Republic of the Philippines
Department of Health
FOOD AND DRUG ADMINISTRATION

FDA CIRCULAR
No. 2022-009

06 OCT 2022

SUBJECT : Implementing Guidelines of Administrative Order No. 2020-0044 "Adoption of the Collaborative Procedure for the Accelerated Registration of World Health Organization (WHO) – Prequalified Pharmaceutical Products and Vaccines"

I. BACKGROUND

Republic Act No. 3720, otherwise known as the "Food, Drugs and Devices, and Cosmetics Act", as amended by Republic Act No. 9711, otherwise known as the "Food and Drug Administration (FDA) Act of 2009", and its Implementing Rules and Regulations, declare that it is the policy of the state to ensure the safety, efficacy, and quality of drug supply in the country so as to protect the health of the Filipino people. The FDA, as the national regulatory authority (NRA) in the country, together with the Department of Health (DOH), are tasked to ensure that there is (1) a constant supply of drugs, including vaccines, and (2) facilitated access to safe, effective, and quality drugs.

In 2013, the World Health Organization (WHO) issued the initial collaborative review procedure under Annex 4 of WHO Technical Report Series (TRS) No. 981, 2013. The FDA signed up as a participating NRA to this collaborative procedure in 2015[1] and has since applied the procedure in the review of applications for initial registration of WHO-prequalified pharmaceutical products including vaccines. In 2016, a revised procedure was issued under Annex 8 of WHO TRS No. 996. This was adopted through Administrative Order (AO) No. 2020-0044 entitled Adoption of the Collaborative Procedure for the Accelerated Registration of World Health Organization (WHO) – Prequalified Pharmaceutical Products and Vaccines.

Given the current resource constraints affecting drug regulation, collaboration and regulatory convergence with international organizations such as the WHO are necessary.

This Circular is issued to guide and provide the activities that must be undertaken by the concerned stakeholders who will be affected by the implementation of the collaborative procedure for accelerated registration.

II. OBJECTIVES

This Circular aims to provide the implementing guidelines of AO No. 2020-0044 which adopted the collaborative procedure for accelerated registration of WHO-prequalified pharmaceutical products including vaccines.

III. SCOPE AND COVERAGE

This Circular covers applications for the registration and the post-approval change/s of WHO-prequalified pharmaceutical products including vaccines and biologicals as

1. *NMRAs Participating in the WHO Collaborative Procedure, https://extranet.who.int/pqweb/sites/default/files/documents/Country_List-21July2022.pdf*

defined in Section IV below, and shall apply to all FDA licensed drug manufacturers, traders, and distributors.

IV. DEFINITION OF TERMS

Collaborative procedure for accelerated registration of WHO-prequalified pharmaceutical products and vaccines, also referred to as **collaborative review procedure** or **collaborative registration procedure (CRP)**, refers to the procedure for collaboration between the WHO Prequalification Team (WHO/PQT) and interested NRAs in the assessment and accelerated national registration of WHO-prequalified pharmaceutical products and vaccine.[2]

National regulatory authority (NRA) is responsible for ensuring that products released for public distribution such as pharmaceuticals, biological products such as vaccines, and medical devices including test kits are evaluated properly and meet international standards of quality and safety and efficacy.[3]

WHO-prequalified pharmaceutical products including vaccines refers to those products which have undergone the WHO prequalification wherein comprehensive ongoing requirements stipulated by the WHO are applied to ensure that the products are safe, efficacious, appropriate, and meet stringent quality standards. The mission of WHO prequalification is to work in close cooperation with NRAs and other partner organizations to make quality priority medical products available for those who urgently need them.[4]

V. IMPLEMENTING DETAILS

A. General Guidelines
   1. The FDA, as a participating NRA for the CRP of WHO-prequalified pharmaceutical products including vaccines, hereby promulgates the implementing details herein for the submission of applications for registration and post-approval change/s through this procedure.
   2. The FDA adopts the WHO CRP of WHO-prequalified pharmaceutical products and vaccines as a registration pathway, consistent with Good Regulatory Practices. Notwithstanding this, the FDA retains its prerogative to use its own assessment of applications which may be combined with verification of compliance with relevant good practices by inspections and testing of product characteristics when applicable, and apply judgements that consider benefits and risks as it applies to the Philippine context.
   3. The applicants shall comply with the existing rules on filing and receiving pursuant to the latest issuances until such time that an automated system has been developed and launched.

B. Eligibility Criteria
   1. Only FDA-licensed drug manufacturers, traders, and distributors with WHO-prequalified pharmaceutical products and vaccines may apply for registration through this procedure.

