalified product.

As a result, applicants are required to submit to participating authorities without delay, at the latest 30 calendar days after acceptance of the variation by WHO/PQT, those variations which are subject to national regulatory requirements. WHO/PQT will inform the NRAs that have registered individual prequalified products, through the restricted-access website, about variations to the prequalification status of such products if and when regulatory action is deemed to be justified. Participating authorities are encouraged to follow the outcomes of the WHO variation procedures for nationally-approved WHO-prequalified products.

If a national variation procedure results in the nationally-registered product being no longer the same (see section 3.2) 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 (in the case that the particular variation is subject to national regulatory requirements), the participating authority informs WHO/PQT of the situation by submitting the form in Appendix 4, clearly specifying the deviations. The deadline for informing WHO/PQT is 30 days after the NRA has been informed by WHO/PQT about variation outcome. The variation approved by WHO/PQT will be considered by WHO/PQT as accepted by the NRA on a non-objection basis 30 days after information-sharing, unless and until the NRA informs WHO/PQT otherwise. Other participating NRAs, which have registered the WHO-

prequalified product in question pursuant to this Procedure, will be made aware of such deviations through the restricted-access website. 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 PQ holder, or is suspended or delisted by WHO/PQT, WHO/PQT will inform each participating authority that has approved, or is in the process of reviewing the product pursuant to this Procedure, of the withdrawal, suspension or delisting and the reasons for taking this action, through the restricted-access website and subject to the obligations of confidentiality contained in Appendix 1, Part A. Similarly, when an NRA deregisters or suspends the registration of a prequalified pharmaceutical product or vaccine for any reason, it will inform WHO/PQT of this decision and of its reasons through the restricted-access website. Other participating NRAs 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 website. 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 by posting on the WHO/PQT website.
- 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 NRAs not to perform repetitive assessment of thoroughly assessed data, but rather to focus on data verification so that they can be assured that the same product is submitted for registration as is prequalified. It is highly recommended not to reinspect the sites that have already been inspected by WHO/PQT inspection teams or by NRAs recognized by WHO as stringent and as functional with respect to inspections of vaccine manufacturing sites.
- 3.12 Sharing of information related to the Procedure between WHO/PQT, WHO PQ holders/applicants and NRAs is governed by Appendices 1, 2, 3 and 4. Completed Appendices 1 and 2 must be submitted to WHO/PQT without any change in their content. 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 vaccine

4.1 The applicant submits the product dossier for a WHO-prequalified pharmaceutical product or a vaccine to a participating NRA. The technical part of the dossier is updated to reflect the data as approved by WHO/PQT 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/PQT. To the extent that national regulatory requirements allow, the technical part of the dossier will be identical to the current version of the WHO/PQT dossier.¹⁰ In specific cases the NRA may prefer a dossier which is abbreviated in line with national requirements;
- an expression of interest reproduced in Part A of Appendix 3;
- data and samples according to country-specific requirements;
- any fees that may be payable to the NRA pursuant to national requirements.

Wherever possible, to minimize the workload of the NRA and facilitate the process, applicants should ensure that they express their interest in using the Procedure (Appendix 3, Part A) to the NRA and to WHO/PQT before submitting a national application for registration. If acceptable to NRAs, 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/PQT, i.e. the common technical document (CTD) format. In the case of vaccines the product summary file format may be also applicable.

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

¹⁰ 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: Annex 6 (WHO Technical Report Series, No. 978)) the submitted data should reflect essential data submitted to the NRA that granted the authorization/licence and additional documents as provided to WHO.

