Republic of the Philippines
Department of Health
FOOD AND DRUG ADMINISTRATION

12 August 2013

FDA CIRCULAR
No. **2013-018**

SUBJECT: **Adoption of the International Conference on Harmonization (ICH) Safety and Efficacy Guidelines**

I. BACKGROUND

Pursuant to Administrative Order No. 2013-0021 known as the "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," enhancing public health and welfare by providing faster access to and increasing availability of quality, safe, and efficacious pharmaceutical products has been promulgated.

The ASEAN Consultative Committee for Standards and Quality – Pharmaceutical Product Working Group (ACCSQ-PPWG), comprised of delegates and observers from the drug regulatory authorities and pharmaceutical industry associations of the 10 Member States, has for years been taking the lead role in developing efficient schemes to harmonize pharmaceutical regulations across the Southeast Asian region with the aim of eliminating technical barriers to trade posed by such regulations, and realize the ASEAN Free Trade Area (AFTA) by 2015.

At its 20th Meeting held in Bali, Indonesia last May 2013, the ACCSQ-PPWG endorsed the adoption of selected International Conference on Harmonization (ICH) Safety and Efficacy Guidelines. The Philippines and Thailand, as the lead countries for Safety and Efficacy guidelines, respectively, presented the updated list of ICH Guidelines that ASEAN considers for adoption based on the following criteria:

(a) ICH guidelines that have reached step 5 and implemented by all three regions will be considered for adoption as ASEAN Guidelines on Safety and/or Efficacy; and
(b) ICH guidelines that have reached step 5 but have not yet been implemented by all 3 member countries/regions shall be considered as references only.

II. RATIONALE

Increasing international harmonization of technical requirements to ensure the efficient and cost-effective development and registration of quality, safe, and efficacious pharmaceutical products is the primary objective of the ICH. This goal is centered toward the promotion of public health, prevention of unnecessary duplication of clinical trials in humans, and minimization of the use of animal testing without compromising safety and efficacy. Despite current global challenges arising from trade and economic and public health, there has been significant progress made in pharmaceutical harmonization.

ICH Safety Guidelines are intended to provide recommendations on which investigational pharmaceutical products warrant carcinogenicity, genotoxicity, and reprotoxicity testing and studies. Furthermore, these guidelines provide assistance for the thorough evaluation and review of information on carcinogenicity studies, genotoxicity studies, toxicokinetics and pharmacokinetics, toxicity testing, reproductive toxicology, biotechnological products, pharmacology studies, immunotoxicology studies, nonclinical evaluation for anticancer pharmaceuticals, and photosafety evaluation.

ICH Efficacy Guidelines are concerned with the design, conduct, safety, and reporting of clinical trials and encompass types of medicines derived from biotechnological processes and pharmacogenetic/pharmacogenomic techniques to produce better targeted medicines. These guidelines are intended to provide assistance for the evaluation and review of information on clinical safety, clinical study reports, dose-response studies, ethnic factors, Good Clinical Practices (GCP), clinical trials, clinical evaluation by therapeutic category, clinical evaluation, and pharmacogenomics.

III. OBJECTIVES

This Circular is hereby issued to formally adopt the ICH Safety and Efficacy Guidelines in order to align the current national requirements with international standard best practices.

IV. SCOPE

This Circular shall cover Phases I, II, and III clinical trial applications of investigational pharmaceutical products.

For purposes of this Circular, an investigational pharmaceutical product shall mean any substance or combination of substances presented as having properties for treating or preventing disease in human beings or may be administered to human beings either with a view to restoring, correcting or modifying physiological functions by exerting a pharmacological, immunological or metabolic action, or to making a medical diagnosis. These include new

chemical entities under the investigational phase of drug development as well as existing drug preparations already in the market seeking approval for new or additional therapeutic indications.

