[FDA CIRCULAR NO. 2014-008, April 01, 2014]

APPLICATION PROCESS AND REQUIREMENTS FOR POST-APPROVAL CHANGES OF PHARMACEUTICAL PRODUCTS

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I. BACKGROUND/RATIONALE

Prior to the full adoption and implementation of the Association of Southeast Asian Nations (ASEAN) Common Technical Dossier (ACTD) and Common Technical Requirements (ACTR), Marketing Authorization Holders (MAHs) referred to the provisions of PSD Memo 02-05, "Updated Checklist of Requirements for Request of Amendment and Revalidation", FDA Circular No. 2011-002, "Application for Revisions/Updates in the Package Insert, Patient Leaflet Information, Prescribing Information, Core Data Sheet, and Basic Succinct Statement", and other national regulations to support post-approval changes to their registered products. However, the said regulations proved to be insufficient to cover many other possible post-approval change scenarios. Therefore, a more comprehensive guideline is needed to address in detail the requirements and applications process for post-approval changes.

The ASEAN Variation Guideline (AVG) for Pharmaceutical Products was established (a) to take into account technical and scientific progress of pharmaceutical products after they have been approved for marketing by the Drug Regulatory Authority (DRA) and (b) to support any post-approval changes that may be required to enable the pharmaceutical products to be manufactured. The AVG is intended to provide supportive information on the requirements for submission of variation application to implement a change to a pharmaceutical product. Although the AVG is a comprehensive guideline, some post-approval changes not covered here are subject to country-specific requirements.

In line with the provisions of Administrative Order No. 2013-021, "Adoption of the Association of Southeast Asian Nations (ASEAN) Common Technical Dossier (ACTD) and Common Technical Requirements (ACTR) for the Registration of Pharmaceutical Products for Human Use", the Food and Drug Administration hereby promulgates the revised application process and requirements for instituting Post-Approval Changes (PACs) to registered pharmaceutical products, which shall cover both the AVG and country-specific requirements.

II. OBJECTIVES

The objectives of this Circular are:

1) To promulgate the revised requirements in instituting post-approval changes to registered pharmaceutical products, incorporating the AVG and countryspecific requirements; and

2) To provide the application process for instituting post-approval changes.

III. SCOPE

This Circular shall apply to all manufacturers, traders and distributors (e.g. exporters, importers and wholesalers) of pharmaceutical products covered by ACTD/ACTR. In the absence of a more specific regulation, the provisions of this Circular also serve as the requirements for manufacturers, traders and distributors of single and multi-component vitamin and mineral products, vaccines and biologics, traditional medicines, over-the-counter preparations, household remedies, medical gases, and veterinary products.

IV. IMPLEMENTING DETAILS

A. *Eligibility*

Any MAH of a pharmaceutical product may apply for PAC, provided:

1. The MAH has a valid License to Operate (LTD); and
2. The pharmaceutical product is covered by a valid Certificate of Product Registration (CPR); provided further, that if the CPR has already expired, the pharmaceutical product is applied for regular renewal registration.

B. *Classification*

Post-approval changes may be classified according to reference:

(a) ASEAN Variation Guideline

- Major Variation (MaV)
- Minor Variation (MiV)

  - Prior Approval (MiV-PA)
  - Notification (MiV-N)

(b) Country-Specific Requirements

- MaV

  - Additional route of administration
  - Change of manufacturing site (same subsidiary) of the drug product

- MiV-PA

  - Change of capsule color
  - Change of brand name
  - Change of MAH
  - Reclassification (ex. Over-the-counter [OTC] to Prescription, OTC to household remedy [HR])

- Such other PACs not covered by AVG