- 4.2 For each application under this Procedure, WHO/PQT is informed by the WHO PQ holder/applicant about the submission to the participating NRA by providing a completed copy of Appendix 3, Part A. The WHO PQ holder provides WHO at this time with its written consent for WHO/PQT to provide the product-related information in compliance with the applicable confidentiality requirements to the NRA of the country concerned (see Appendix 2).
- 4.3 The participating NRA informs WHO/PQT and the respective applicant of each application which it accepts or declines to include in this Procedure (Appendix 3, Part B). It is for the individual NRAs to decide whether to apply the Procedure for individual submissions. The Procedure applies only to applications that the NRA has accepted as complete.
- 4.4 Within 30 calendar days of receipt of the WHO PQ holder's consent, WHO/PQT shares the most recent product-related information and assessment, inspection and laboratory-testing outcomes through the restricted-access website 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/PQT provides explanations and/or more detailed information. If NRAs have significant concerns or questions which would preclude the registration of the prequalified pharmaceutical product or vaccine in their country, questions may be sent to WHO/PQT, preferably within 60 calendar days from the first day of the regulatory time. WHO/PQT will facilitate the problem resolution in cooperation with relevant parties.
- 4.5 After receiving the information and documentation from WHO/PQT, 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 of regulatory time.¹¹ Within 30 days of having taken its decision the participating authority reports this decision, together with an indication of the dates of submission, registration and, if applicable, the length of the non-regulatory time. The participating authority also reports any deviations from the WHO PQ conclusion and the reasons for such deviations, or, if a decision

¹¹ See footnote 7.

has been made to discontinue the Procedure for a product, the reasons for such discontinuation, to WHO/PQT through the restricted-access website. This report is provided to WHO/PQT using Part C of Appendix 3 and is copied to the applicant. WHO/PQT lists pharmaceutical products and vaccines registered according to this Procedure by participating NRAs on its public website. The steps in the collaboration for national registration of a pharmaceutical product or vaccine are summarized in Figure A8.1.

