

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, 240-402-7500.

**FOR FURTHER INFORMATION CONTACT:**

Jeanmaire Hryshko, Center for Food Safety and Applied Nutrition, Food and Drug Administration, 5001 Campus Dr., College Park, MD 20740, 240-402-2371; or Philip Chao, Center for Food Safety and Applied Nutrition, Office of Regulations and Policy (HFS-024), Food and Drug Administration, 5001 Campus Dr., College Park, MD 20740, 240-402-2378.

**SUPPLEMENTARY INFORMATION:** In the **Federal Register** of February 23, 2023 (88 FR 11449), we published a notice of availability for a draft guidance entitled "Labeling of Plant-Based Milk Alternatives and Voluntary Nutrient Statements; Draft Guidance for Industry; Availability; Agency Information Collection Activities; Proposed Collection; Comment Request." This action opened a docket with a 60-day comment period.

We have received requests for a 90-day extension of the comment period for the draft guidance. We have concluded that it is reasonable to reopen the comment period for 90 days, until July 31, 2023. We are reopening the comment period because the request for an extension of the comment period arrived too late for us to extend the comment period. We believe that an additional 90 days allows adequate time for interested persons to submit comments.

Dated: April 26, 2023.

**Lauren K. Roth,**

*Associate Commissioner for Policy.*

[FR Doc. 2023-09176 Filed 4-28-23; 8:45 am]

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**DEPARTMENT OF HEALTH AND HUMAN SERVICES**

**Food and Drug Administration**

[Docket No. FDA-2021-D-0875]

**S12 Nonclinical Biodistribution Considerations for Gene Therapy Products; International Council for Harmonisation; 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 for industry entitled "S12 Nonclinical Biodistribution Considerations for Gene Therapy Products." The guidance was prepared under the auspices of the International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH). The final guidance provides harmonized recommendations for the conduct and overall design of nonclinical biodistribution (BD) studies for gene therapy (GT) products. The recommendations in the guidance endeavor to facilitate the development of investigational GT products, while avoiding unnecessary use of animals, in accordance with the 3Rs (reduce/refine/replace) principles. The final guidance replaces the draft guidance entitled "S12 Nonclinical Biodistribution Considerations for Gene Therapy Products" issued on September 9, 2021.

**DATES:** The announcement of the guidance is published in the **Federal Register** on May 1, 2023.

**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-2021-D-0875 for "S12 Nonclinical Biodistribution Considerations for 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, 240-402-7500.

- *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, 240-402-7500.

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

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, 10001 New Hampshire Ave., Hillandale Building, 4th Floor, Silver Spring, MD 20993-0002, or 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 that 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:

**Regarding the guidance:** Alyssa Galaro, Center for Biologics Evaluation and Research, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 71, Rm. 6260, Silver Spring, MD, 20993-0002, 301-796-6589.

**Regarding the ICH:** Jill Adleberg, Center for Drug Evaluation and Research, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 51, Rm. 6364, Silver Spring, MD 20993-0002, 301-796-5259, [Jill.Adleberg@fda.hhs.gov](mailto:Jill.Adleberg@fda.hhs.gov).

#### SUPPLEMENTARY INFORMATION:

##### I. Background

FDA is announcing the availability of a guidance for industry entitled "S12 Nonclinical Biodistribution Considerations for Gene Therapy Products." The guidance was prepared under the auspices of ICH. ICH has the mission of achieving greater regulatory harmonization worldwide to ensure that safe, effective, high-quality medicines are developed, registered, and

maintained in the most resource-efficient manner.

By harmonizing the regulatory requirements in regions around the world, ICH guidelines enhance global drug development, improve manufacturing standards, and increase the availability of medications. For example, ICH guidelines have substantially reduced duplicative clinical studies, prevented unnecessary animal studies, standardized the reporting of important safety information, and standardized marketing application submissions.

The six Founding Members of the ICH are FDA; the Pharmaceutical Research and Manufacturers of America; the European Commission; the European Federation of Pharmaceutical Industries Associations; the Japanese Ministry of Health, Labour, and Welfare; and the Japanese Pharmaceutical Manufacturers Association. The Standing Members of the ICH Association include Health Canada and Swissmedic. ICH membership continues to expand to include other regulatory authorities and industry associations from around the world (refer to <https://www.ich.org/>).

ICH works by engaging global regulatory and industry experts in a detailed, science-based, and consensus-driven process that results in the development of ICH guidelines. The regulators around the world are committed to consistently adopting these consensus-based guidelines, realizing the benefits for patients and for industry.

As a Founding Regulatory Member of ICH, FDA plays a major role in the development of each of the ICH guidelines, which FDA then adopts and issues as guidance for industry. FDA's guidance documents do not establish legally enforceable responsibilities. Instead, they describe the Agency's current thinking on a topic and should be viewed only as recommendations, unless specific regulatory or statutory requirements are cited.

In the **Federal Register** of September 9, 2021 (86 FR 50536), FDA published a notice announcing the availability of a draft guidance entitled "S12 Nonclinical Biodistribution Considerations for Gene Therapy Products." The notice gave interested persons an opportunity to submit comments by November 8, 2021.

After consideration of the comments received and revisions to the guideline, a final draft of the guideline was submitted to the ICH Assembly and endorsed by the regulatory agencies on March 14, 2023.

This guidance finalizes the draft guidance of the same title issued on

September 9, 2021. The guidance is intended to promote harmonization of recommendations for the BD assessment for investigational GT products and facilitate a more efficient and timely nonclinical development program. The revisions to the draft guidance aimed to clarify key elements of the BD assessment by providing additional information on selecting dose levels and identifying a biologically relevant model. Additional details were provided on what product and study characteristics should be considered to determine if previous BD data can be leveraged.

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 "S12 Nonclinical Biodistribution Considerations for 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 contains no collection of information. Therefore, clearance by the Office of Management and Budget under the Paperwork Reduction Act of 1995 is not required.

##### III. Electronic Access

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

Dated: April 26, 2023.

**Lauren K. Roth,**

*Associate Commissioner for Policy.*

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