2. *Annex 8, WHO-TRS No. 996, 2016 p.264*
3. *National Regulatory Agencies, https://www.who.int/southeastasia/activities/national-regulatory-agencies*
4. *Prequalification of Medical Products, https://extranet.who.int/pqweb/medicines/overview-history-mission*

2. Prior to the submission of the registration application with the FDA, the applicant shall ensure that the form provided under Appendix 2 of WHO TRS 996 Annex 8, *Consent of WHO prequalification holder for WHO to share information with the national regulatory authority confidentially under the Procedure* (Annex A), has been duly accomplished and submitted by the Manufacturer or Prequalification Holder to the WHO/PQT.
3. The eligible product shall be the same as the product prequalified by the WHO/PQT.
    a. All aspects of the drug product's quality, including but not limited to the formulation, manufacturing site/s, release and shelf-life specifications, primary packaging, and commercial presentation must be the same as those currently approved by the WHO/PQT at the time of submission.
    b. The proposed indication/s, dosing regimen/s, patient group/s, and/or direction/s for use should be the same as those approved by the WHO/PQT.
4. For post-approval change/s, only applications submitted to FDA not later than thirty (30) calendar days after approval of the change/s by WHO/PQT may be applied through CRP of WHO-prequalified pharmaceutical products and vaccines. Applications for post approval change/s which have not undergone WHO prequalification shall be evaluated through the regular FDA registration pathway following FDA Circular (FC) No. 2014-008, its amendment FC No. 2014-008-A, supplement FC No. 2016-017, and succeeding issuances for the same purposes.
5. The applicant may choose to avail of the CRP of WHO-prequalified pharmaceutical products and vaccines only if the application has not been applied through other types of facilitated review pathway (i.e. abridged review and verification review). If any of the requirements of CRP of WHO-prequalified pharmaceutical products and vaccines cannot be complied with, the application shall not be accepted and the applicant shall be advised to submit their application following the regular registration pathway.

C. Specific Guidelines
1. Regulatory time
    a. Within five (5) working days after acceptance of the application, the FDA shall notify the WHO/PQT of its consent to apply the procedure, and request for access to the product-specific information.
    The regulatory time is stopped (stop clock) until the WHO/PQT has provided the FDA with the requested product-related information and documentation, through the restricted-access website.
    b. The regulatory review time shall resume after the acceptance of the application and access to confidential information has been granted by the WHO/PQT and shall continue until the date of decision on the application. These shall be sixty (60) working days for the review of registration applications and twenty (20) working days for the review of post-approval change/s applications.
    The regulatory review time does not include the time granted to the applicant to complete lacking parts of the documentation, provide additional data, or respond to queries and clarifications found during the review as–communicated by FDA through an electronic notice of deficiencies. The regulatory time is stopped until necessary compliance documents have been submitted.

2. Applications for Registration
    a. Documentary requirements
        i. Accomplished application form as per FC No. 2014-003, as prescribed in FA No. 2022-0001, or any future issuance providing for its amendment, repeal, or modification;
        ii. Application dossier compliant with the existing requirements [e.g. Association of Southeast Asian Nations (ASEAN) – Common Technical Dossier (CTD) (ACTD), or International Council on Harmonization (ICH) – CTD (ICH-CTD)];
        iii. Appendix 3, Part A of WHO TRS 996 Annex 8, *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* (Annex B). In cases where the applicant company is not the original WHO PQ holder, the applicant company must submit an authorization letter that indicates agreement of the original WHO PQ holder, following the prescribed format in Appendix 3, Part A of WHO TRS 996 to the FDA;
        iv. Country specific requirements such as:
            (1) Current Good Manufacturing Practice (cGMP) Clearance of Foreign Drug Manufacturers issued by FDA;
            (2) Labeling materials consistent with country-specific requirements;
            (3) Stability studies conducted under Climatic Zone IVb (hot and very humid) for applicable products;
            (4) Tabulated summary of WHO/PQT post-approval change/s prior to the registration application through CRP of WHO-prequalified pharmaceutical products and vaccines, obtained by the manufacturer/prequalification holder;
            (5) Additional requirement for pharmaceutical products under Monitored Release (MR) registration status: Risk Management Plan (RMP) and RMP Philippine-Specific Annex, with Periodic Safety Update Reports (PSUR)/Periodic Benefit-Risk Evaluation Reports (PBRER), as applicable;
            (6) Representative sample with corresponding Certificate of Analysis (upon request of the evaluator); and
            (7) Additional requirements for vaccines and biological products:
                (a) Identification of the medical director who will monitor event/s reactions, and prepare appropriate report to be submitted to FDA;
                (b) Person/s responsible for production and control of the product (Name/s, Position, Department, and Sample of Signature);
                (c) Information/procedure on the numbering system of the lots or batches;
                (d) System for the reprocessing of the product in event of rejection of the lot or batch by the manufacturer's Quality Assurance/Quality Control;
                (e) Demonstration of lot-to-lot consistency from three (3) consecutive lots or batches;