Figure A8.1
Flowchart showing the principal steps of the collaborative procedure

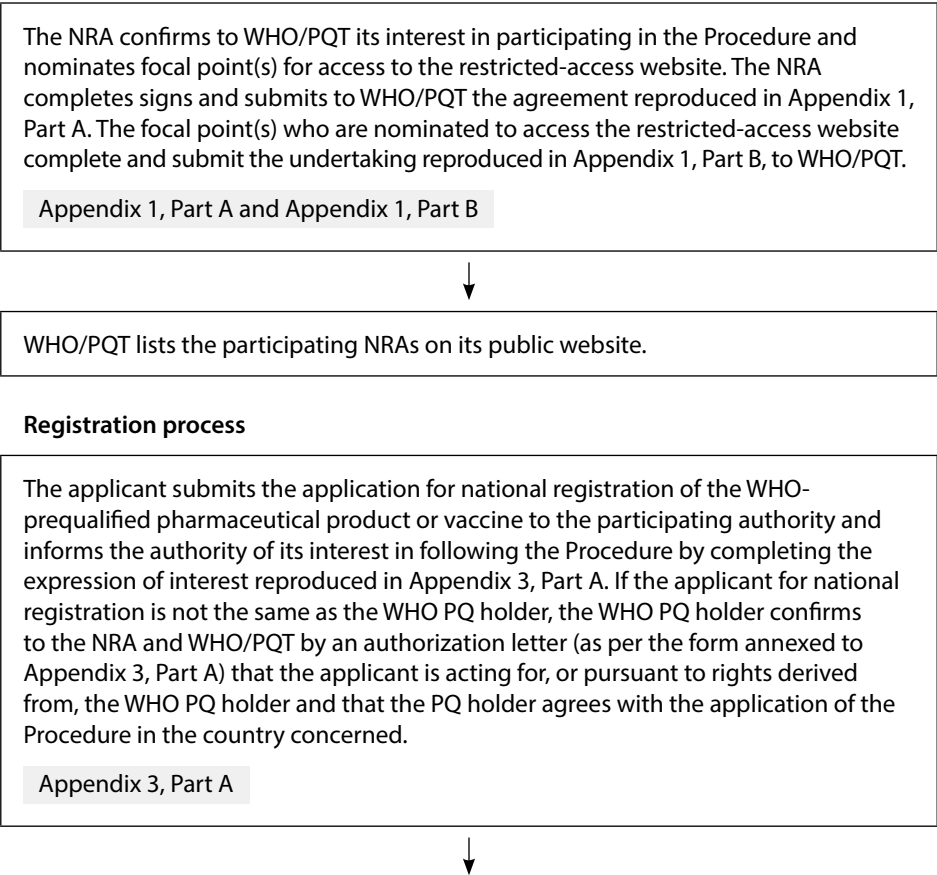


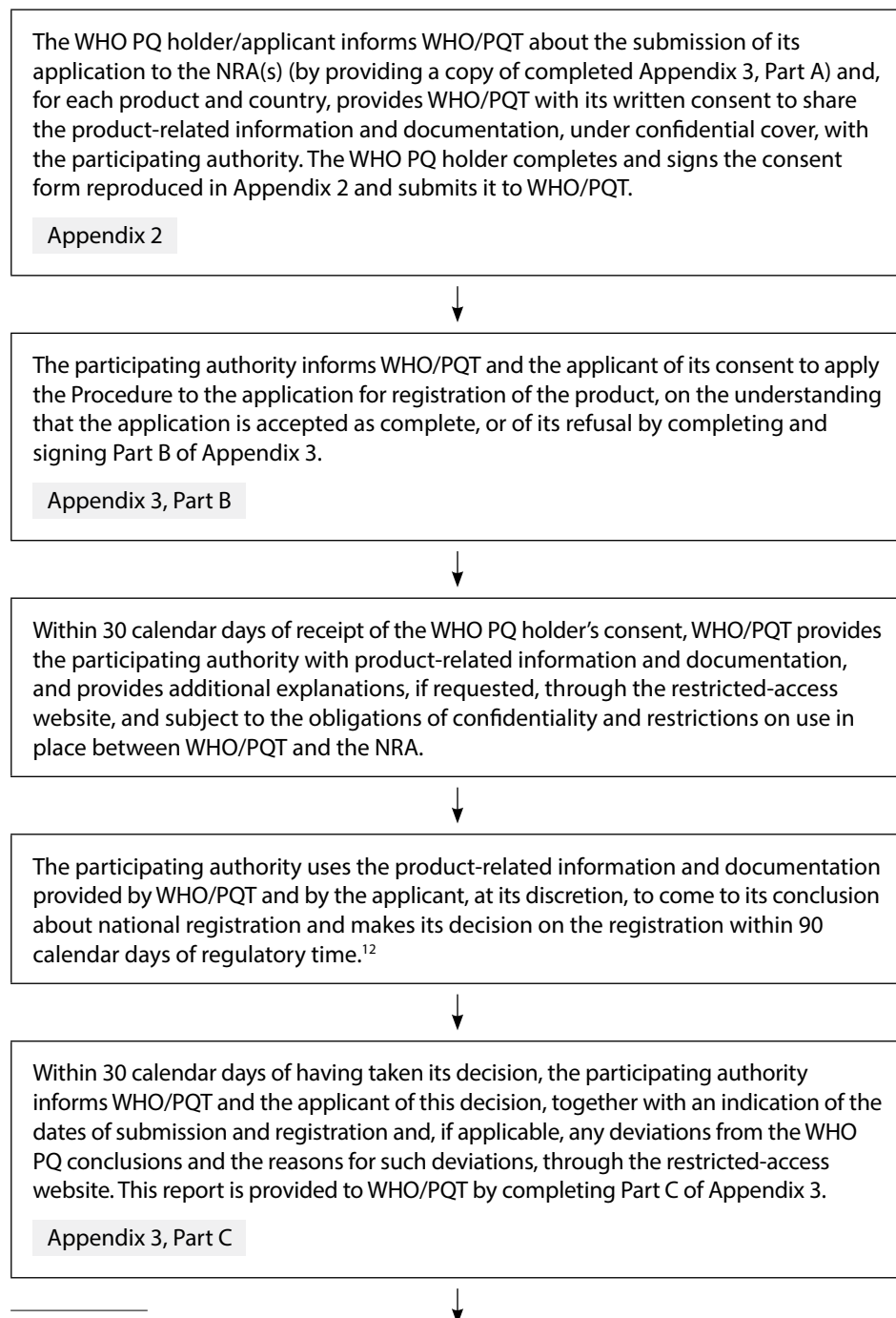
Figure A8.1 *continued*¹² See footnote 7.

Figure A8.1 *continued*

WHO/PQT lists pharmaceutical products registered by participating NRAs according to this Procedure on its public website

Post-registration processes

The WHO PQ holder/applicant submits to participating authorities at the latest 30 calendar days after acceptance of the variation by WHO/PQT those variations which are subject to national regulatory requirements. If regulatory action is deemed to be justified, WHO/PQT promptly provides the participating authorities concerned, through the restricted-access website, and subject to the above-mentioned obligations of confidentiality and restrictions on use, with outcomes of its variation assessment and relevant 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 same (see section 3.2) 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/PQT, by submitting the form reproduced in Appendix 4, clearly specifying the deviations. Other participating NRAs that have registered the WHO-prequalified product in question pursuant to this Procedure will be made aware of such deviations through the restricted-access website.

