4160-01-P

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. FDA-2011-D-0082]

Guidance for Industry on Clinical Pharmacogenomics: Premarket Evaluation in Early-Phase Clinical Studies and Recommendations for Labeling; Availability

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice.

SUMMARY: The Food and Drug Administration (FDA) is announcing the availability of a guidance for industry entitled "Clinical Pharmacogenomics: Premarket Evaluation in Early-Phase Clinical Studies and Recommendations for Labeling." This guidance is intended to assist the pharmaceutical industry and other investigators engaged in new drug development in evaluating how variations in the human genome, specifically DNA sequence variants, could affect a drug's pharmacokinetics (PK), pharmacodynamics (PD), efficacy, or safety. The guidance provides recommendations on when and how genomic principles should be considered and applied in early-phase clinical studies to address questions arising during drug development and regulatory review.

DATES: Submit either electronic or written comments on Agency guidances at any time.

ADDRESSES: Submit written requests for single copies of this guidance to the Division of Drug Information, Center for Drug Evaluation and Research, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 51, rm. 2201, Silver Spring, MD 20993-0002; or the Office of Communication, Outreach and Development (HFM-40), Center for Biologics Evaluation and Research (CBER), Food and Drug Administration, 1401 Rockville Pike, Rockville, MD 20852-

1448. The guidance may also be obtained by mail by calling CBER at 1-800-835-4709 or 301-827-1800. Send one self-addressed adhesive label to assist that office in processing your requests. See the SUPPLEMENTARY INFORMATION section for electronic access to the guidance document.

Submit electronic comments on the guidance to http://www.regulations.gov. Submit written comments to the Division of Dockets Management (HFA-305), Food and Drug Administration, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852.

FOR FURTHER INFORMATION CONTACT:

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Center for Biologics Evaluation and Research (HFM-17),

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1401 Rockville Pike, suite 200N,

Rockville, MD 20852-1448,

301-827-6210.

SUPPLEMENTARY INFORMATION:

I. Background

FDA is announcing the availability of a guidance entitled "Clinical Pharmacogenomics: Premarket Evaluation in Early-Phase Clinical Studies and Recommendations for Labeling." This guidance should help sponsors, researchers, and other interested persons engaged in new drug development in evaluating how variations in the human genome, specifically DNA sequence variants, could affect a drug's pharmacokinetics, pharmacodynamics, efficacy, or safety. The guidance provides recommendations on when and how genomic principles should be considered and applied in early-phase clinical studies to address questions arising during drug development and regulatory review. The guidance does not address trial design or statistical analysis considerations for later-phase randomized controlled clinical trials that are intended to draw definitive conclusions about treatment effects in a genomic subgroup or codevelopment of a drug and in vitro diagnostic. Rather, the considerations here are more relevant for exploratory and observational studies intended to generate genomic hypotheses that may then be tested in confirmatory trials.

Drug development is commonly described in "phases" (21 CFR 312.21). The first two phases provide initial information about safety and efficacy, and ideally examine a broad range of doses, so that the larger, later adequate, and well-controlled trials (phase 3) that are needed to support marketing approval can be efficiently designed. Across the drug development continuum, genomic data may be used for several purposes, including: (1) Identifying the basis for PK outliers and intersubject variability in clinical response; (2) ruling out the role of polymorphic pathways as clinically significant contributors to variable PK, PD, efficacy, or safety; (3) estimating the magnitude of potential drug-drug interactions; (4) investigating the

molecular or mechanistic basis for lack of efficacy or occurrence of adverse reactions; and (5) designing clinical trials to test for greater effects in specific subgroups (i.e., use in study enrichment strategies).

On February 18, 2011 (76 FR 9583), FDA issued a draft of this guidance to solicit comments from the public. After carefully reviewing received comments and in light of increased regulatory experience and the evolution of the science, FDA has revised the guidance. In addition to making clarifying changes, FDA added content to describe when pharmacogenomics (PGx) studies are warranted, including circumstances when full sample ascertainment is expected to evaluate a specific hypothesis. In addition, a number of topics were further elaborated, including targeted sample collection, sample retention, genotyping approaches, pooled analyses, dedicated prospective PGx studies, genetic substudies, and safety PGx.

This guidance is being issued consistent with FDA's good guidance practices regulation (21 CFR 10.115). The guidance represents the Agency's current thinking on conducting pharmacogenomic studies in early-phase clinical studies. It does not create or confer any rights for or on any person and does not operate to bind FDA or the public. An alternative approach may be used if such approach satisfies the requirement of the applicable statutes and regulations.

II. Paperwork Reduction Act of 1995

This guidance refers to previously approved collections of information that are subject to review by the Office of Management and Budget (OMB) under the Paperwork Reduction Act of 1995 (44 U.S.C. 3501-3520). The collections of information have been approved under OMB control numbers 0910-0014 and 0910-0572.

III. Comments

Interested persons may submit either electronic comments regarding this document to http://www.regulations.gov or written comments to the Division of Dockets Management (see ADDRESSES). It is only necessary to send one set of comments. Identify comments with the docket number found in brackets in the heading of this document. Received comments may be seen in the Division of Dockets Management between 9 a.m. and 4 p.m., Monday through Friday, and will be posted to the docket at http://www.regulations.gov.

IV. Electronic Access

Persons with access to the Internet may obtain the document at either http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/Guidances, http://www.fda.gov/BiologicsBloodVaccines/GuidanceComplianceRegulatoryInformation/default.htm or http://www.regulations.gov.

Dated: January 22, 2013.

Leslie Kux,

Assistant Commissioner for Policy.

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