



DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. FDA-2016-D-4317]

Compounding and Repackaging of Radiopharmaceuticals by Outsourcing Facilities; Draft Guidance for Industry; Availability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SUMMARY: The Food and Drug Administration (FDA or Agency) is announcing the availability of a draft guidance for industry entitled "Compounding and Repackaging of Radiopharmaceuticals by Outsourcing Facilities." Specifically, this guidance sets forth FDA's policy regarding compounding and repackaging of radiopharmaceuticals for human use by entities that are registered with FDA as outsourcing facilities. This guidance describes how FDA intends to apply section 503B of the Federal Food, Drug, and Cosmetic Act (the FD&C Act) to radiopharmaceuticals compounded by outsourcing facilities, and it describes the conditions under which FDA does not intend to take action for violations of certain provisions of the FD&C Act when an outsourcing facility repackages radiopharmaceuticals.

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on any guidance at any time (see 21 CFR 10.115(g)(5)), to ensure that the Agency considers your comment on this draft guidance before it begins work on the final version of the guidance, submit either electronic or written comments on the draft guidance by [INSERT DATE 60 DAYS AFTER DATE OF PUBLICATION IN THE FEDERAL REGISTER].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

collection of information proposed in the draft guidance by [INSERT DATE 60 DAYS AFTER DATE OF PUBLICATION IN THE FEDERAL REGISTER].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: <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): 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-2016-D-4317 for "Compounding and Repackaging of Radiopharmaceuticals by Outsourcing Facilities." 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 <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 Division of Dockets Management, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852.

Submit written requests for single copies of the draft 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. Send one self-addressed adhesive label to assist that office in processing your requests. See the SUPPLEMENTARY INFORMATION section for electronic access to the draft guidance document.

FOR FURTHER INFORMATION CONTACT: Sara Rothman, Center for Drug Evaluation and Research, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 51, rm. 5197, Silver Spring, MD 20993, 301-796-3110.

SUPPLEMENTARY INFORMATION:

I. Background

In 2013, the Drug Quality and Security Act created a new section 503B of the FD&C Act (21 U.S.C. 353b), which describes a new category of compounders called outsourcing facilities. Section 503B of the FD&C Act describes the conditions that must be satisfied for human drug products compounded by or under the direct supervision of a licensed pharmacist in an

outsourcing facility to qualify for exemptions from the following three sections of the FD&C Act:

- Section 502(f)(1) (21 U.S.C. 352(f)(1)) (concerning labeling with adequate directions for use);
- section 505 (21 U.S.C. 355) (concerning drug approval requirements); and
- section 582 (21 U.S.C. 360eee-1) (concerning drug supply chain security requirements).

In contrast to section 503A (21 U.S.C. 353a), section 503B of the FD&C Act does not exclude radiopharmaceuticals. In general, FDA's policies regarding section 503B of the FD&C Act apply to the compounding of radiopharmaceutical drug products. However, the Agency has developed specific policies, applicable only to the compounding of radiopharmaceuticals by outsourcing facilities, with respect to bulk drug substances for use in compounding radiopharmaceuticals and compounding radiopharmaceuticals that are essentially copies of approved drugs when such compounding is limited to minor deviations, as that term is defined in the guidance.

In addition, because outsourcing facilities may sometimes repackage radiopharmaceuticals for patients, but repackaged radiopharmaceuticals are not eligible for the exemptions in section 503B of the FD&C Act, the draft guidance describes the conditions under which the Agency does not intend to take action for violations of sections 505 and 502(f)(1) of the FD&C Act when an outsourcing facility repackages radiopharmaceuticals for human use.

Elsewhere in this issue of the Federal Register, FDA is announcing the availability of a separate draft guidance document concerning compounding and repackaging of radiopharmaceuticals by State-licensed nuclear pharmacies and Federal facilities that are not

registered as outsourcing facilities entitled "Compounding and Repackaging of Radiopharmaceuticals by State-Licensed Nuclear Pharmacies and Federal Facilities."

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 "Compounding and Repackaging of Radiopharmaceuticals by Outsourcing Facilities." 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 draft guidance contains information collection provisions that are subject to review by the Office of Management and Budget under the Paperwork Reduction Act of 1995 (the PRA) (44 U.S.C. 3501-3520). The title, description, and respondent description of the information collection are given under this section with an estimate of the annual reporting and recordkeeping burdens. Included in the estimate is the time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing and reviewing the collection of information.