Appendix 4



WHO/PQT informs the participating authority, through the restricted-access website, 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/PQT, through the restricted-access website, of national de-registration or suspension (for any reason) of a prequalified pharmaceutical product or vaccine and the reasons for doing so. Other participating NRAs which have registered the WHO-prequalified product in question pursuant to this Procedure will be made aware of such national de-registration or suspension, through the restricted-access website.

Appendix 4



Figure A8.1 *continued*

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

- if the nationally-registered product is no longer the same (see section 3.2) as the WHO-prequalified product, or
- if the NRA deregisters a WHO-prequalified product, or
- if WHO/PQT delists a WHO-prequalified product.

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

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

- 5.1 Those post-prequalification variations submitted to WHO/PQT, which are subject to national regulatory requirements, are expected to be submitted to any relevant participating authorities without delay at the latest 30 calendar days after acceptance of the variation by WHO/PQT. Submission of variations to NRAs should respect national regulatory requirements. Applicants for national variations should inform participating authorities that the same application for a variation is being processed by WHO/PQT.
- 5.2 WHO/PQT promptly shares the outcomes of variation assessment and of related post-prequalification inspection (if applicable), through the restricted-access website, 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/PQT’s variation procedures (3)) 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/PQT, each participating authority informs WHO/PQT through the restricted-access website if and to what extent a variation of a WHO-prequalified product is not followed by the same accepted variation of the nationally-registered product and, as a consequence, the nationally-registered product is no longer the same (see section 3.2) as the WHO-prequalified product. The variation approved by WHO/PQT will be considered by WHO/PQT as accepted by the NRA on a non-objection basis 30 days after information-sharing, unless and until the NRA informs WHO/PQT otherwise.

- 5.3 If a national variation procedure occurs independently of a variation submitted to WHO/PQT and results in the nationally-registered product

being no longer the same (see section 3.2) as the WHO-prequalified product, the participating authority informs WHO/PQT 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/PQT guidelines (3). Differences in brand name, name of applicant or WHO PQ 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 conclusions during the prequalification of pharmaceutical products. For vaccines, such changes must be reported to WHO/PQT, which provides its opinion on the extent to which the difference represents deviation from conclusions during prequalification.
- 5.5 If a national variation procedure results in the nationally-registered product being no longer the same (see section 3.2) 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 PQ holder will inform WHO/PQT of the differences and their reasons.
- 5.6 WHO/PQT removes a product from the list published in line with this Procedure if the nationally-registered product is no longer the same (see section 3.2) 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 by the WHO PQ holder, or if a product is suspended or delisted by WHO/PQT, WHO/PQT will promptly, through the restricted-access website, 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 NRA deregisters or suspends the registration of a prequalified pharmaceutical product or vaccine for any reason, the participating authority informs WHO/PQT of the decision (together with an indication of the reasons), through the restricted-access website. The information should be provided promptly whenever there are concerns about product quality, safety or efficacy and in all other cases within 30 days. A participating authority is encouraged to consult WHO/PQT before adopting a decision about deregistration or suspension of registration of a WHO-prequalified product.
- 6.3 In the case that a WHO-prequalified product is deregistered at the national level, or in the case that WHO/PQT delists a prequalified product, WHO/PQT adjusts the information about this product on its website accordingly.

References

1. Procedure for prequalification of pharmaceutical products. In: WHO Expert Committee on Specifications for Pharmaceutical Preparations: forty-fifth report. Geneva: World Health Organization; 2011: Annex 10 (WHO Technical Report Series, No. 961).
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: Annex 6 (WHO Technical Report Series, No. 978).
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: Annex 3 (WHO Technical Report Series, No. 981), (and any updates thereto).
For vaccines: http://www.who.int/immunization_standards/vaccine_quality/variations_pq_vaccine/en/ (and any updates thereto).

