Annex 5

Guidelines on submission of documentation for prequalification of finished pharmaceutical products approved by stringent regulatory authorities

Scope

The revision of the WHO *Guidelines on submission of documentation for prequalification of innovator finished pharmaceutical products approved by stringent regulatory authorities*[1] is extended to include not only innovator products, but also multisource products. The title is accordingly changed to *Guidelines on submission of documentation for prequalification of finished pharmaceutical products approved by stringent regulatory authorities*. These guidelines apply to both innovator[2] and multisource (generic) finished pharmaceutical products (FPPs) approved by SRAs.

Introduction

The World Health Organization (WHO) recognizes the scientific evaluation of finished pharmaceutical products (FPPs) by SRAs,[1] which apply similarly stringent standards for quality, safety and efficacy to those recommended by WHO. Where an applicant shares with WHO information on an FPP that has been approved by a stringent SRA (hereinafter called the reference SRA) and that is invited for prequalification, WHO will consider such FPPs 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.

---

[1] Stringent regulatory authority (SRA): a regulatory authority which is: (a) a member of the International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH) (as specified on www.ich.org); or (b) an ICH observer, being the European Free Trade Association (EFTA), as represented by Swissmedic 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 (WHO Technical Report Series, No. 937, 2006, Annex 7).

Guidelines on submission of documentation

The following should be submitted:

1. A covering letter, which should include:
   - a statement indicating that the information submitted is true and correct;
   - a statement confirming that for WHO prequalification, the FPP – including but not limited to composition/formulation, strength, manufacturing, specifications, packaging, product information – will, at the time of submission and after prequalification, in all respects be the same as the product registered with the reference SRA;
   - a statement indicating that the product is actually on the market of the reference SRA's country or region.
2. A copy of the marketing authorization, or the equivalent thereof, issued by the reference SRA to demonstrate that the product is registered or licensed in accordance with the reference SRA requirements. 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 website 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(s)) 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 that are not publicly available may be requested.

8. A tabular listing of the batches manufactured for the market of the reference SRA's region or country since approval or during the past five years, whichever is shorter. 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 most recent product quality review, prepared according to the requirements of the reference SRA.
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 or certified 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 (http://apps.who.int/prequal/), 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, and must include certified English translations of product information and other documents, if applicable. These documents should be made available electronically. The English language version of 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 or regions relevant for prequalified products. If necessary, this additional information, relevant for use of the product within the scope of the Prequalification Programme, will be included in the WHO public assessment report (WHOPAR) as a separate piece of information. Such information could be communicated to the reference SRA where appropriate. The SRA-approved product information will not be changed. WHO would normally not inspect the manufacturing site(s) of an SRA-approved product; however, there may be circumstances necessitating an inspection to be conducted 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 approval letter of any changes to the key information on the

FPP (as captured in the QIS-SRA), the product information, the revised QIS-SRA, 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. The clean version (in English language) of the updated product information should also be submitted. Other supporting 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% relative humidity (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 Food and Drug Administration (US-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 these guidelines. Such products can be co-listed on the WHO list of prequalified products in accordance with mutual agreements between WHO and these regulatory authorities.