DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. FDA–2022–D–2424]

Protein Efficiency Ratio Rat Bioassay Studies To Demonstrate That a New Infant Formula Supports the Quality Factor of Sufficient Biological Quality of Protein; Draft Guidance for Industry; Availability; Agency Information Collection Activities; Proposed Collection; Comment Request

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice of availability.

SUMMARY: The Food and Drug Administration (FDA or we) is announcing the availability of a draft guidance entitled ''Protein Efficiency Ratio (PER) Rat Bioassay Studies To Demonstrate That a New Infant Formula Supports the Quality Factor of Sufficient Biological Quality of Protein.'' The draft guidance, when finalized, will provide information for manufacturers and contract laboratories that perform PER studies to assist in designing, conducting, evaluating, and reporting PER studies. The draft guidance, when finalized, will explain ''appropriate modifications'' of AOAC Official Method 960.48 (the AOAC Method) with the aim of supporting industry in successfully conducting PER studies that demonstrate that a new infant formula meets the quality factor of sufficient biological quality of protein when fed as the sole source of nutrition.

DATES: Submit either electronic or written comments on the draft guidance by May 11, 2023 to ensure that we consider your comment on the draft guidance before we begin work on the final version of the guidance. Submit electronic or written comments on the proposed collection of information in the draft guidance by May 11, 2023.

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–2424 for ''Protein Efficiency Ratio (PER) Rat Bioassay Studies To Demonstrate That a New Infant Formula Supports the Quality Factor of Sufficient Biological Quality of Protein.'' 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.'' We will review this copy, including the claimed confidential information, in our 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 Office of Nutrition and Food Labeling (HFS–800), Center for Food Safety and Applied Nutrition, Food and Drug Administration, 5001 Campus Dr., College Park, MD 20740. Send one self-addressed adhesive label to assist that office in processing your request or include a Fax number to which the draft guidance may be sent. See the **SUPPLEMENTARY INFORMATION** section for information on electronic access to the draft guidance.

FOR FURTHER INFORMATION CONTACT:

With regard to the draft guidance: Andrea Lotze, Center for Food Safety and Applied Nutrition, Office of Nutrition and Food Labeling (HFS–800), Food and Drug Administration, 5001 Campus Dr., College Park, MD 20740, 240–402–1450, email: *Andrea.Lotze@fda.hhs.gov;* or Keronica Richardson, 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.

With regard to the proposed collection of information: Rachel Showalter, Office of Operations, Food and Drug Administration, Three White Flint North, 10A–12M, 11601 Landsdown St., North Bethesda, MD 20852, 240–994–7399, *PRAStaff@fda.hhs.gov.*

SUPPLEMENTARY INFORMATION:

I. Background

FDA is announcing the availability of a draft guidance for industry entitled

''Protein Efficiency Ratio (PER) Rat Bioassay Studies To Demonstrate That a New Infant Formula Supports the Quality Factor of Sufficient Biological Quality of Protein.'' Our regulations, at 21 CFR 106.96, establish requirements for quality factors for infant formulas, including the quality factor of sufficient biological quality of protein. Subject to a limited exception (see § 106.96(g)), each manufacturer of an infant formula that is not an eligible infant formula must demonstrate that the formula meets the quality factor of sufficient biological quality of protein by establishing the biological quality of the protein in the infant formula when fed as the sole source of nutrition using an appropriate modification of the AOAC Official Method 960.48 (the AOAC Method) Protein Efficiency Ratio (PER) Rat Bioassay (§ 106.96(f)).[1]

The AOAC Method provides a procedure by which the quality of a protein in food can be evaluated and compared with those of other proteins. Protein ''quality'' can be defined as the ability of a protein to meet the essential amino acid needs of an animal. The AOAC Method is a standardized bioassay with published collaborative study data. The AOAC Method permits the calculation of a PER as the ratio of the average animal body weight gain per gram of protein consumed of a test protein versus casein after a 28-day feeding period. Typically, the protein concentration of both the test and casein reference diet is set at about 10 percent, a level that is below the estimated requirement for growth of rats of 15 percent, to improve the sensitivity of the method. While growth is slower at 10 percent protein than at 15 percent protein, the lower protein level assures that available protein is efficiently utilized.

In the PER study described in the AOAC Method, a protein ingredient was assayed at 10 percent and other potential variables were standardized so that their numbers and potential effects were minimized. Vitamin composition, moisture, ash, carbohydrates, fat, and fiber were adjusted between the casein reference diet and the test diet. Use of a test diet that contains an infant formula in its entirety introduces matrices of high fat content and additional vitamins, minerals, and other ingredients, as well as the low protein source. A major challenge in analyzing infant formulas by the AOAC Method is matching the casein reference diet and test diet to achieve dietary groups with as few confounding variables as possible.