Appendix 1

National regulatory authority participation agreement and undertaking for national regulatory authority focal point(s)

Appendix 1, Part A

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

Details of NRA

Name of NRA: _____ (“the NRA”)

Postal address: _____

Country: _____ (“the Country”)

Telephone number (please include codes): _____

Email (please indicate contact details as appropriate for inclusion in the list of participating NRAs maintained on the WHO website): _____

Scope of agreement

Applicants for national registration of a particular WHO-prequalified pharmaceutical product or vaccine (hereafter referred to as “Applicants”) may express their interest to the NRA in the assessment and accelerated registration of this product (“the Product”) in the Country under the “Collaborative Procedure between WHO/PQT and NRAs in the assessment and accelerated national registration of WHO-prequalified pharmaceutical products or vaccines” (hereafter referred to as “the Procedure”).¹

Subject to the NRA agreeing to conduct such assessment and consider such accelerated registration of the Product under the Procedure (by submitting

¹ If the applicant for national registration is not the same as the WHO prequalification (PQ) holder, the WHO PQ holder must confirm to the NRA and to WHO/PQT 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 PQ holder, and that the WHO PQ holder agrees with the application of the Procedure in the country concerned.

the form reproduced in Part B of Appendix 3 attached to the Procedure to WHO/PQT through the restricted-access website), the NRA hereby confirms for each such Product that it will adhere to, and collaborate with the WHO/PQT and the Applicant for registration of the Product in accordance with the terms of the Procedure.

Confidentiality of information

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

- the full WHO/PQT 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/PQT or NRAs 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 PQ holder and WHO/PQT are shared. Sharing of any other data is subject to additional agreement of the data owners concerned.

WHO/PQT agrees to make such information available to the NRA through a restricted-access website 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 NRA agrees to treat any Information provided by WHO/PQT as aforesaid as strictly confidential and proprietary to WHO/PQT, the WHO PQ holder/Applicant and/or parties collaborating with WHO/PQT and/or the WHO PQ holder/Applicant. In this regard, the NRA agrees to use such Information only for the Purpose and to make no other use thereof. Thus, the NRA undertakes to maintain the Information received from WHO/PQT 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: Annex 3 (WHO Technical Report Series, No. 981), (and any updates thereto).
For vaccines: http://www.who.int/immunization_standards/vaccine_quality/variations_pq_vaccine/en/ (and any updates thereto).

- the Information received from WHO/PQT 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 NRA 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 NRA is clearly able to demonstrate:

- was in the public domain or the subject of public knowledge at the time of disclosure by WHO/PQT to the NRA under the Procedure; or
- becomes part of the public domain or the subject of public knowledge through no fault of the NRA; or
- is required to be disclosed by law, provided that the NRA shall in such event immediately notify WHO/PQT and the Applicant in writing of such obligation and shall provide adequate opportunity to WHO/PQT 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/PQT and/or as submitting WHO/PQT to any national court jurisdiction).

Upon completion of the Purpose, the NRA 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/PQT which is in tangible or other form, except that the NRA 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 PQ holder/Applicant discontinues participation in the Procedure for the particular product;

- the Product is deregistered by the NRA and/or delisted by WHO/PQT.

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

The NRA 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 NRA to use the Information other than for the Purpose.

Timelines

In respect of each Product that the NRA agrees to assess and consider for accelerated registration under the Procedure, the NRA 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 regulatory time³ after obtaining access (through the restricted access website) to:
 - the data submitted to WHO/PQT for prequalification of the Product and owned by the WHO PQ holder,
 - the full WHO/PQT assessment and inspection outcomes (reports),
 the NRA undertakes to take a decision on the national registration of the Product;
- within 30 working days of the NRA's decision on national registration of the Product, the NRA undertakes to inform WHO/PQT of this decision and of any deviations from WHO conclusions during prequalification (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/PQT through the restricted-access website;

³ Regulatory time starts after a valid application for the registration according to the Procedure has been received and access to the confidential information has been granted (whichever is the later) and continues until the date of decision on registration. The regulatory time does not include the time granted to the applicant to complete missing parts of the documentation, provide additional data or respond to queries raised by NRAs.

- if a national variation procedure results in the nationally-registered product being no longer the same⁴ 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 same as the WHO-prequalified product, the NRA undertakes to inform WHO/PQT 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/PQT, as the case may be (i.e. by completing and submitting the form attached to the Procedure as Appendix 4 to WHO/PQT through the restricted-access website);⁵
- the NRA undertakes to inform WHO/PQT in the case that the NRA 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/PQT through the restricted-access website, and to do so promptly if this decision is based on quality, safety or efficacy concerns, and within 30 days if this decision is based on other reasons.

