

WHO PQ dossier Module I

*DCVMN Common Technical Document
(CTD) Workshop*

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Introduction

- The WHO Vaccines prequalification programme has made the decision to use the CTD as their dossier format to replace the Product Summary File used earlier
- In order to organize the switch they have developed a WHO specific module 1 to address the UN related requirements

Items of WHO-proposed module I

1.1 and 1.2

Administrative and Product information

1.1 Table of Contents

- The overall table of contents should include all modules from 1 to 5.

1.2 Correspondence

- 1.2.1 Copy of the letter from the manufacturer indicating the intention to submit an application for prequalification of the vaccine and of the acknowledgement from WHO of the acceptability for submission.
- 1.2.2 Agreed minutes of any pre-submission meetings between WHO/PQT and the applicant.

Items proposed for WHO-PQ module I

1.3

1.3 Site Master file

(consistent with WHO Guidance document: WHO Technical Report Series, No 961, Annex 14, 2011)

[http://apps.who.int/iris/bitstream/10665/44079/1/WHO TRS 961 eng.pdf](http://apps.who.int/iris/bitstream/10665/44079/1/WHO_TRS_961_eng.pdf)

Items proposed for WHO-PQ module I

1.4

1.4. Compliance information

- 1.4.1. Certificate of Establishment Licensing, if required by the National Regulatory Authority (NRA) of the country of manufacture.
- 1.4.2. Copy of GMP certificate issued by the NRA of the country of manufacture. Report (English translation if required) of the last GMP inspection (which included in its scope the production of the product submitted for prequalification) by the NRA of the country of manufacture.
- 1.4.3. Copy of marketing authorizations for all formulations and presentations of the vaccine submitted for prequalification.
- 1.4.4. Policy for assignment of date of manufacture of each component as well as the final product and diluents.
- 1.4.5 If the vaccine is a Genetically Modified Organism, supply a copy of the Environmental Risk Assessment.

Items proposed for WHO-PQ module I

1.5

1.5. Vaccine composition, presentations and scheduling information

- 1.5.1. Description of presentations available to UN agencies, including diluent (if applicable), combination products, forms, dose, sizes and type of containers and indicate Vaccine Vial Monitor (VVM) type and location.
- 1.5.2 Vaccine temperature stability profile
- Additional to stability information in 3.2.P.8, please provide any additional stability data required to support the assignment of VVM type or to support any on-label claim for elevated temperature storage according to Extended Controlled Temperature Conditions guideline (<http://who.int/biologicals/areas/vaccines/ectc/en/>).
- 1.5.3 Description of immunization /administration devices to be delivered with the vaccine
- 1.5.4 Recommended schedule and route of administration

Items proposed for WHO-PQ module I

1.5 (continued)

- 1.5.5 Samples of labels of primary containers and of secondary packaging for the product (including diluents. If applicable)
- 1.5.6. Samples of package inserts (in English) to be used for supply through UN agencies. After finalization of the review of the English version, translation to other languages required by UN procurement agencies (currently French, Portuguese, Russian and Spanish) should be provided.
- 1.5.7. Sample of lot summary protocol to be provided to UN agencies, in compliance with WHO-recommended format.

Items proposed for WHO-PQ module I

1.6

1.6. Supplemental pre-clinical and clinical Information (Pre and post marketing)

- 1.6.1 List of pre-clinical studies sponsored by applicant including any important conclusion(s) including and preclinical studies performed after initial licensure of product (and the reasons for these studies)
- 1.6.2 List of all clinical trials sponsored by the applicant relevant for the application which must contain:-
 - Location of study sites
 - Number and age of subject
 - Date of study
 - Evidence of registration in clinical registry (part of ICTRP)
 - Indication of whether the study complied with GCP
 - Rational of each study must be included in the summary table
 - Statement of final conclusions on safety and immunogenicity (and/or efficacy)

Items proposed for WHO-PQ module I

1.6

1.6. Supplemental pre-clinical and clinical Information (Pre and post marketing)

- 1.6.3 Final approved protocol by ERC and NRA
- 1.6.4 List of any clinical trials that are known to be currently ongoing not relevant to the current application including the summary of details of the study plan and expected date of result
- 1.6.5 List of other studies with applicant product for which the applicant is not the sponsor.

The applicant should make every effort to provide a list of all trials and, where applicable, observational studies relevant to the application that were not sponsored by the applicant but in which the product was evaluated. This list should be compiled from publications identified using an extensive literature search (details of which should be provided) and, in the case of co-licensure agreements, from any other company that holds a license for or a right to market the same product.

