4160-01-P

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. FDA-2010-D-0616]

Guidance for Industry on Codevelopment of Two or More New Investigational Drugs for Use in Combination; Availability

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice.

SUMMARY: The FDA is announcing the availability of a guidance for industry entitled "Codevelopment of Two or More New Investigational Drugs for Use in Combination." This guidance is intended to assist sponsors in the codevelopment of two or more investigational drugs that have not been previously developed for any indication (i.e., "new investigational drugs") to be used in combination to treat a disease or condition. The guidance provides recommendations and advice on how to address certain scientific and regulatory issues that may arise during codevelopment of two or more new investigational drugs. It is not intended to apply to development of combinations of already approved drugs or to development of a single new investigational drug to be used in combination with an already approved drug or drugs. The guidance is not intended to apply to biological products regulated by the Center for Biologics Evaluation and Research or medical devices.

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

ADDRESSES: Submit written requests for single copies of the 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. 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 See the SUPPLEMENTARY INFORMATION section for electronic access to the draft guidance document.

Submit electronic comments on the draft guidance to http://www.regulations.gov.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: Colleen Locicero, Center for Drug Evaluation and Research, Food and Drug Administration, Bldg. 22, rm. 4216, 10903 New Hampshire Ave., Silver Spring, MD 20993-0002, 301-796-1114.

SUPPLEMENTARY INFORMATION:

I. Background

The FDA is announcing the availability of a guidance for industry entitled "Codevelopment of Two or More New Investigational Drugs for Use in Combination." The guidance is intended to assist sponsors in the codevelopment[1] of two or more investigational drugs that have not been previously developed for any indication (i.e., "new investigational drugs") to be used in combination to treat a disease or condition. Recent scientific advances have increased our understanding of the pathophysiological processes that underlie many complex diseases, such as cancer, cardiovascular disease, and infectious diseases. This increased understanding has provided further impetus to develop therapeutic approaches that rely primarily

[1] The term codevelopment as used in the guidance refers to the concurrent development of two or more new investigational drugs that are intended to be used in combination to treat a disease or condition. A sponsor may elect to codevelop two or more new investigational drugs intended to be marketed as individual agents or to be used in combination as a fixed-combination or copackaged drug.

or exclusively on combinations of drugs directed at multiple therapeutic targets to improve treatment response and minimize development of resistance. In settings in which combination therapy provides significant therapeutic advantages, there is growing interest in the development of combinations of investigational drugs not previously developed for any indication.

Because existing developmental and regulatory pathways focus primarily on assessment of the safety and effectiveness of a single new investigational drug acting alone, or in combination with an already approved drug, FDA believes guidance is needed to assist sponsors in the codevelopment of two or more new investigational drugs. This guidance is intended to describe a high-level, generally applicable approach. It describes the criteria for determining when codevelopment may be an appropriate option, makes recommendations about nonclinical and clinical development strategies, and addresses certain regulatory process issues. The guidance is not intended to apply to biological products regulated by the Center for Biologics Evaluation and Research or medical devices.

In the Federal Register of December 15, 2010 (75 FR 78259), FDA announced the availability of a draft of this guidance. FDA received a number of comments, including multiple comments seeking clarification of the scope and applicability of the guidance, the criteria for determining when codevelopment is appropriate, the evidentiary expectations for the individual new investigational drugs and their use in combination, and the types of regulatory submissions needed for codeveloped products. FDA has carefully considered these comments. The final guidance clarifies the criteria for determining when codevelopment is appropriate and elaborates on strategies for clinical development of the individual new investigational drugs and their use in combination. it also provides a detailed discussion of considerations for submitting

Investigational New Drug Applications (INDs) and New Drug Applications (NDAs) . The final guidance clarifies the scope of the drugs to which it applies; it uses the term "new investigational drug" to refer to drugs that have not previously been developed for any indication. We have also revised the title of the guidance to reflect this term.

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 development of two or more new investigational drugs for use in combination. 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. The Paperwork Reduction Act of 1995

This guidance refers to previously approved collections of information found in FDA regulations. These collections of information 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 part 312 have been approved under OMB control number

0910-0014. The collections of information in 21 CFR part 314 have been approved under OMB control number 0910-0001. 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 in 21 CFR 310.305 and 314.80 have been approved under OMB control number 0910-0230. The collections of information in 21 CFR 208.20, 208.24, and 314.70(b) have been approved under OMB control number 0910-0393.

IV. Electronic Access

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

Dated: June 11, 2013.

Leslie Kux,

Assistant Commissioner for Policy.

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