Focal points for access to restricted-access website

The NRA has designated the person(s) listed below to act as focal point(s) for access to WHO/PQT's restricted-access website. 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/PQT without delay in writing and will be subject to the new focal point having signed and submitted to WHO/PQT the undertaking reproduced in Appendix 1, Part B to the Procedure. The NRA also undertakes to inform WHO/PQT if and as soon as a designated focal point ceases to be an employee of the NRA.

⁴ Within the context of this Procedure, the same pharmaceutical product/same vaccine is characterized by the same product dossier; the same manufacturing chain, processes and control of materials and finished product, in the case of vaccines also by the same batch release scheme; the same active ingredient and finished product specifications; and the same essential elements of product information for pharmaceutical products, in the case of vaccines by the same product information, packaging presentation and labelling.

⁵ 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 also be made public.

Focal point for inspections

If applicable, this should be the same focal point as for the “WHO/PQT Collaborative Procedure with NRAs in inspection activities” (<http://who.int/prequal>, “Inspections”). 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 NRA: _____

Email: _____

Telephone: _____

☐ 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 dossier assessment. If additional person(s) are nominated for dossier assessment, please complete the 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 NRA: _____

Email: _____

Telephone: _____

☐ 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 NRA: _____

Email: _____

Telephone: _____

☐ A signed Undertaking is attached**Miscellaneous**

The NRA agrees that WHO/PQT may list its name on the WHO/PQT website as a participant in the Procedure. Except as provided hereinbefore, 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 NRA in writing. The NRA furthermore undertakes to promptly inform WHO/PQT 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 NRA

Signature: _____

Name: _____

Title: _____

Place and date: _____

Attachments:

Signed Undertaking(s) of NRA focal point(s) (Appendix 1, Part B)

Appendix 1, Part B

Undertaking for NRA focal point(s)

The undersigned:

Mr/Ms/Dr

First name (and initials): _____

Surname/family name: _____

Title in NRA: _____

Name of NRA: _____ (“the NRA”)

Country: _____ (“the Country”)

Email: _____

Telephone: _____

Applicants for national registration of WHO-prequalified pharmaceutical products or vaccines (hereafter referred to as “Applicants”) may express their interest to the national regulatory authority (NRA) in the assessment and accelerated national registration of such products under the “Collaborative Procedure between the World Health Organization (WHO) Prequalification Team (WHO/PQT) and national regulatory authorities in the assessment and accelerated national registration of WHO-prequalified pharmaceutical products and vaccines” (hereafter referred to as “the Procedure”).⁶

Subject to the NRA agreeing to conduct such assessment and consider such accelerated registration of a WHO-prequalified product under the Procedure, WHO/PQT will communicate confidential Information (as hereinafter defined) relating to each such product to the NRA, and the NRA will communicate outcomes of the national registration procedure and post-registration actions in respect of such products to WHO/PQT, through a restricted-access website, which can be accessed only by the focal points designated by the NRA, including the undersigned. For the purpose of accessing the restricted-access website and downloading Information and uploading reports in accordance with and subject to the terms of the Procedure, WHO/PQT will provide the undersigned with a secret access code. The undersigned undertakes to treat this access code as strictly confidential and not to disclose it to any other person whatsoever. The undersigned furthermore undertakes

⁶ If the applicant for national registration is not the same as the WHO PQ holder, the WHO PQ holder must confirm to the NRA and to WHO/PQT 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 PQ holder, and that the PQ holder agrees with the application of the Procedure in the country concerned.

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 website (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/PQT to the NRA under the Procedure, including but not necessarily limited to:

- the full WHO/PQT assessment and inspection outcomes (reports) and if relevant, also results of laboratory testing;
- information and documentation on subsequent variations (as defined in WHO guidelines⁷), as well as information and documentation on any actions taken by WHO/PQT or NRAs post-prequalification of the Product.

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

The undersigned confirms that:

1. the NRA has bound him or her to obligations of confidentiality and restrictions on use no less stringent than those contained in Appendix 1, Part A 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 NRA.