(f) Description of the cold-chain procedures employed from the origin to the port of entry and storage in the Philippines (how and where);
(g) Summary Lot Protocol (for vaccines, toxoids and immunoglobulins only); and
(h) List of Countries where the product is already licensed and the date of approval (for vaccines only).
(i) Head-to-head comparability studies (for biosimilars only)

b. Processing
   i. Notification to the WHO and request for access to product-specific information.
   The FDA shall inform, within five (5) working days starting from acceptance of the application, the WHO/PQT and the applicant of its consent to apply the procedure through Appendix 3, Part B of WHO TRS 996 Annex 8, *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* (Annex C).
   ii. Review and evaluation.
      - Upon grant of access to the shared documents by WHO/PQT, the FDA is given a maximum of sixty (60) working days of regulatory time for the accelerated evaluation of the registration application using information provided by WHO, make a decision, and inform the applicant.
      - The information shared by WHO/PQT and the documents submitted by the applicant shall be reviewed and evaluated. Suitability of use under local conditions and regulatory requirements while relying on the prior assessment of the WHO/PQT shall be assessed.
      - Only the product details/aspects provided in the application shall be considered for evaluation and approval. The FDA shall consider the benefits and risks as they apply to the Philippine context based on the available data provided by the applicant.
   iii. Notification of WHO.
   Within twenty (20) working days of issuing a regulatory decision to the applicant, FDA shall inform WHO/PQT through Appendix 3, Part C of WHO TRS 996 Annex 8, *Notification of outcomes of national registration procedure by the NRA* (Annex D).

3. Post-Approval Changes
   a. Documentary requirements:
      i. Accomplished application form as per FC No. 2014-003, as prescribed in FA No. 2022-0001, subject to any future issuance providing for its amendment, repeal, or modification;
      ii. Letter of Request for Post-Approval Changes (Annex E);
      iii. The official post-prequalification variation approval document issued by the WHO/PQT; and
      iv. Documentary requirements following FC No. 2014-008 (Application Process and Requirements for Post-approval Changes of Pharmaceutical Products) and its amendment, FC No. 2014-008-A,

or any future issuance providing for its repeal, further amendment, or modification.

b. Processing

i. Notification to the WHO and request for access to product-specific information.

The FDA shall inform, within five (5) working days starting from acceptance of application, the WHO/PQT and the applicant of its consent to apply the procedure through Appendix 3, Part B of WHO TRS 996 Annex 8 (Annex C).

ii. Evaluation of application.

Upon grant of access to the shared documents by WHO/PQT, the FDA is given a maximum of twenty (20) working days of regulatory time starting from acceptance of application to evaluate the post-approval change/s application using information provided by WHO, make a decision, and inform the applicant.

iii. Notification of WHO

If the evaluation of the application for post-approval changes results in the FDA-registered product being no longer the same as the WHO-prequalified product, or if an approved change of the WHO-prequalified product is not followed by an application for post-approval change of the FDA-registered product and, as a consequence, the FDA-registered product is no longer the same, the FDA shall inform the WHO of the situation within twenty (20) working days of obtaining access to the information and documentation provided by WHO/PQT, by submitting the form reproduced in Appendix 4 of the WHO TRS 996 Annex 8, *Report on post-registration actions in respect of a product registered under the procedure* (Annex F), clearly specifying the deviations.

D. Fees

The appropriate fees as prescribed under existing regulations shall apply, including a Legal Research Fee (LRF) following A.O. No. 50 s. 2001, or any amendment or latest issuance thereafter.

VI. PENALTY CLAUSE

The applicable penalties under Republic Act No. 9711 and its Implementing Rules and Regulations shall apply for any violations of this Circular or of AO No. 2020-0044.

VII. IMPLEMENTATION REVIEW

FDA shall conduct a review of the implementation of this order after a period of five (5) years from its effectivity or earlier, as needed, i.e. to address any emerging process issues or changes in the WHO/PQT procedures.

VIII. SEPARABILITY CLAUSE

If any provision in this Circular, or application of such provision to any circumstances, is held invalid, the remainder of the provisions in this Circular shall not be affected.

IX. EFFECTIVITY DATE

This Circular shall take effect fifteen (15) calendar days after publication in one (1) newspaper of general circulation and upon filing with the University of the Philippines, Office of the National Administrative Register (ONAR).

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Director General