V. IMPLEMENTING DETAILS

The following ICH technical guidelines are hereby adopted:

Safety Guidelines

		Date Finalized
S1A	Guideline on the Need for Carcinogenicity Studies of Pharmaceuticals	Nov. 1995
S1B	Testing for Carcinogenicity of Pharmaceuticals	July 1997
S1C(R2)	Dose Selection for Carcinogenicity Studies of Pharmaceuticals	Mar. 2008
S2(R1)	Guidance on Genotoxicity Testing and Data Interpretation for Pharmaceuticals Intended for Human Use	Nov. 2011
S3A	Note for Guidance on Toxicokinetics: The Assessment of Systemic Exposure in Toxicity Studies	Oct. 1994
S3B	Pharmacokinetics: Guidance for Repeated Dose Tissue Distribution Studies	Oct. 1994
S4	Duration of Chronic Toxicity Testing in Animals (Rodent and Non Rodent Toxicity Testing)	Sept. 1998
S5(R2)	Detection of Toxicity to Reproduction for Medicinal Products and Toxicity to Male Fertility	Nov. 2000
S6(R1)	Preclinical Safety Evaluation of Biotechnology-Derived Pharmaceuticals	June 2011
S7A	Safety Pharmacology Studies for Human Pharmaceuticals	Nov. 2000
S7B	The Non-clinical Evaluation of the Potential for Delayed Ventricular Repolarization (QT Interval Prolongation) by Human Pharmaceuticals	May 2005
S8	Immunotoxicity Studies for Human Pharmaceuticals	Sept. 2005
S9	Nonclinical Evaluation for Anticancer Pharmaceuticals	Oct. 2009
M3(R2)	Guidance on Nonclinical Safety Studies for the Conduct of Human Clinical Trials and Marketing Authorization for Pharmaceuticals	June 2009

Efficacy Guidelines

		Date Finalized
E1	The Extent of Population Exposure to Assess Clinical Safety for Drugs Intended for Long-Term Treatment of Non-Life-Threatening Conditions	Oct. 1994
E2A	Clinical Safety Data Management: Definitions and Standards for Expedited Reporting	Oct. 1994
E2D	Post-Approval Safety Data Management: Definitions and Standards for Expedited Reporting	Nov. 2003
E2E	Pharmacovigilance Planning	Nov. 2004
E2F	Development Safety Update Report	Aug. 2010
E3	Structure and Content of Clinical Study Reports*	Nov. 1995
E4	Dose-Response Information to Support Drug Registration	Mar. 1994
E5(R1)	Ethnic Factors in the Acceptability of Foreign Clinical Data*	Mar. 1998
E6(R1)	Good Clinical Practice: Consolidated Guideline	May 1996
E7	Studies in Support of Special Populations: Geriatrics*	June 1993
E8	General Considerations for Clinical Trials	July 1997
E9	Statistical Principles for Clinical Trials	Feb. 1998
E10	Choice of Control Group and Related Issues in Clinical Trials	July 2000
E11	Clinical Investigation of Medicinal Products in the Pediatric Population	July 2000
E12	Principles for Clinical Evaluation of New Antihypertensive Drugs	Mar. 2000
E14	The Clinical Evaluation of QT/QTc Interval Prolongation and Proarrhythmic Potential for Non-Antiarrhythmic Drugs*	May 2005
E15	Definitions for Genomic Biomarkers, Pharmacogenomics, Pharmacogenetics, Genomic Data and Sample Coding Categories	Nov. 2007
E16	Biomarkers Related to Drug or Biotechnology Product Development: Context, Structure and Format of Qualification Submissions	Aug. 2010

**This contains an additional guidance in the form of Questions and Answers (Q&As).*

VI. REPEALING CLAUSE/SEPARABILITY CLAUSE

Provisions on previous circulars and memoranda that are inconsistent with this issuance are hereby withdrawn, repealed, and/or revoked accordingly. In case any part, term or provision of this Circular is declared contrary to law or unconstitutional, other provisions which are not affected remain in force and effect.

VII. EFFECTIVITY

This Circular shall take effect immediately.

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