

- Subpart C—Quality Assurance—212.20
- Subpart D—Facilities and Equipment—212.30
- Subpart E—Control of Components, Containers, and Closures—212.40
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Records must be maintained at the PET drug production facility or another location that is reasonably accessible to responsible officials of the production facility and to employees of FDA designated to perform inspections. All records, including those not stored at the inspected establishment, must be legible, stored to prevent deterioration or loss, and readily available for review and copying by FDA employees. All

records and documentation referenced in this part must be maintained for a period of at least 1 year from the date of final release, including conditional final release, of a PET drug product.

The regulations contain what we believe are the minimum standards for quality production of PET drugs at all types of PET drug production facilities. These CGMP requirements are designed according to the unique characteristics of PET drugs, including their short half-lives and because most PET drugs are produced at locations close to the patients to whom the drugs are administered. We have also taken into account that time spent on recording procedures, processes, and specifications may be somewhat higher in the year in which records are first established and correspondingly lower in subsequent years, when only updates and revisions will be required.

We have also issued Agency guidance entitled, “PET Drugs—Current Good

Manufacturing Practice (CGMP),” (December 2009), available for download from our website at <https://www.fda.gov/regulatory-information/search-fda-guidance-documents/pet-drug-products-current-good-manufacturing-practice-cgmp>. The guidance document communicates FDA’s thinking concerning compliance with the CGMP regulations. The guidance document addresses resources, procedures, and documentation for all PET drug production facilities, academic and commercial. In some cases, the guidance provides practical examples of methods or procedures that PET drug production facilities can use to comply with the CGMP requirements.

Respondents to the information collection include are PET production facilities, including academic or hospital facilities as well as commercial facilities.

We estimate the burden of the collection of information as follows:

TABLE 1—ESTIMATED ANNUAL RECORDKEEPING BURDEN¹

Required recordkeeping activity; 21 CFR 212	Number of recordkeepers	Records per recordkeeper	Total annual records	Average burden per record	Total hours
Academia, Small Firms, & High-Risk Component Manufacture Records.	76	~824.26	62,644	~.81 (50 minutes)	50,862
Corporate Firm Records	91	~1,447.10	131,686	~.35 (21 minutes)	45,728
External Control Testing Laboratory Records.	23	145	3,335	~.67 (40 minutes)	2,243
Total			197,665		98,833

¹ There are no capital costs or operating and maintenance costs associated with this collection of information.

TABLE 2—ESTIMATED ANNUAL DISCLOSURE BURDEN

Notifications required under 21 CFR 212.70	Number of respondents	Number of disclosures per respondent	Total annual disclosures	Average burden per disclosure	Total hours
Sterility Testing Failures	11	3	33	2.5	83

¹ There are no capital costs or operating and maintenance costs associated with this collection of information.

² Totals have been rounded to the nearest whole number.

³ Two reports are sent to FDA per incident, and one notification is sent to the receiving site.

Our estimated burden for the information collection reflects an overall increase of 14,348 hours and a corresponding increase of 12,851 records. We attribute this adjustment to an increase in our estimate of the number of small firms due to new facilities.

Grace R. Graham,

Deputy Commissioner for Policy, Legislation, and International Affairs.

[FR Doc. 2025–18620 Filed 9–24–25; 8:45 am]

BILLING CODE 4164-01-P

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. FDA–2025–D–3403]

Innovative Designs for Clinical Trials of Cellular and Gene Therapy Products in Small Populations; Draft Guidance for Industry; Availability

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice of availability.

SUMMARY: The Food and Drug Administration (FDA, the Agency, or

we) is announcing the availability of a draft document entitled “Innovative Designs for Clinical Trials of Cellular and Gene Therapy Products in Small Populations.” The draft guidance document provides recommendations to sponsors who are planning clinical trials of cell and gene therapy (CGT) products intended for use in a disease or condition that affects a small population, generally one that meets the definition of a rare disease or condition under section 526(a)(2) of the FD&C Act (21 U.S.C. 360bb(a)(2)). It describes FDA requirements and provides considerations for the use of various

clinical trial designs and endpoints to generate clinical evidence to support product licensure. The recommendations are intended for sponsors developing CGTs intended for use in small populations to leverage the use of innovative trial designs to simultaneously expedite drug development and generate data necessary to demonstrate substantial evidence of effectiveness.

DATES: Submit either electronic or written comments on the draft guidance by November 24, 2025 to ensure that the Agency considers your comment on this draft guidance before it begins work on the final version of the guidance.

ADDRESSES: You may submit comments on any guidance 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-

2025-D-3403] for "Innovative Designs for Clinical Trials of Cellular and Gene Therapy Products in Small Populations; Draft 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, 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 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. 3103, 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 or emailing industry.biologics@fda.hhs.gov. See the **SUPPLEMENTARY INFORMATION** section for electronic access to the draft guidance document.

FOR FURTHER INFORMATION CONTACT: Janet Goldberg, Center for Biologics Evaluation and Research, Food and Drug Administration, 240-402-7911.

