

manufacturers and clinical investigators involved in the development of therapeutic protein products for human use in evaluating and reducing the risk of adverse events caused by immune responses to these products. The guidance: (1) Outlines and recommends adoption of a risk-based approach to evaluating and mitigating potential immune responses to therapeutic protein products that may affect their safety and efficacy, (2) describes various product- and patient-specific factors that affect the immunogenicity of or immune responses to therapeutic protein products and provides recommendations pertaining to each factor that may reduce the likelihood that an immune response will be generated to the product, (3) offers a series of recommendations for risk mitigation in the clinical phase of development of therapeutic protein products, (4) provides supplemental information on the diagnosis and management of particular adverse consequences of immune responses to therapeutic protein products, and (5) discusses briefly the use of animal studies and the conduct of comparative immunogenicity studies.

In the **Federal Register** of February 11, 2013 (78 FR 9702), FDA announced the availability of the draft guidance of the same title dated February 2013. FDA received numerous comments on the draft guidance, and those comments were considered as the guidance was finalized. In addition, editorial changes were made to improve clarity.

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 immunogenicity assessments for therapeutic protein products. 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 requirements of the applicable statutes and regulations.

II. 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>.

III. Electronic Access

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

Dated: August 8, 2014.

Leslie Kux,

Assistant Commissioner for Policy.

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DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. FDA-2014-N-1108]

Revised Draft Guidance for Industry on Clinical Pharmacology Labeling for Human Prescription Drug and Biological Products—Considerations, Content, and Format; Availability

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice.

SUMMARY: The Food and Drug Administration (FDA) is announcing the availability of a revised draft guidance for industry entitled “Clinical Pharmacology Labeling for Human Prescription Drug and Biological Products—Considerations, Content, and Format.” This draft guidance is one of a series of guidance documents intended to assist applicants in complying with FDA regulations on the content and format of labeling for human prescription drug and biological products. The guidance describes the recommended information to include in the *Clinical Pharmacology* section of labeling that pertains to the safe and effective use of human prescription drug and biological products. This revised draft guidance replaces the 2009 draft guidance for industry entitled “Clinical Pharmacology Section of Labeling for Human Prescription Drug and Biological Products—Content and Format.”

DATES: Although you can comment on any guidance at any time (see 21 CFR 10.115(g)(5)), to ensure that the Agency considers your comment on this draft guidance before it begins work on the final version of the guidance, submit either electronic or written comments on the draft guidance by October 14, 2014.

ADDRESSES: Submit written requests for single copies of the draft 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 Office of Communication, Outreach, and Development, Center for Biologics Evaluation and Research, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 71, Rm. 3128, Silver Spring, MD 20993. Send one self-addressed adhesive label to assist that office in processing your requests. See the **SUPPLEMENTARY INFORMATION** section for electronic access to the draft guidance document.

Submit electronic comments on the draft 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: Lei Zhang, Office of Clinical Pharmacology, Office of Translational Sciences, Center for Drug Evaluation and Research, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 51, Rm. 3177, Silver Spring, MD 20993-0002, 301-796-5008 or Stephen Ripley, Center for Biologics Evaluation and Research, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 71, Rm. 7301, Silver Spring, MD 20993-0002, 240-402-7911.

SUPPLEMENTARY INFORMATION:

I. Background

In the **Federal Register** of January 24, 2006 (71 FR 3922), FDA published a final rule entitled “Requirements on Content and Format of Labeling for Human Prescription Drug and Biological Products” to revise the Agency's previous regulations on labeling (effective June 30, 2006). The final rule, commonly referred to as the Physician Labeling Rule (PLR), is designed to make information in prescription drug labeling easier for health care practitioners to access, read, and use, thereby increasing the extent to which practitioners rely on labeling for prescribing decisions. In the **Federal Register** of March 3, 2009 (74 FR 9250), FDA announced the availability of a draft guidance for industry entitled “Clinical Pharmacology Section of Labeling for Human Prescription Drug and Biological Products—Content and Format” as one of a series of guidance documents intended to assist applicants in complying with FDA regulations on the content and format of labeling for human prescription drug and biological

products. The 2009 draft guidance provided guidance on the *Clinical Pharmacology* section of the prescription drug labeling under the PLR.