We invite comments on the following topics: (1) Whether the proposed collection of information is necessary for the proper performance of FDA's functions, including whether the information will have practical utility; (2) the accuracy of FDA's estimate of the burden of the proposed collection of information, including the validity of the methodology and assumptions used; (3) ways to enhance the quality, utility, and clarity of the information to be collected; and (4) ways to minimize the burden of the collection of information on respondents, including

through the use of automated collection techniques, when appropriate, and other forms of information technology.

The draft guidance includes the following collections of information under the PRA:

One condition in the draft guidance is that if a radiopharmaceutical is repackaged by an outsourcing facility, the label on the immediate container (primary packaging, e.g., the syringe) of the repackaged product includes the following information:

- The statement "This radiopharmaceutical was repackaged by [name of outsourcing facility].";
- the address and phone number of the outsourcing facility that repackaged the radiopharmaceutical;
- the established name of the original, approved radiopharmaceutical that was repackaged;
- the lot or batch number of the repackaged radiopharmaceutical;
- the dosage form and radioactive dose of the repackaged radiopharmaceutical;
- a statement of either the quantity or volume of the repackaged radiopharmaceutical, whichever is appropriate;
- the date the radiopharmaceutical was repackaged;
- the beyond-use-date of the repackaged radiopharmaceutical;
- storage and handling instructions for the repackaged radiopharmaceutical;
- the National Drug Code (NDC) number of the repackaged radiopharmaceutical, if available¹;

¹ The NDC number of the original approved drug product should not be placed on the repackaged drug product.

- the statement "Not for resale," and, if the repackaged radiopharmaceutical is distributed by an outsourcing facility other than pursuant to a prescription for an individual identified patient, the statement "Office Use Only"; and
- a list of the active and inactive ingredients, unless such information is included on the label for the container from which the individual units are removed, as described in this document.

Another condition in the draft guidance is that the label on the container from which the individual units are removed for administration (secondary packaging, e.g., the bag, box, or other package in which the repackaged products are distributed) includes the active and inactive ingredients, if the immediate product label is too small to include this information, and directions for use, including, as appropriate, dosage and administration, and the following information to facilitate adverse event reporting: <http://www.fda.gov/medwatch> and 1-800-FDA-1088.

We estimate that annually a total of approximately 2 outsourcing facilities ("No. of Respondents" in table 1, row 1) will each design, test, and produce approximately 5 different labels ("No. of Disclosures per Respondent" in table 1, row 1) for a total of 10 labels that include the information described previously (including directions for use) ("Total Annual Disclosures" in table 1, row 1). We also estimate that designing, testing, and producing each label will take approximately 0.5 hours for each repackaged radiopharmaceutical ("Average Burden Hours per Disclosure" in table 1, row 1). The provision to add the statement <http://www.fda.gov/medwatch> and 1-800-FDA-1088 is not included in this burden estimate because it is not considered a collection of information under the PRA because the information is "originally supplied by the Federal Government to the recipient for the purpose of disclosure to the public" (5 CFR 1320.3(c)(2)).

The draft guidance also references registration, adverse event reporting, product reporting, and current good manufacturing practices (CGMP) requirements for outsourcing facilities. The collection of information for outsourcing facility registration has been approved by the Office of Management and Budget (OMB) under OMB control number 0910-0777 (79 FR 69859, November 24, 2014). The collection of information for adverse event reporting by outsourcing facilities has been approved by OMB under OMB control number 0910-0800 (80 FR 60917, October 8, 2015). In the Federal Register of August 1, 2016 (81 FR 50523), FDA estimated the burden resulting from outsourcing facility electronic drug product reporting. In the Federal Register of July 2, 2014 (79 FR 37743), FDA estimated the burden resulting from outsourcing facility compliance with CGMP requirements.

The total estimated third-party disclosure burden resulting from the draft guidance is as follows:

Table 1.--Estimated Annual Third-Party Disclosure Burden

Repackaging by Outsourcing Facilities	No. of Respondents	No. of Disclosures per Respondent	Total Annual Disclosures	Average Burden per Disclosure	Total Hours
Designing, testing, and producing each label on immediate containers, packages and/or outer containers	2	5	10	.5 (30 minutes)	5

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

III. Electronic Access

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

Dated: December 22, 2016.

Leslie Kux,

Associate Commissioner for Policy.

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