4164-01-P

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. FDA-2015-D-3399]

Recommendations for Microbial Vectors Used for Gene Therapy; Draft Guidance for Industry; Availability

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice.

SUMMARY: The Food and Drug Administration (FDA or Agency) is announcing the availability of a draft document entitled "Recommendations for Microbial Vectors Used for Gene Therapy; Draft Guidance for Industry." The draft guidance provides investigational new drug application (IND) sponsors, with recommendations concerning IND submissions for microbial vectors used for gene therapy (MVGTs) in early-phase clinical trials. MVGTs meet the regulatory definition of "biological product", when such products are applicable to the prevention, treatment, or cure of a disease or condition of human beings. The draft guidance focuses on the chemistry, manufacturing, and control (CMC) information that sponsors should submit in an IND for MVGTs and provides an overview of preclinical and clinical considerations for these products. The draft guidance, when finalized, will supplement the guidance entitled, "Guidance for FDA Reviewers and Sponsors: Content and Review of Chemistry, Manufacturing, and Control (CMC) Information for Human Gene Therapy Investigational New Drug Applications (INDs)," dated April 2008 (April 2008 Guidance).

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comment on any guidance at any time (see 21 CFR 10.115(g)(5)), to ensure that the Agency considers your comment on this draft guidance before it begins work on the final version of the guidance, submit either electronic or written comments on the draft guidance by [INSERT DATE 60 DAYS AFTER DATE OF PUBLICATION IN THE FEDERAL REGISTER].

ADDRESSES: You may submit comments as follows:

Electronic Submissions

Submit electronic comments in the following way:

- Federal eRulemaking Portal: http://www.regulations.gov. Follow the instructions for submitting comments. Comments submitted electronically, including attachments, to http://www.regulations.gov will be posted to the docket unchanged. Because your comment will be made public, you are solely responsible for ensuring that your comment does not include any confidential information that you or a third party may not wish to be posted, such as medical information, your or anyone else's Social Security number, or confidential business information, such as a manufacturing process. Please note that if you include your name, contact information, or other information that identifies you in the body of your comments, that information will be posted on http://www.regulations.gov.
- If you want to submit a comment with confidential information that you do not wish to be made available to the public, submit the comment as a written/paper submission and in the manner detailed (see "Written/Paper Submissions" and "Instructions").

Written/Paper Submissions

Submit written/paper submissions as follows:

- Mail/Hand delivery/Courier (for written/paper submissions): Division of Dockets Management (HFA-305), Food and Drug Administration, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852.
- For written/paper comments submitted to the Division of Dockets Management, FDA will post your comment, as well as any attachments, except for information submitted, marked and identified, as confidential, if submitted as detailed in "Instructions."

Instructions: All submissions received must include the Docket No. FDA-2015-D-3399 for "Recommendations for Microbial Vectors Used for Gene Therapy; Draft Guidance for Industry." Received comments will be placed in the docket and, except for those submitted as "Confidential Submissions" publicly viewable at http://www.regulations.gov or at the Division of Dockets Management between 9 a.m. and 4 p.m., Monday through Friday.

- Confidential Submissions--To submit a comment with confidential information that you do not wish to be made publicly available, submit your comments only as a written/paper submission. You should submit two copies total. One copy will include the information you claim to be confidential with a heading or cover note that states "THIS DOCUMENT CONTAINS CONFIDENTIAL INFORMATION". The Agency will review this copy, including the claimed confidential information, in its consideration of comments. The second copy, which will have the claimed confidential information redacted/blacked out, will be available for public viewing and posted on http://www.regulations.gov. Submit both copies to the Division of Dockets Management. If you do not wish your name and contact information to be made publicly available, you can provide this information on the cover sheet and not in the body of your comments and you must identify this information as

"confidential." Any information marked as "confidential" will not be disclosed except in accordance with 21 CFR 10.20 and other applicable disclosure law. For more information about FDA's posting of comments to public dockets, see 80 FR 56469, September 18, 2015, or access the information at: http://www.fda.gov/regulatoryinformation/dockets/default.htm.

Docket: For access to the docket to read background documents or the electronic and written/paper comments received, go to http://www.regulations.gov and insert the docket number, found in brackets in the heading of this document, into the "Search" box and follow the prompts and/or go to the Division of Dockets Management, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852.

Submit written requests for single copies of the draft guidance to the Office of Communication, Outreach and Development, Center for Biologics Evaluation and Research (CBER), Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 71, rm. 3128, Silver Spring, MD 20993-0002. Send one self-addressed adhesive label to assist the office in processing your requests. The draft guidance may also be obtained by mail by calling CBER at 1-800-835-4709 or 240-402-8010. See the SUPPLEMENTARY INFORMATION section for electronic access to the draft guidance document.

FOR FURTHER INFORMATION CONTACT: Paul E. Levine, Jr., 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

FDA is announcing the availability of a draft document entitled, "Recommendations for Microbial Vectors Used for Gene Therapy; Draft Guidance for Industry." The draft guidance provides IND sponsors, with recommendations concerning IND submissions for MVGTs in early-phase clinical trials. MVGTs meet the definition of "biological product" in section 351(i) of the Public Health Service Act (42 U.S.C. 262), when such products are applicable to the prevention, treatment, or cure of a disease or condition of human beings. MVGTs include bacterial vectors such as Salmonella, Listeria, or E. coli genetically modified to express human tumor antigens, cytokines, growth factors, enzymes, therapeutic proteins, or nucleotides. MVGTs may also be generated by the modification (deletion, truncation, or point mutation) of chromosomal or episomal genes and by the insertion of foreign genetic material into the chromosome, or into naturally occurring episomes; or by the introduction of one or more plasmids. The MVGTs may consist of microbes that are either live, replication restricted (division under specific growth conditions), capable of limited or no cell divisions, or killed, or a combination of these forms. The guidance focuses on the CMC information that sponsors should submit in an IND for MVGTs and provides an overview of preclinical and clinical considerations for these products.

In the Federal Register of April 10, 2008 (73 FR 19511), FDA announced the availability of the April 2008 Guidance. In that guidance, FDA provided sponsors of a human gene therapy IND, including those with combination products that contain a human gene therapy biological product with a drug or device as part of the final product, with recommendations on CMC information that is to be included in an original IND. That guidance also provided instruction to

FDA CMC reviewers about the information to record and assess as part of an IND review. The draft guidance, when finalized, will supplement the April 2008 Guidance.

The draft guidance is being issued consistent with FDA's good guidance practices regulation (21 CFR 10.115). The draft guidance, when finalized, will represent FDA's current thinking on recommendations for MVGTs. It does not establish 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

The draft 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 parts 211, 610, and 312 have been approved under OMB control numbers 0910-0139 and 0910-0114, respectively.

III. Electronic Access

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

Dated: October 7, 2015.

Leslie Kux,

Associate Commissioner for Policy

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