GUIDELINES ON SUBMISSION OF DOCUMENTATION FOR PREQUALIFICATION OF FINISHED PHARMACEUTICAL PRODUCTS APPROVED BY STRINGENT REGULATORY AUTHORITIES

REVISED DRAFT FOR COMMENT

Please address any comments on this proposal by 15 September 2013 to Dr. S. Kopp, Medicines Quality Assurance Programme, World Health Organization, 1211 Geneva 27, Switzerland, fax: (+41 22) 791 4730 or e-mail: kopp@who.int with a copy to gaspardm@who.int.

We are sending out our working documents electronically only and they are also placed on the Medicines web site for comment. If you do not already receive our documents please let us have your e-mail address (to bonnyw@who.int) and we will add it to our electronic mailing list.

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### SCHEDULE FOR THE PROPOSED ADOPTION PROCESS OF DOCUMENT QAS/13.531:

**GUIDELINES ON SUBMISSION OF DOCUMENTATION FOR**

**PREQUALIFICATION OF FINISHED PHARMACEUTICAL PRODUCTS**

**APPROVED BY STRINGENT REGULATORY AUTHORITIES**

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INTRODUCTION

The World Health Organization (WHO) recognizes the scientific evaluation of finished pharmaceutical products (FPPs) by regulatory authorities which apply similarly stringent standards for quality, safety and efficacy as those recommended by WHO. Where an applicant and a stringent regulatory authority (SRA) \(^1\) (hereinafter called the reference SRA) can agree to share the following information on an FPP with WHO, WHO will consider such FPP for inclusion in the list of WHO-prequalified products, as and when information about such a product becomes available to WHO and when the applicant in question expresses interest in the product being prequalified by WHO.

These guidelines apply to both innovator \(^2\) and multisource (generic) FPPs approved by SRAs.

The following should be submitted:

1. A covering letter, which should include:

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\(^1\) Stringent regulatory authority (SRA): a regulatory authority which is: (a) a member of the International Conference on Harmonisation (ICH) (as specified on [www.ich.org](http://www.ich.org)); or (b) an ICH observer, being the European Free Trade Association (EFTA), as represented by Swiss Medic and Health Canada (as may be updated from time to time); or (c) a regulatory authority associated with an ICH member through a legally-binding, mutual recognition agreement including Australia, Iceland, Liechtenstein and Norway (as may be updated from time to time).

\(^2\) Generally the innovator pharmaceutical product is that which was first authorized for marketing, on the basis of documentation of quality, safety and efficacy (reference: WHO Technical Report Series, No. 937, 2006, Annex 7).
– a statement indicating that the information submitted is true and correct;
– a statement confirming that for WHO prequalification the FPP – including composition/formulation, strength, manufacturing, specifications, packaging, product information, etc., will at the time of submission and after prequalification in all respects be the same as the product registered with the reference SRA.

2. A copy of the marketing authorization issued by the reference SRA. If applicable, a copy of the latest renewal of the marketing authorization should also be provided.

3. A copy of the current WHO-type certificate of a pharmaceutical product issued and fully completed, including answers to each question, by the reference SRA.

4. The latest SRA approved product information (summary of product characteristics (SmPC), or an equivalent thereof, the patient information leaflet (PIL), or equivalent thereof, and the labelling). Provide a web link to the SRA-approved product information, preferably on the web site of the SRA itself, if available.

5. A list of the SRA-approved manufacturer(s) of the FPP, including manufacturers of intermediates, primary packaging sites and release-testing sites, with the physical address of the manufacturing site(s) (and unit if applicable).

6. A list of the SRA-approved manufacturer(s) of the active pharmaceutical ingredient(s) (API) used in the manufacture of the FPP, with the physical address of the manufacturing site(s) (and unit if applicable).

7. If available, a public assessment report, such as the Scientific Discussion of the European Public Assessment Report (EPAR), issued by the reference SRA. Assessment report(s) issued by the reference SRA and that are not publically available may be requested.

8. A tabular listing of the batches manufactured for the market of the reference SRA’s region/country since approval, but not exceeding the last five years. The table should
include at least the batch number, batch size (number of units), date of manufacture and pack type/size. Also provide a copy of the last product quality review (PQR).

9. A sample(s) of the product in market packaging(s). This should be provided with the submission to enable visual inspection thereof. Attach the respective certificate of analysis.

10. A copy of the currently approved FPP specifications (release and shelf-life), dated and signed by authorized personnel, with the analytical test procedures.

11. The quality information summary (QIS-SRA). The QIS-SRA template, available on the WHO Prequalification Programme website, should be fully completed and submitted with the application. The QIS-SRA provides a condensed summary of key information on the FPP as approved by the reference SRA at the time of application for prequalification of the FPP.

Please note that the submission must be in English, which includes certified English translations of product information and other documents if applicable. These documents should be made available as hard copies and electronically. The product information, in the case of English translations, should also be submitted as Word files.

WHO may request additional data, when considered necessary for the use of the product in populations/settings/regions relevant for prequalified products. WHO may also inspect the manufacturing site(s) in collaboration with the reference SRA, upon application or after prequalification of the FPP.

Variations to and renewal of the marketing authorization of an FPP that has been prequalified by WHO based on the approval by an SRA, remain the responsibility of the reference SRA.

Once the product has been prequalified, WHO should be provided with a copy of the regulatory acceptance letter of any changes to the key information on the FPP (as captured in the QIS-SRA), the product information, the FPP specification and test procedures, where appropriate, immediately after the variation has been approved by the reference SRA.
Changes to the QIS-SRA, the product information, the specification and test procedures should be shown in track-change mode in Word files. Other supportive information may be requested once the variation notification has been submitted.

WHO should be informed immediately in case of discontinuation of the product with the relevant SRA and of any critical safety or quality-related issues reported for batches on the market.

The preferred storage condition for WHO-prequalified products is “do not store above 30 °C”, based on demonstrated stability at long-term storage conditions of 30 °C/75% RH and at accelerated storage conditions (40 °C/75% RH). If this storage condition is not indicated on the SmPC, PIL and labels of the product, applicants are encouraged to apply for a variation in this respect with the relevant SRA. This could also be done after prequalification of the product.

Products that received United States FDA tentative approval or positive opinions under Article 58 of European Union Regulation (EC) No. 726/2004 or the Canada S.C. 2004, c. 23 (Bill C-9) procedure, are not within the scope of this guide. Such products can be co-listed on the WHO list of prequalified products in accordance with mutual agreements between WHO and these regulatory authorities.

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