Since we promulgated § 106.96, we have found that industry is experiencing difficulties in consistently meeting its requirements. Therefore, we are announcing the availability of a draft guidance for industry entitled ''Protein Efficiency Ratio (PER) Rat Bioassay Studies To Demonstrate That a New Infant Formula Supports the Quality Factor of Sufficient Biological Quality of Protein.'' This draft guidance, when finalized, will help infant formula manufacturers and contract laboratories that perform PER studies in designing, conducting, evaluating, and reporting PER studies. The draft guidance, when finalized, will explain ''appropriate modifications'' of the AOAC Method to help manufacturers and contract laboratories conduct PER studies that demonstrate to FDA that a new infant formula meets the quality factor of sufficient biological quality of protein.

FDA's work on this draft guidance document began prior to significant infant formula supply chain concerns that arose in early 2022. Although this guidance was not prepared specifically to alleviate supply chain concerns, this guidance will help ensure that infant formula products meet FDA's regulatory requirements and will contribute to ensuring a more resilient infant formula supply. We are issuing the draft guidance consistent with our good guidance practices regulation (21 CFR 10.115). The draft guidance, when finalized, will represent the current thinking of FDA on this topic. It does not establish any rights for any person and is not binding on FDA or the public. You can use an alternate approach to make ''appropriate modifications'' if it satisfies the requirements of the applicable statutes and regulations. Topics discussed in the draft guidance include:

- Purpose of the AOAC Method;
- Overview of the AOAC Method as originally described;
- Need for ''appropriate modifications'' to update the AOAC Method and for use of infant formulas in PER bioassays;
- Conduct and analysis of a PER study with ''appropriate modifications'' (matching the reference and test diets);
- Protocols and reports;
- Reference guidelines; and
- *Appendices:* AOAC Official Method 960.48, composition of vitamin and mineral mixtures, compositions of diets, and examples of an approach for matching vitamin, mineral, and (methionine + cystine) compositions of PER study diets.

II. Paperwork Reduction Act of 1995

Under the Paperwork Reduction Act of 1995 (PRA) (44 U.S.C. 3501–3521), Federal Agencies must obtain approval from the Office of Management and Budget (OMB) for each collection of information they conduct or sponsor. ''Collection of information'' is defined in 44 U.S.C. 3502(3) and 5 CFR 1320.3(c) and includes Agency requests or requirements that members of the public submit reports, keep records, or provide information to a third party. Section 3506(c)(2)(A) of the PRA (44 U.S.C. 3506(c)(2)(A)) requires Federal Agencies to provide a 60-day notice in the **Federal Register** concerning each proposed collection of information before submitting the collection to OMB for approval. To comply with this requirement, FDA is publishing notice of the proposed collection of information set forth in this document.

With respect to the following collection of information, FDA invites comments on these 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.

Protein Efficiency Ratio (PER) Rat Bioassay Studies To Demonstrate That a New Infant Formula Supports the Quality Factor of Sufficient Biological Quality of Protein

OMB Control Number 0910–0256—Revision

Under § 106.96(e), an infant formula must meet the quality factor of sufficient biological quality of protein, and § 106.96(f) provides how an infant formula manufacturer must demonstrate that a formula meets this quality factor. PER studies are used to demonstrate to FDA that a new infant formula meets

[1] We support the principles of the ''3Rs'' to reduce, refine, and replace animal use in testing when feasible. We encourage sponsors to consult with us if they wish to use a non-animal testing method they believe is suitable, adequate, and validated to demonstrate that the formula supports the quality factor for the biological quality of the protein as described in 21 CFR 106.96(g)(3). We support alternative methods by exemption in 21 CFR 106.96(f) which allows the manufacturer to request an exemption and provide certain required assurances described in 21 CFR 106.96(g). The applicability of this exemption is not the subject of this guidance.

the quality factor of sufficient biological quality of protein when fed as the sole source of nutrition. This draft guidance, when finalized, would help manufacturers and laboratories performing PER studies in the design, conduct, evaluation, and reporting of such studies. When finalized, the draft guidance would provide recommendations for additional recordkeeping and reporting of protocols and PER studies related to the composition of test and control diets, as well as conditions, adverse effects, and attrition in rats. The draft guidance, when finalized, also will explain ''appropriate modifications'' of the AOAC Method to help manufacturers and contract laboratories conduct PER studies that demonstrate to FDA that a new infant formula meets the quality factor of sufficient biological quality of protein.

Description of Respondents: Respondents to the information collection are manufacturers of infant formula. Respondents are from the private sector (for-profit businesses).