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

This Undertaking shall not be modified except by mutual agreement of WHO and the undersigned in writing. The undersigned furthermore undertakes

⁷ 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: Annex 3 (WHO Technical Report Series, No. 981), (and any updates thereto). For vaccines: http://www.who.int/immunization_standards/vaccine_quality/variations_pq_vaccine/en/ (and any updates thereto).

to promptly inform WHO/PQT 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 NRA: _____

Place and date: _____

Appendix 2

Consent of WHO prequalification holder for WHO to share information with the national regulatory authority confidentially under the Procedure

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

☐ pharmaceutical product

☐ vaccine

WHO prequalification details:

WHO prequalification (PQ) reference number: _____

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

Date of requalification (if applicable): _____

WHO PQ holder:² _____

Application details:

Name of entity: _____ (“the Applicant”)

Street: _____

City and country: _____

Email: _____

Telephone: _____

The WHO PQ holder hereby consents to the WHO Prequalification Team (WHO/PQT) providing the following information and documentation to the national regulatory authority (NRA) of _____ [country]

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

² If the applicant for national registration is not the same as the WHO PQ holder, the WHO PQ holder must confirm to the NRA and to WHO/PQT 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 PQ holder, and that the PQ holder agrees with the application of the Procedure in the country concerned.

(“the NRA”) for the assessment and accelerated registration of the Product in the country under the Procedure and to freely discuss the same with the aforesaid NRA for this purpose:

- the full WHO/PQT 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;
- information and documentation on subsequent variations (as defined in WHO guidelines³), as well as information and documentation on any actions taken by WHO/PQT 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 PQ holder and WHO/PQT are shared. Sharing of any other data is subject to additional agreement of the data owners concerned.⁴

Such consent is subject to the NRA having entered into an agreement with WHO/PQT as per Part A of Appendix 1 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/PQT.

The WHO PQ holder/Applicant commits to submit post-prequalification variations to WHO/PQT and any relevant participating authorities respecting national regulatory requirements. Variations should be submitted to participating authorities at the latest 30 calendar days after acceptance of the variation by WHO/PQT. Participating authorities should be informed about the fact that the same application for a variation is being processed by WHO/PQT. If a national variation procedure results in the nationally-registered product being no longer

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: Annex 3 (WHO Technical Report Series, No. 981), (and any updates thereto). For vaccines: http://www.who.int/immunization_standards/vaccine_quality/variations_pq_vaccine/en/ (and any updates thereto).

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

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

For the WHO PQ holder

Signature: _____

Name: _____

Title: _____

Place: _____

Date (dd/mm/yyyy): _____

⁵ Within the context of this Procedure, the same pharmaceutical product/same vaccine is characterized by the same product dossier; the same manufacturing chain, processes and control of materials and finished product, and in the case of vaccines also by the same batch release scheme; the same active ingredient and finished product specifications; as well as the same essential elements of product information for pharmaceutical products, and, in the case of vaccines, by the same product information, packaging presentation and labelling.

Appendix 3

Expression of interest to national regulatory authority (NRA) in the assessment and accelerated national registration, acceptance by NRA and notification of Procedure outcomes

Appendix 3, Part A

Expression of interest to the national regulatory authorities (NRAs) in the assessment and accelerated national registration of a World Health Organization (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 NRA of _____ [country] (“the NRA”) in respect of the following submission for national registration:

- ☐ pharmaceutical product
- ☐ vaccine

Application details:

Name of entity: _____ (“the Applicant”)

Street: _____

City and country: _____

Email: _____

Telephone: _____

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

Product name in national system (if known): _____

National reference number (if known): _____

¹ If the applicant for national registration is not the same as the WHO prequalification (PQ) holder, the WHO PQ holder must confirm to the NRA and to WHO/Prequalification Team (PQT) 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 PQ holder, and that the PQ holder agrees with the application of the Procedure in the country concerned.

Product details for pharmaceutical products:

Active pharmaceutical ingredient(s) (API(s)) (international nonproprietary name (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 PQ reference number: _____

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

WHO PQ 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 approved by WHO/PQT during the initial prequalification procedure, and consecutive variation procedures and

² Within the context of this Procedure, the same pharmaceutical product/same vaccine is characterized by the same product dossier; the same manufacturing chain, processes and control of materials and finished product, and in the case of vaccines also by the same batch release scheme; the same active ingredient and finished product specifications; as well as the same essential elements of product information for pharmaceutical products, and, in the case of vaccines, by the same product information, packaging presentation and labelling.