SUPPLEMENTARY INFORMATION:

I. Background

FDA is announcing the availability of a draft document entitled "Innovative Designs for Clinical Trials of Cellular and Gene Therapy Products in Small Populations; Draft Guidance for Industry." The draft guidance document provides recommendations to sponsors who are planning clinical trials of CGT products intended for use in a disease or condition that affects a small population, generally one that meets the definition of a rare disease or condition under section 526(a)(2) of the FD&C Act (21 U.S.C. 360bb(a)(2)). It describes FDA requirements and provides considerations for the use of various clinical trial designs and endpoints to generate clinical evidence to support product licensure. The guidance expands on principles described in FDA's existing guidance documents related to this topic, by providing additional recommendations for the planning, design, conduct, and analysis of cell and gene therapy trials to facilitate FDA's assessment of product effectiveness. The recommendations are intended for sponsors developing CGTs intended for use in small populations to leverage the use of innovative trial designs to simultaneously expedite drug development and generate data necessary to demonstrate substantial evidence of effectiveness.

FDA is issuing this draft guidance in accordance with a commitment outlined in the reauthorization of the Prescription Drug User Fee Act (PDUFA VII) under the 2022 FDA User Fee Reauthorization Act.

This draft guidance is being issued consistent with FDA's good guidance practices regulation (21 CFR 10.115). The draft guidance, when finalized, will represent the current thinking of FDA on "Innovative Designs for Clinical Trials of Cellular and Gene Therapy Products in Small Populations." 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.

As we develop final guidance on this topic, FDA will consider comments on costs or cost savings the guidance may generate, relevant for Executive Order 14192.

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 50 and 56 pertaining to institutional review boards and the protection of human subjects, respectively, have been approved under OMB control number 0910–0130. The collections of information under 21 CFR part 312 pertaining to Investigational New Drug Applications, including clinical trials and formal meetings, have been approved under OMB control number 0910–0014. The collections of information in 21 CFR part 601 pertaining to the submissions of biologics license application product for development have been approved under OMB control number 0910–0338. The collections of information described in FDA’s guidance entitled “Formal Meetings Between the FDA and Sponsors or Applicants of PDUFA Products” have been approved under OMB control number 0910–0297.

III. Electronic Access

Persons with access to the internet may obtain the draft 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.

[FR Doc. 2025–18651 Filed 9–24–25; 8:45 am]

BILLING CODE 4164–01–P

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. FDA–2025–N–0373]

Agency Information Collection Activities; Submission for Office of Management and Budget Review; Comment Request; Registration of Food Facilities

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice.

SUMMARY: The Food and Drug Administration (FDA) is announcing that a proposed collection of information has been submitted to the Office of Management and Budget (OMB) for review and clearance under the Paperwork Reduction Act of 1995.

DATES: Submit written comments (including recommendations) on the collection of information by October 27, 2025.

ADDRESSES: To ensure that comments on the information collection are received, OMB recommends that written comments be submitted to <https://www.reginfo.gov/public/do/PRAMain>. Find this particular information collection by selecting “Currently under Review—Open for Public Comments” or by using the search function. The OMB control number for this information collection is 0910–0502. Also include the FDA docket number found in brackets in the heading of this document.

FOR FURTHER INFORMATION CONTACT:

Domini Bean, Office of Operations, Food and Drug Administration, Three White Flint North, 10A–12M, 11601 Landsdown St., North Bethesda, MD 20852, 301–796–5733, PRAStaff@fda.hhs.gov.

SUPPLEMENTARY INFORMATION: In compliance with 44 U.S.C. 3507, FDA has submitted the following proposed collection of information to OMB for review and clearance.

Registration of Food Facilities

OMB Control Number 0910–0502—Extension

This information collection supports FDA regulations. The Public Health Security and Bioterrorism Preparedness and Response Act of 2002 (the Bioterrorism Act) amended the Federal Food, Drug, and Cosmetic Act (FD&C Act), to require, among other things, domestic and foreign facilities that manufacture, process, pack, or hold food for human or animal consumption

in the United States to register with FDA. Sections 1.230 to 1.235 of our regulations (21 CFR part 1, subpart H) set forth the requirements for the registration of food facilities.

Information provided to us under these regulations helps us to quickly notify the facilities that might be affected by a deliberate or accidental contamination of the food supply. In addition, data collected through registration is used to support FDA enforcement activities and to screen imported food shipments.

Advanced notice of imported food allows FDA, with the support of U.S. Customs and Border Protection, to target import inspections more effectively and help protect the nation’s food supply against terrorist acts and other public health emergencies. If a facility is not registered or the registration for a facility is not updated when necessary, we may not be able to contact the facility and may not be able to target import inspections effectively in case of a known or potential threat to the food supply or other food-related emergency, putting consumers at risk of consuming hazardous food products that could cause serious adverse health consequences or death.

To assist respondents of the information collection we developed the following forms. Each facility that manufactures, processes, packs, or holds food for human or animal consumption in the United States must register with FDA using Form FDA 3537 entitled, “Food Facility Registration” (§ 1.231), unless exempt under § 1.226 from the requirement to register. To cancel a registration, respondents must use Form FDA 3537a entitled, “Cancellation of Food Facility Registration” (§ 1.235). The terms “Form FDA 3537” and “Form FDA 3537a” refer to both the paper version of each form and the electronic system known as the Food Facility Registration Module, which is available at <https://www.access.fda.gov>.

Registrations, updates, and cancellations are required to be submitted electronically. Domestic facilities are required to register regardless of whether food from the facility enters interstate commerce. Foreign facilities that manufacture, process, pack, or hold food also are required to register unless food from that facility undergoes further processing (including packaging) by another foreign facility outside the United States. However, if the further manufacturing/processing conducted by the subsequent facility consists of adding labeling or any similar activity of a de minimis nature, the former facility is required to register. In addition to the initial registration requirements, a