II. Revised Draft Guidance

FDA is announcing the availability of a draft guidance entitled “Clinical Pharmacology Labeling for Human Prescription Drug and Biological Products—Considerations, Content, and Format,” which is a revision of the 2009 draft guidance. The revised draft guidance provides clarifications of recommendations in the 2009 draft guidance based on consideration of public comments on the 2009 draft guidance and the Agency’s increased regulatory experience implementing the PLR. This draft guidance provides clarity on the information that should be included in section 12 *Clinical Pharmacology* and provides guidance on the inclusion of clinical recommendations based on clinical pharmacology findings in other sections of the labeling.

A. Clinical Pharmacology Section of Labeling

The draft guidance is intended to assist applicants in preparing the *Clinical Pharmacology* section of product labeling to meet the requirements of FDA regulations (21 CFR 201.57(c)(13)). The draft guidance is also intended to ensure consistency, as appropriate, in labeling of the *Clinical Pharmacology* section for all prescription drug products approved by FDA.

The draft guidance outlines the use of subsections, headings, and subheadings to provide organization to the *Clinical Pharmacology* section. The draft guidance also emphasizes the importance of providing variability measures related to pharmacokinetic measures and parameters, pharmacodynamic measures, and other clinical pharmacology study results.

This draft guidance provides a general framework and set of recommendations that should be adapted to specific drugs and their conditions of use. Not all of the information identified in this draft guidance for inclusion in the *Clinical Pharmacology* section of product labeling will be applicable for every drug. For the purposes of this notice, all references to drugs include both human drugs and biological products unless otherwise specified.

B. Cross-Referencing of Clinical Pharmacology Information

Detailed information on clinical pharmacology topics is included in the

Clinical Pharmacology section, while other sections of labeling contain summary information and clinical recommendations that may be related to clinical pharmacology information. Optimal pharmacotherapy is driven by an understanding of a drug product’s clinical pharmacology as well as the clinical context in which the drug will be used. Important clinical pharmacology attributes to consider in therapeutic decisionmaking include, but are not limited to, drug mechanism of action, pharmacodynamic effects (e.g., on target, on pathway, and off target/pathway), and pharmacokinetic properties in a variety of settings and specific populations. Clinical pharmacology information collected throughout a drug product’s life can contribute to the product’s labeling. Specifically, FDA considers what clinical pharmacology information can be directly translated to patient care management and provides specific recommendations that should be included in relevant sections of the labeling. Examples include strategies for dose selection, therapeutic individualization, and adverse reaction risk minimization. In these cases, supportive information (i.e., the clinical pharmacology basis for the specific recommendation) is expected to be concise to enable unambiguous application to patient care. Occasionally, depending on the complexity of the patient care recommendations, it can be appropriate to provide expanded versions of this supportive information in the labeling. The reason for including this information is to provide sufficient detail for the health care provider to determine the relevance of the information for a given patient or clinical scenario; this information is typically included in the *Clinical Pharmacology* section of product labeling and is the main focus of the guidance.

This draft guidance is being issued consistent with FDA’s good guidance practices regulation (21 CFR 10.115). The draft guidance, when finalized, will represent the Agency’s current thinking on inclusion of clinical pharmacology information in section 12 *Clinical Pharmacology* of product labeling. 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.

III. Paperwork Reduction Act of 1995

This revised draft 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 in 21 CFR 201.56 and 201.57 have been approved under OMB control number 0910–0572; the collections of information related to pharmacogenomic data have been approved under OMB control number 0910–0557.

IV. 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>.

V. Electronic Access

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Dated August 8, 2014.

Leslie Kux,

Assistant Commissioner for Policy.

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DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. FDA–2011–D–0689]

De Novo Classification Process (Evaluation of Automatic Class III Designation); Draft Guidance for Industry and Food and Drug Administration Staff; Availability

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice.

SUMMARY: The Food and Drug Administration (FDA) is announcing the availability of the draft guidance entitled “De Novo Classification Process