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

TABLE 1—ESTIMATED ANNUAL RECORDKEEPING BURDEN [1]

Activity; guidance document section	Number of recordkeepers	Number of records per recordkeeper	Total annual records	Average burden per recordkeeping	Total hours
Records for composition of the test and control diets during PER studies; Section IV.	15	2	30	1	30
Records for conditions, adverse effects, and attrition in rats during PER studies; Section IV.	15	140	2,100	0.083 (5 minutes).	174
Total					204

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

The estimates in tables 1 and 2 are based on experience with our infant formula safety and nutrition programs. We estimate that fifteen manufacturers annually will each create and maintain two records for the composition of test and control diets of PER studies. We estimate the recordkeeping burden to be 1 hour per record for an annual burden of 30 hours (15 manufacturers × 2 records). These estimates are based on numerous PER study protocols, reports, and laboratory experiences.

We estimate that fifteen manufacturers annually will each create and maintain 140 records to account for conditions, adverse effects, and attrition in rats during PER studies. We estimate these records will take 5 minutes per record for an annual burden of 174.3 hours, rounded to 174 (15 manufacturers × 140 records × 0.083/hours). We calculate the total recordkeeping burden will be 204 hours annually.

TABLE 2—ESTIMATED ANNUAL REPORTING BURDEN [1]

Activity; guidance document section	Number of respondents	Number of responses per respondent	Total annual responses	Average burden per response	Total hours
Development and submission of a PER study protocol; Section V	15	1	15	70	1,050
Development and submission of a PER study final report; Section V	15	1	15	40	600
Total					1,650

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

We estimate that fifteen manufacturers will prepare and submit to FDA a protocol to ensure that the specifications of the AOAC Method and FDA's ''appropriate modifications'' are met. A protocol is a detailed plan for the conduct of the PER study that helps the manufacturer meet the requirements of § 106.96. In Table 1 in Appendix 6 of the draft guidance, we offer an illustration of how the values can be recorded as part of a protocol. An interested manufacturer will call FDA to discuss the manner in which a protocol will be submitted. We estimate each protocol will take 70 hours for an annual burden of 1,050 hours (15 protocols × 70 hours).

In addition, we estimate that fifteen manufacturers will submit a final report on all aspects of the PER study, including Certificates of Analyses (*i.e.,* a full specification of results) for relevant ingredients to FDA. A final report is submitted in the same manner as a protocol. We estimate each final report will take 40 hours for an annual burden of 600 hours (15 final reports × 40 hours). We calculate the total reporting burden will be 1,650 hours annually.

This draft guidance also refers to previously approved FDA collections of information. The collections of information in 21 CFR part 106 have been approved under OMB control number 0910–0256.

III. Electronic Access

Persons with access to the internet may obtain an electronic version of the draft guidance at *https://www.fda.gov/RegulatoryInformation/Guidances/default.html, https://www.fda.gov/regulatory-information/search-fda-guidance-documents,* or *https://www.regulations.gov.*

IV. Other Issues for Consideration

Although FDA welcomes comments on any aspect of the draft guidance, we particularly invite comments on the following sections, issues, and questions related to the compositions of PER study test (infant formula) and reference (casein control) diets. We ask that your

comments explain how suggestions will meet the overall requirement of demonstrating that the quality factor has been met using an ''appropriate modification.'' When commenting on a particular question, please use the question numbers below as this will make it easier for us to determine how a specific comment relates to a particular question or topic.

A. Questions for Section IV.B.1.c. Fats and Carbohydrates

1. Fats

Question 1. Companies have expressed difficulties in qualitative matching of fat in test and reference diets (*e.g.,* problems with physical consistency of reference diets when qualitative matching is attempted) and difficulties in quantitative matching because of the much lower fat requirement of rats. We invite comments on whether the fat compositions of the test and reference diets should be matched: (a) on a quantitative basis only; or (b) on both a quantitative and qualitative basis. Please explain your reasoning. If your answer is (b), please describe what additional flexibilities might be needed to reduce problems with formulation and palatability of the reference diets (*e.g.,* use of more saturated fat in place of the unsaturated (liquid) fats in infant formulas; partial substitution of the unsaturated fat in the infant formula with saturated fat in the reference diet). Please describe your experience with use of fat compositions in the reference diets that differ from that of the infant formula.

Question 2. Would reducing the fat content of the reference diet to about 80 percent that of the infant formula test diet (*e.g.,* to about 17–20 percent fat in the reference diet versus about 22–25 percent fat in the test diet) help to avoid issues (*e.g.,* problems with physical consistency of reference diets when qualitative matching is attempted) reported with high-fat reference diets? If your answer is ''yes,'' please describe other compositional changes that might be needed to keep the test and reference diets isocaloric. If your answer is ''no,'' please explain your reasoning.

