TABLE 2—ESTIMATED ANNUAL RECORDKEEPING BURDEN [1]—Continued

| Activity; guidance document section | Number of recordkeepers | Number of records per recordkeeper | Total annual records | Average burden per recordkeeping | Total hours |
|---|---|---|---|---|---|
| Records regarding qualifications to receive FDA recognition as a 3PRO; Section V.C | 9 | 1 | 9 | 1 | 9 |
| Recordkeeping system regarding complaints; Section V.C | 9 | 1 | 9 | 2 | 18 |
| Total | | | | | 1,287 |

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

Upon review of this information collection, we have adjusted our burden estimate for the average burden hours required per response for initial requests for accreditation from 24 to 40 hours to more accurately reflect the time required based on recent experience of FDA program staff. This adjustment has resulted in an increase of 15 hours to the currently approved burden.

Dated: June 26, 2025.

**Grace R. Graham,**

*Deputy Commissioner for Policy, Legislation, and International Affairs.*

[FR Doc. 2025–12416 Filed 7–2–25; 8:45 am]

**BILLING CODE 4164–01–P**

## DEPARTMENT OF HEALTH AND HUMAN SERVICES

### Food and Drug Administration

**[Docket No. FDA–2022–D–2301]**

### Small Volume Parenteral Drug Products and Pharmacy Bulk Packages for Parenteral Nutrition: Aluminum Content and Labeling Recommendations; Draft Guidance for Industry; Availability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**SUMMARY:** The Food and Drug Administration (FDA or Agency) is announcing the availability of a draft guidance for industry entitled ''Small Volume Parenteral Drug Products and Pharmacy Bulk Packages for Parenteral Nutrition: Aluminum Content and Labeling Recommendations.'' This draft guidance is intended to clarify the key factors in calculating the aluminum content to ensure that the total aluminum exposure in parenteral nutrition (PN) does not exceed an acceptable threshold. It also provides FDA's recommendations regarding the aluminum concentration limits for small volume parenterals (SVPs) packaged as single doses or SVPs packaged in pharmacy bulk packages (PBPs). Additionally, this draft guidance is intended to assist sponsors and applicants in determining the appropriate placement of information on aluminum toxicity in SVP and large volume parenteral (LVP) Prescribing Information and container and carton labeling. This draft guidance revises and replaces the draft guidance for industry of the same name published on December 7, 2022.

**DATES:** Submit either electronic or written comments on the draft guidance by September 2, 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–2022–D–2301 for ''Small Volume Parenteral Drug Products and Pharmacy Bulk Packages for Parenteral Nutrition: Aluminum Content and Labeling Recommendations.'' 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 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:** Thao Vu, Center for Drug Evaluation and Research, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 22, Rm. 5232, Silver Spring, MD 20993–0002, 240–402–2690.

**SUPPLEMENTARY INFORMATION:**

## I. Background

FDA is announcing the availability of a revised draft guidance for industry entitled ''Small Volume Parenteral Drug Products and Pharmacy Bulk Packages for Parenteral Nutrition: Aluminum Content and Labeling Recommendations.'' Aluminum, one of the most abundant metallic elements on earth, occurs naturally in several minerals, ores, oxides, and silicates. Although humans are exposed to aluminum through drinking water, food, and drugs, absorption of aluminum through the gastrointestinal tract (oral bioavailability) is low; therefore, healthy individuals typically face little risk of aluminum toxicity. However, in the settings of chronic kidney failure or prolonged PN treatment in neonates, aluminum toxicity has manifested as osteomalacia and reduced bone mineralization, neurological dysfunction including dialysis encephalopathy, microcytic hypochromic anemia, and cholestasis.

A long-implicated, major source of aluminum exposure is PN, resulting from contamination of ingredients or leaching through the container during manufacturing. Patients with underlying renal impairment who receive prolonged courses of PN are at greatest risk of exposure to toxic levels of aluminum from PN. Preterm neonates and infants, who have immature kidneys that are incapable of excreting aluminum efficiently and may require weeks of PN before transitioning to oral nutrition, are at particularly high risk.

This draft guidance is intended to clarify the key factors in calculating the aluminum content to ensure that the total aluminum exposure in PN does not exceed an acceptable threshold. It also provides FDA's recommendations regarding the aluminum concentration limits for SVPs packaged as single doses or SVPs packaged in PBPs. Additionally, this draft guidance is intended to assist sponsors and applicants in determining the appropriate placement of information on aluminum toxicity in SVP and LVP Prescribing Information and container and carton labeling; it revises and replaces the draft guidance for industry of the same name published on December 7, 2022 (87 FR 75052). Interested parties' comments were considered, and the following key changes were made:

- Revised the Introduction section to clarify the intended purpose; the key factors in calculating the aluminum content; the need for aluminum mitigation and control strategies for SVP, PBP, and LVP development; and labeling considerations for aluminum toxicity in SVPs, PBPs, and LVPs;
- Clarified the examples showing the calculations of total aluminum exposure, individual aluminum exposure, and aluminum concentration limits, as well as the data supporting FDA's recommendation for total aluminum exposure; and
- Added section VI to provide advice regarding implementation of this guidance, particularly steps manufacturers should take if a drug shortage arises.

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 ''Small Volume Parenteral Drug Products and Pharmacy Bulk Packages for Parenteral Nutrition: Aluminum Content and Labeling Recommendations.'' 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 any final guidance on this topic, FDA will consider comments on the applicability of Executive Order 14192, per the Office of Management and Budget (OMB) guidance M–25–20, and in particular, on any costs or cost savings.

## 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 OMB under the Paperwork Reduction Act of 1995 (PRA) (44 U.S.C. 3501–3521). The collections of information in 21 CFR part 314 have been approved under OMB control number 0910–0001. The collections of information in 21 CFR part 312 have been approved under OMB control number 0910–0014. The collections of information in FDA's guidance entitled ''Formal Meetings Between the FDA and Sponsors or Applicants of PDUFA Products'' (available at *https://www.fda.gov/media/109951/download*) have been approved under OMB control number 0910–0001. The collections of information in 21 CFR 201.56 and 201.57 have been approved under OMB control number 0910–0572. The collections of information in FDA's guidance entitled ''Formal Meetings Between FDA and ANDA Applicants of Complex Products Under GDUFA'' (available at *https://www.fda.gov/media/107626/download*) and in FDA's guidance entitled ''Controlled Correspondence Related to Generic Drug Development'' (available at *https://www.fda.gov/media/109232/download*) have been approved under OMB control number 0910–0727.

## III. Electronic Access

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

Dated: June 27, 2025.

**Grace R. Graham,**

*Deputy Commissioner for Policy, Legislation, and International Affairs.*

[FR Doc. 2025–12403 Filed 7–2–25; 8:45 am]

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