

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 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 guidance document.

FOR FURTHER INFORMATION CONTACT:

Shruti Modi, 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

The Orphan Drug Act of 1983 (Pub. L. 97-414) defines a rare disease as a disease or condition that affects fewer than 200,000 persons in the United States. Since most rare diseases have no approved therapies, there is a significant unmet need for effective treatments. However, developing safe and effective products to treat rare diseases can be challenging. For example, it may be more difficult to find and recruit such patients into clinical trials, and many rare diseases exhibit a number of variations or subtypes. Consequently, patients may have highly diverse clinical manifestations and rates of disease progression with unpredictable clinical courses. Despite these challenges, GT-related research and development continue to grow at a rapid rate, with several products advancing in clinical development.

FDA is announcing the availability of a document entitled “Human Gene Therapy for Rare Diseases; Guidance for Industry.” This guidance provides recommendations to stakeholders developing human GT product intended to treat a rare disease in adult and/or pediatric patients regarding the manufacturing, preclinical, and clinical trial design issues for all phases of the clinical development program. Such information is intended to assist sponsors in designing clinical development programs for such products, where there may be limited study population size and potential feasibility and safety issues as well as issues relating to the interpretability of bioactivity/efficacy outcomes that may be unique to rare diseases or to the nature of the GT product itself.

In the **Federal Register** of July 12, 2018 (83 FR 32303), FDA announced the availability of the draft guidance of the

same title. FDA received several comments on the draft guidance and those comments were considered as the guidance was finalized. The guidance announced in this notice finalizes the draft guidance dated July 2018.

Elsewhere in this issue of the **Federal Register**, FDA is announcing the availability of two other human gene therapy guidance documents entitled “Human Gene Therapy for Hemophilia; Guidance for Industry” and “Human Gene Therapy for Retinal Disorders; Guidance for Industry.”

This guidance is being issued consistent with FDA’s good guidance practices regulation (21 CFR 10.115). The guidance represents the current thinking of FDA on recommendations for stakeholders developing human GT products for retinal disorders affecting adult and pediatric patients. It does not establish any rights for any person and is not binding on FDA or the public. You can use an alternative approach if it satisfies the requirements of the applicable statutes and regulations.

II. Paperwork Reduction Act of 1995

This guidance refers to previously approved collections of information subject to review by the Office of Management and Budget (OMB) under the Paperwork Reduction Act of 1995 (44 U.S.C. 3501-3521). The collections of information in 21 CFR part 50 have been approved under OMB control number 0910-0755; the collections of information in 21 CFR part 58 have been approved under OMB control number 0910-0119; 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 601 have been approved under OMB control number 0910-0338; the collections of information in the guidance entitled “Expedited Programs for Serious Conditions—Drugs and Biologics” have been approved under OMB control number 0910-0765; and the collections of information in the guidance entitled “Formal Meetings Between the FDA and Sponsors or Applicants” have been approved under OMB control number 0910-0429.

III. Electronic Access

Persons with access to the internet may obtain the guidance at either <https://www.fda.gov/vaccines-blood-biologics/guidance-compliance-regulatory-information-biologics/biologics-guidances> or <https://www.regulations.gov>.

Dated: January 27, 2020.

Lowell J. Schiller,

Principal Associate Commissioner for Policy.

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DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. FDA-2018-D-2173]

Long Term Follow-Up After Administration of Human Gene Therapy Products; Guidance for Industry; Availability

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice of availability.

SUMMARY: The Food and Drug Administration (FDA or Agency) is announcing the availability of a final guidance entitled “Long Term Follow-Up After Administration of Human Gene Therapy Products.” The guidance document provides sponsors, who are developing a human gene therapy (GT) product, recommendations regarding the design of long term follow-up (LTFU) observational studies for the collection of data on delayed adverse events following administration of a GT product. This guidance finalizes the draft guidance of the same title dated July 2018 and supersedes the document entitled “Guidance for Industry: Gene Therapy Clinical Trials—Observing Subjects for Delayed Adverse Events” dated November 2006. This guidance also supplements the guidance entitled “Testing of Retroviral Vector-Based Human Gene Therapy Products for Replication Competent Retrovirus during Product Manufacture and Patient Follow-up; Guidance for Industry.”

DATES: The announcement of the guidance is published in the **Federal Register** on January 30, 2020.

ADDRESSES: You may submit either electronic or written comments on Agency guidances at any time as follows:

Electronic Submissions

Submit electronic comments in the following way:

- *Federal eRulemaking Portal:* <https://www.regulations.gov>. Follow the instructions for submitting comments. Comments submitted electronically, including attachments, to <https://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 <https://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):* Dockets Management Staff (HFA-305), Food and Drug Administration, 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852.

- For written/paper comments submitted to the Dockets Management Staff, 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-2018-D-2173 for "Long Term Follow-Up After Administration of Human Gene Therapy Products." Received comments will be placed in the docket and, except for those submitted as "Confidential Submissions," publicly viewable at <https://www.regulations.gov> or at the Dockets Management Staff 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 <https://www.regulations.gov>. Submit both copies to the Dockets Management Staff. 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: <https://www.gpo.gov/fdsys/pkg/FR-2015-09-18/pdf/2015-23389.pdf>.