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 NRAs under exceptional circumstances, additional technical data can be provided (e.g. bioequivalence with a country-specific comparator).

requalification (where applicable). Minor differences⁴ from the information submitted to WHO/PQT are the following:

Subject to the NRA 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 NRA and WHO/PQT in accordance with the terms of the Procedure; and
2. will authorize WHO/PQT⁵ to provide the NRA confidential access to the following information and documentation and to freely discuss the same with the aforesaid NRA for the above-mentioned Purpose:
 - the full WHO/PQT 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,
 - information and documentation on subsequent variations (as defined in WHO guidelines⁶), as well as information and documentation on any actions taken by WHO/PQT post-prequalification of the Product.

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

⁴ As defined in section 3.2 of the Procedure, in the case of pharmaceutical products, examples of minor differences which are not considered essential may include differences in administrative information, brand name, name of applicant (provided that the applicant is acting for, and has the authority to represent the WHO PQ holder), format of product information, level of detail of product information, labelling of internal and external packaging and language of product information.

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

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: Annex 3 (WHO Technical Report Series, No. 981), (and any updates thereto).
For vaccines: http://www.who.int/immunization_standards/vaccine_quality/variations_pq_vaccine/en/ (and any updates thereto).

3. authorizes the NRA to freely share and discuss all registration-related and Product-related information provided by the Applicant to the NRA, with WHO/PQT, subject to the obligations of confidentiality and restrictions on use as contained in the NRA'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 NRA 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 PQ holder. An authorization letter from the WHO PQ holder is attached.

For the Applicant

Signature: _____

Name: _____

Title: _____

Place: _____

Date (dd/mm/yyyy): _____

Template for authorization letter

[To be provided if the applicant is not the WHO PQ holder. Please provide a separate letter for each NRA concerned, with a copy to WHO/PQT.]

This is to confirm that _____ (*name of applicant*) seeking registration for prequalified product number _____ (*WHO PQ number*) in _____ (*name of 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 PQ holder*) and that _____ (*name of WHO PQ holder*) agrees with the application of the Procedure in the country concerned.

For _____ (*name of WHO PQ holder*):

Signature: _____

Name: _____

Title: _____

Date: _____

Appendix 3, Part B

Decision on acceptance by the NRA to apply the Procedure to a specified WHO-prequalified 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: _____

Email: _____

Telephone: _____

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

Product name in national system (if known): _____

*National reference number: _____

Product details for pharmaceutical products:

Active pharmaceutical ingredient(s) (API(s)) (international nonproprietary name (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 PQ reference number: _____

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

WHO PQ holder: _____

Please complete either section A or section B below:☐ **Section A**

The NRA 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/PQT and the NRA dated ____ / ____ / ____ (dd/mm/yyyy).

☐ **Section B**

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

*For the NRA of _____ (indicate country)

Signature: _____

Name: _____

Title: _____

Place: _____

*Date (dd/mm/yyyy): _____

Appendix 3, Part C

Notification of outcomes of national registration procedure by the NRA

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

Please complete either section A or section B below:

☐ Section A

Registration has been granted under the terms of the Procedure, 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): _____

Non-regulatory time (days): _____

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: _____

Email: _____

Telephone: _____

Are the national registration conclusions different from prequalification outcomes?⁷ _____ (yes/no)

If you answered yes to the above question, please specify:

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**

Please complete as appropriate:

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

☐ The collaborative procedure was discontinued for this application for the following reasons: _____

For the NRA

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/PQ 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 a deviation from the PQ 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/PQT 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 PQ reference number: _____
 Date of prequalification (dd/mm/yyyy): _____
 WHO PQ 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/same vaccine is characterized by the same product dossier; the same manufacturing chain, processes and control of materials and finished product, and in the case of vaccines also by the same batch release scheme; the same active ingredient and finished product specifications; as well as the same essential elements of product information for pharmaceutical products, and, in the case of vaccines, by the same product information, packaging presentation and labelling.

- ☐ The variation notified to the NRA by WHO/PQT has not been followed by a variation of the nationally-registered Product and, as a consequence, the nationally-registered product is no longer the same¹ 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 NRA

Signature: _____

Name: _____

Title: _____

Place: _____

Date (dd/mm/yyyy): _____