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4164-01-P

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. FDA-2023-D-4299]

Potency Assurance for Cellular and 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 titled "Potency Assurance for Cellular and Gene Therapy Products." The guidance document provides recommendations to help assure the potency of human cellular therapy or gene therapy (CGT) products at all stages of the product lifecycle. FDA is recommending a comprehensive approach to potency assurance of CGT products that is grounded in quality risk management. For investigational products, we describe how to progressively implement a strategy for potency assurance during product development and provide additional considerations to help assure the potency of products that are undergoing rapid clinical development. For licensed products, we describe requirements for potency assurance, including testing required for lot release assays. The guidance announced in this notice finalizes the draft guidance of the same title issued on December 28, 2023.

DATES: The announcement of the guidance is published in the *Federal Register* on [INSERT DATE OF PUBLICATION IN THE *FEDERAL REGISTER*].

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-2023-D-4299 for "Potency Assurance for Cellular and 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 the guidance to the Center for Biologics Evaluation and Research (CBER), Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 71, Rm. 3103, 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: Myrna Hanna, Center for Biologics Evaluation and Research, Food and Drug Administration, 240-402-7911.

SUPPLEMENTARY INFORMATION:

I. Background

FDA is announcing the availability of a document titled "Potency Assurance for Cellular and Gene Therapy Products." This guidance provides recommendations to help assure the potency of human CGT products that are regulated as biological products under section 351 of the Public Health Service Act (42 U.S.C. 262).

This final guidance provides recommendations for developing a science- and risk-based strategy to help assure the potency of human CGT products. A potency assurance strategy is a multifaceted approach that reduces risks to the potency of a product through: (1) manufacturing process design, (2) manufacturing process control, (3) material control, (4) in-process testing, and (5) potency lot release assays. The goal of a potency assurance strategy is to ensure that every lot of a product released will have the specific ability or capacity to achieve the intended therapeutic effect.

The guidance emphasizes that potency assays and their corresponding acceptance criteria should be designed to make meaningful contributions to potency assurance by reducing risks to product potency. We provide illustrative examples of approaches to potency assay development that are grounded in quality risk management. Due to the diversity of CGT products and the product-specific nature of potency assays, the recommendations in this final guidance regarding the selection and design of potency assays are necessarily general.

In the *Federal Register* of December 28, 2023 (88 FR 89707), FDA announced the availability of the draft guidance of the same title dated December 28, 2023. FDA received several comments on the draft guidance and those comments were considered as the guidance

was finalized. A summary of changes includes: advice on integration of potency assurance into existing quality systems, expanded risk assessment guidance, advice on regulatory engagement pathways, and additional practical examples with refined terminology throughout. In addition, editorial changes were made to improve clarity. The guidance announced in this notice finalizes the draft guidance dated December 28, 2023.

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 "Potency Assurance for Cellular and 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

While this guidance contains no collection of information, it does refer to previously approved FDA collections of information. The previously approved collections of information are subject to review by the Office of Management and Budget (OMB) under the Paperwork Reduction Act of 1995 (PRA) (44 U.S.C. 3501-3521). The collections of information in 21 CFR parts 210 and 211 pertaining to manufacturing, processing, packing, and holding of finished pharmaceuticals and biological products for human use have been approved under OMB control number 0910-0139. The collections of information in 21 CFR 312.23(a)(7)(i) and (ii) pertaining to submission of chemistry, manufacturing, and control information sufficient to assure the proper identification, quality, purity, and strength of an investigational drug in an IND application, and 21 CFR 312.47(a) pertaining to meetings between FDA and sponsors, including pre-IND meetings, have been approved under OMB control number 0910-0014. The collections of information in 21 CFR 600.14(b) pertaining to biological product deviation reporting is included in OMB control number 0910-0458. The collections of information in 21 CFR part 601 pertaining to biologics license applications have been approved under OMB control number 0910-0338.

III. Electronic Access

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

Grace R. Graham,

Deputy Commissioner for Policy, Legislation, and International Affairs.

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