Docket: For access to the docket to read background documents or the electronic and written/paper comments received, go to <https://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 Dockets Management Staff, 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852.

You may submit comments on any guidance at any time (see 21 CFR 10.115(g)(5)).

Submit written requests for single copies of the 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 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 guidance document.

FOR FURTHER INFORMATION CONTACT:

Jessica Walker Udechukwu, 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 document entitled "Long Term Follow-Up After Administration of Human Gene Therapy Products; Guidance for Industry." This guidance provides a brief introduction of the product characteristics, patient-related factors, and the preclinical and clinical data that should be considered when assessing the need for LTFU observations for your GT product. This guidance also describes the Agency's current recommendations for the conduct of LTFU studies, specifically the information/data to support a

sponsor's rationale for the duration and design of a LTFU protocol when clinical trials are initiated. Also included this guidance are GT product-specific clinical considerations for monitoring subjects under a LTFU protocol and recommendations on patient monitoring for licensed GT products. This guidance is intended to supersede the guidance entitled "Guidance for Industry: Gene Therapy Clinical Trials—Observing Participants for Delayed Adverse Events" dated November 2006. This guidance supplements the guidance entitled "Testing of Retroviral Vector-Based Human Gene Therapy Products for Replication Competent Retrovirus during Product Manufacture and Patient Follow-up; Draft Guidance for Industry".

In the **Federal Register** of July 12, 2018 (83 FR 32311), FDA announced the availability of the draft guidance of the same title dated July 2018. FDA received several comments on the draft guidance and those comments were considered as the guidance was finalized. The guidance announced in this notice finalizes the draft guidance dated July 2018.

This guidance is being issued consistent with FDA's good guidance practices regulation (21 CFR 10.115). The guidance represents the current thinking of FDA on "Long Term Follow-Up After Administration of Human Gene Therapy Products." It does not establish any rights for any person and is not binding on FDA or the public. You can use an alternative approach if it satisfies the requirements of the applicable statutes and regulations.

II. 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. 3501-3521). The collections of information in 21 CFR parts 50 and 56 have been approved under OMB control number 0910-0755; the collections of information in 21 CFR part 58 have been approved under OMB control number 0910-0119; and the collections of information in 21 CFR part 312 have been approved under OMB control number 0910-0014.

III. Electronic Access

Persons with access to the internet may obtain the guidance at either <https://www.fda.gov/vaccines-blood-biologics/guidance-compliance-regulatory-information-biologics/>

biologics-guidances or <https://www.regulations.gov>.

Dated: January 27, 2020.

Lowell J. Schiller,

Principal Associate Commissioner for Policy.

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DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. FDA-2018-D-2236]

Human Gene Therapy for Retinal Disorders; Guidance for Industry; Availability

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice of availability.

SUMMARY: The Food and Drug Administration is announcing the availability of a final guidance entitled “Human Gene Therapy for Retinal Disorders; Guidance for Industry.” The final guidance provides recommendations to stakeholders developing human gene therapy (GT) products for retinal disorders affecting adult and pediatric patients. The guidance focuses on issues specific to GT products for retinal disorders and provides recommendations related to product development, preclinical testing, and clinical trial design for such GT products. The guidance announced in this notice finalizes the draft guidance of the same title dated July 2018.

DATES: The announcement of the guidance is published in the **Federal Register** on January 30, 2020.

ADDRESSES: You may submit either electronic or written comments on Agency guidances at any time as follows:

Electronic Submissions

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- **Federal eRulemaking Portal:** <https://www.regulations.gov>. Follow the instructions for submitting comments. Comments submitted electronically, including attachments, to <https://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 <https://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):** Dockets Management Staff (HFA-305), Food and Drug Administration, 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852.

- For written/paper comments submitted to the Dockets Management Staff, 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-2018-D-2236 for “Human Gene Therapy for Retinal Disorders; Guidance for Industry.” Received comments will be placed in the docket and, except for those submitted as “Confidential Submissions,” publicly viewable at <https://www.regulations.gov> or at the Dockets Management Staff 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 <https://www.regulations.gov>. Submit both copies to the Dockets Management Staff. 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: <https://www.govinfo.gov/content/pkg/FR-2015-09-18/pdf/2015-23389.pdf>.

Docket: For access to the docket to read background documents or the electronic and written/paper comments received, go to <https://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 Dockets Management Staff, 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852.

You may submit comments on any guidance at any time (see 21 CFR 10.115(g)(5)).

Submit written requests for single copies of the 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 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 guidance document.

FOR FURTHER INFORMATION CONTACT:

Jenifer Stach, 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 document entitled “Human Gene Therapy for Retinal Disorders; Guidance for Industry.” This guidance provides recommendations to stakeholders developing human GT products for retinal disorders affecting adult and pediatric patients. These disorders vary in etiology, prevalence, diagnosis, and management, and include genetic as well as age-related diseases. These disorders manifest with central or peripheral visual impairment and often with progressive visual loss. This guidance focuses on issues specific to GT products for retinal disorders and provides recommendations related to product development, preclinical testing, and clinical trial design for such GT products.