Items proposed for WHO-PQ module I

1.6 (continued)

1.6.6 Complementary Clinical summary supporting the use of the product worldwide by UN agencies

Provide a detailed summary and interpretation of the safety and efficacy data obtained from the pre-licensure clinical studies and all studies performed in the post-licensure period that support the current prescribing information. The summary should pay particular attention to any data that are relevant to the use of the product worldwide in WHO recommended schedules (e.g. co-administration of other vaccines). In the absence of such data, the summary should provide a preclinical and/or clinical justification for the extrapolation of the existing data to the likely circumstances of use after prequalification. This summary should complement, and not replace, the summary written by an independent clinical expert described in 1.6.8.

Items proposed for WHO-PQ module I

1.6.6 (continued)

- Consistency of manufacture for the vaccine lots used in clinical trials demonstrated and documented. Ideally three lots with the same formulation intended for marketing are used in late stages of the clinical development. However, a formal lot-to-lot consistency clinical study is considered on a case-by-case basis.
- Issues to be considered when the manufacturer performs a lot-to-lot consistency clinical study to fulfil the requirements a NRA. Vaccines used in clinical-consistency trials must have been manufactured at full production scale. The study should be designed (and analysed) as an equivalence trial and have pre-defined criteria and choice of parameters to conclude comparability.
- Changes to the batch size used to produce the clinical lots will require additional information to support the change (e.g. scale-up). Depending on the manufacturing consistency data, additional clinical studies to support comparability to the clinical lots may be required. These issues should be decided in consultation with the WHO Prequalification Secretariat.

Items proposed for WHO-PQ module I

1.6 (continued)

1.6.7 Assessment Report from the NRA(s)

- Whenever possible, the applicant should provide the clinical sections of the NRA assessment reports from the country of origin and/or country where the vaccine is initially licensed. Assessment reports for both initial licensure and any subsequent variations to the licence for changes relevant to clinical data are requested.

1.6.8. Clinical Independent expert report

- Provide an independent clinical expert report on the clinical studies (evidence of expertise and independence should be provided). If the application for prequalification is based on the extrapolation of the existing clinical data to the likely circumstances of use after prequalification, and if the data are old or there is a doubt regarding the ethical or regulatory oversight of the trial, the report should discuss the degree of compliance with WHO GCP recommendations and current guidance regarding preclinical and clinical trials with vaccines.

Items proposed for WHO-PQ module I

1.6 (continued)

1.6.9 Post marketing Safety documentation

Safety data should be submitted both in the case of the initial application for prequalification evaluation and for reassessment purposes.

- 1.6.9.1 Outline of the post-marketing pharmacovigilance plan for the product
- 1.6.9.2. Initial evaluation of vaccines that have been in the market for a long time or reassessment of already prequalified vaccines

Outline of the applicant's procedures for the collection, onward notification and assessment of adverse events.

Listing of all reported AEFIs for the vaccine in question in the last five years or since the last WHO reassessment. As far as possible from the reports received, applicants should list the type of reaction, lot number, date and place of immunization, patients' initials and age and, for immunization series, the dose number. A judgment of seriousness and whether or not the event was expected, should be included.

- 1.6.9.3 List of ongoing clinical studies for recently licensed vaccines.
This includes Phase IV studies or any active monitoring of safety profile of the vaccine.

Items proposed for WHO-PQ module I

1.7

- **1.7. Regulatory actions**
- 1.7.1 Information on refusals, withdrawals, suspensions, including those initiated by the manufacturer
- 1.7.2. List of lots rejected by an NRA, if applicable
- 1.7.3. Restrictions on distributions and recalls, including those initiated by the manufacturer
- 1.7.4. Clinical trial suspensions
- 1.7.5. Dosage or schedule changes since the initial marketing authorization
- 1.7.6. Changes in target populations since the initial marketing authorization

Items proposed for WHO-PQ module I

1.8

1.8. Distribution information

1.8.1. Quantity of finished product distributed in the domestic market and exported in the previous three years, by presentation.

Clearly indicate if numbers refer to vials or doses

1.8.2. List of countries where the product has received a Marketing Authorization, with an indication as to whether the product has been supplied in those countries

1.8.3. Description of recording system for distribution, including the release process by the manufacturer and by the NRA/NCL

1.8.4 Summarize the packaging procedures for international shipments for UN agencies and the validation (according to relevant, current WHO guidelines) of this packaging.

THANK YOU
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