Republic of the Philippines
Department of Health
FOOD AND DRUG ADMINISTRATION

21 SEP 2021

FDA CIRCULAR
No. 2021-020

SUBJECT: Revised Post-Marketing Surveillance Requirements for New Drugs under Monitored Release

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I. BACKGROUND

On 15 March 1989, Department of Health Administrative Order (AO) No. 67 s. 1989 was issued to provide rules and regulations for the registration of pharmaceutical products. Under the said AO, a 'new drug' refers to a new chemical or structural modification of a tried and tested or established drug proposed to be used for a specific therapeutic indication, which has undergone adequate clinical pharmacology Phase I, II, and III studies but which needs further Phase IV clinical studies before it can be given regular 'initial' registration. Under Bureau Circular (BC) No. 5 s. 1997, new drugs will be required to pass a 3-year 'monitored-release' registration and complete the additional clinical study requirement described as "*an uncontrolled clinical study*" that are "*observational or non-experimental in nature*".

On 10 August 2006, AO No. 2006-0021 was issued to serve as a supplement to the abovementioned regulations. Under Section III, item 1, the FDA was authorized to "*adopt measures and methods that would address drug evaluation issues... to ensure adaptive efficiency of rules as a consequence of new technologies, doctrines, and harmonization of standards in the evaluation of new drugs that are intended to enter the Philippine market*". Further, under Section IV, item B, the FDA was authorized to allow applicants the use of other indicators/measures deemed reasonable to ensure safety, efficacy, and quality of new drugs.

In order to monitor the safety and efficacy of drug products, AO No. 2011-0009 was issued establishing the National Policy and Program on Pharmacovigilance. Subsequently, pharmacovigilance related guidelines were issued including FDA Circular (FC) No. 2013-003: Post Market Surveillance and Periodic Safety Update Report, FC No. 2013-004: Post Market Surveillance of Authorized Drug Products, and FC No. 2018-012: Rescinding FC No. 2013-004 and Instituting Post-Marketing Surveillance (PMS) Requirements for New Drugs under Monitored Release.

On 26 February 2020, FC No. 2020-003 was issued which provided clear guidelines for marketing authorization holders on their pharmacovigilance requirements, including those for new drugs under monitored release. While FC No. 2018-012 describes the guidelines on the Risk Management Plan (RMP) and the conduct of local Phase IV clinical trials for drug products that are classified as monitored release, it is imperative to update existing guidelines. The guidelines for the RMP are already updated in FC No. 2020-003 while guidelines for the local Phase IV clinical trial need further clarification, thus, this issuance.

With the changes in regulatory requirements brought about by new technologies, regulatory strengthening, and harmonization among countries, there is a need for FDA to align its drug registration requirements.

II. OBJECTIVE

This Circular is hereby issued to provide updated post-marketing surveillance (PMS) requirements for new drugs under monitored release, streamlined with AO No. 67 s. 1989, AO No. 2006-0021, and FC No. 2020-003.

III. SCOPE

This Circular shall apply to all applicants and marketing authorization holders (MAH) of new drugs, vaccines, and biologics under monitored release.

IV. GUIDELINES

A. PMS Requirements for New Drugs classified as Monitored Release

1. Consistent with Section V, letter E of FC No. 2020-003, all biological and new drug product applications shall have an accompanying RMP. The contents of the RMP shall comply with the requirements provided in such guideline.

2. The Pharmacovigilance (PV) Plan contained in the RMP shall discuss the plans of the applicant company to further characterize the safety concerns on the product. It shall identify, among others, the need to conduct additional PV activities, either as non-clinical studies, clinical trials, or non-interventional studies (including Phase IV clinical studies).

    a. If on the basis of available safety information, there is a need to conduct additional PV activity(ies), the requirements under Section V, letter E, item 4 of FC No. 2020-003 shall be complied with and provided by the applicant.

b. If on the basis of available safety information, there is no need to conduct such studies, appropriate justification (discussed under Section 3.2 RMP – Philippine-Specific Annex) shall be provided by the applicant.

3. Studies including Phase IV clinical studies which have been conducted or are proposed to be conducted in other countries as additional PV activity(ies) shall not be required to be duplicated to include the local study population, as such studies are already recognized by the FDA. However, if the FDA finds through its review that there are specific safety concerns affecting the Filipino population requiring further identification and characterization, the applicant shall be required to conduct, as appropriate, additional local PV activity(ies). The applicant shall be informed in writing of the safety concern(s) that prompted the FDA request.

4. Upon submission of the complete and correct requirements, review, and approval of the application, the FDA shall grant a marketing authorization (MA) distinctly indicating that the product is classified as a monitored release, with validity of five (5) years. After such validity, the MAH may apply for Initial Registration of the product.

5. Consistent with FC No. 2020-003, the MAH shall comply with all the requirements of pharmacovigilance stated therein.

B. Processing of Pending Applications

Previously submitted applications without upfront local phase IV clinical study protocol shall be evaluated by the FDA following the guidance above. If upon review it was found that the applicant satisfactorily met all the requirements, but the FDA deems it necessary to conduct additional local PV activity(ies), a post-approval letter shall be issued. Section IV, letter A, item 4 above shall apply.

Additional fees should be settled first by the MAH, per A.O. No. 50 s. 2001, to be granted with up to 5-year validity upon the approval of the application.

V. PENALTY CLAUSE

Any violation shall be grounds for filing appropriate administrative charges and/or imposition of administrative sanctions such as but not limited to imposition of fines, suspension, cancellation or revocation of any license, permit or registration issued by the FDA.

VI. SEPARABILITY CLAUSE

If any provisions 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.

VII. REPEALING CLAUSE

FC No. 2018-012 is hereby rescinded. Provisions in previous circulars and memoranda that are inconsistent with this Circular are hereby repealed or modified accordingly.

VIII. EFFECTIVITY

This Circular shall take effect fifteen (15) days after publication in a newspaper of general circulation and/or the Official Gazette and filing of the required copies with the University of the Philippines - Office of the National Administrative Register.

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