Question 3. The need for vitamin E increases with an increase in dietary polyunsaturated fatty acids (PUFA) and with the degree of unsaturation of PUFA. We are proposing the use of a minimum ratio value for vitamin E:PUFA of 0.48 ± 0.28 milligrams (mg) of d-α-tocopherol to grams (g) of PUFAs in the PER study diets. We suggest that the total PUFA content of the test and reference diets be estimated from the Certificates of Analysis or other information and used with dietary concentrations of vitamin E to calculate the ratio of vitamin E:PUFA for both diets. The minimum ratio value of 0.48 can be used as a guideline for adjusting the concentration of vitamin E in the reference diet. Is this adjustment for using vitamin E needed? If you think the adjustment for vitamin E is needed, please explain your reasoning. If your answer is ''no,'' please explain why not. Is the mean ratio of 0.48 mg d-α-tocopherol per gram of PUFA reasonable or is there a more appropriate value? Please explain your reasoning.

2. Carbohydrates

Question 4. In explaining appropriate modifications to the AOAC Method, the IFR states that, among other things, if an infant formula contains a carbohydrate source other than lactose, the source(s) of carbohydrate in the formula should be added in the reference diet as well (see FDA's interim final rule, *Current Good Manufacturing Practices, Quality Control Procedures, Quality Factors, Notification Requirements, and Records and Reports, for Infant Formula,* 79 FR 7933 at 8024, Feb. 10, 2014)).

The simultaneous qualitative matching of fat and carbohydrate composition has proven difficult during formulation of PER study reference diets (*e.g.,* problems from adding sugars such as sucrose; hardening of mixture and compromised oil absorption when water is added to liquid oils). Our current thinking is that use of the same oil blend in the infant formula and reference diet may be one approach if there is not a need to qualitatively match all the carbohydrates. We invite comments on potential solutions to these difficulties. For example, would altering the type of fat used in the reference diet while retaining quantitative matching of the fat contents of the test and reference diets be sufficient to overcome these problems? Would the use of corn starch as a carbohydrate source in the reference diet allow the reference diet to be formulated with the same oil blends used in the infant formula? Please explain your reasoning.

B. Questions for Section IV.B.1.d. Removal of Water From Liquid Infant Formulas and Determination of Moisture in PER Study Diets

Question 5. The AOAC Method specifies a moisture content of 5 percent in the PER study test and reference diets. Some laboratories have had difficulty preparing diets to match fat and water contents, leading to physical consistencies in diets that makes it difficult to accurately record food consumption. We invite comments on specific problems that have arisen when attempting to match dietary contents of fat and water, as well as solutions that have been identified to help limit the occurrence of such problems. Should flexibility be provided in matching the water and fat contents of the diets? If your answer is ''yes,'' please describe an approach (*i.e.,* explain the types of flexibilities) that might be needed to reduce problems with the physical consistencies of the reference diets. If your answer is ''no,'' please explain your reasoning.

C. Questions for Section IV.B.1.e. Mineral Content

Question 6. FDA's regulations require that the infant formula be studied in a PER assay (§ 106.96(f)). Further, the AOAC Method specifies that both the PER study test and reference diets contain similar contents of minerals based on matched ash contents. We invite comments on how this matching could be achieved while meeting the requirement that the infant formula be tested. Is ash content alone an adequate surrogate when matching minerals in test and reference diets? If your answer is ''no,'' please described why not and discuss another approach that might be used to achieve the matching of minerals in test and reference diets.

Question 7. Multielement analysis (*e.g.,* ICP–AES (inductively coupled plasma-atomic emission spectroscopy), ICP–MS (inductively coupled plasma-mass spectrometry)) is currently used for the simultaneous analysis of many minerals. We invite comments on whether use of multielement analysis for the quantitation and subsequent matching of all minerals would be preferable to continued use of ash as a surrogate for mineral content. If your answer is ''yes,'' please describe reasonable expectations regarding how such analyses can be used.

Question 8. In Appendix 6 of the draft guidance, FDA has suggested a process by which mineral compositions of the test and reference diets can be matched to within ±20 percent. We invite comments on whether this is a reasonable approach. If your answer is ''no,'' please explain your reasoning and suggest an alternate approach.

D. Questions for Section IV.B.1.f. Vitamin Content

Question 9. The AOAC Method specifies that both the PER study test and reference diets contain the same vitamin composition. For the purpose of studying infant formula, we understand this to mean that the vitamin

composition of the test and reference diets in a PER study should be comparable. We invite comments on how such comparability should be defined and how it might be achieved.

Question 10. In Appendix 6 of the draft guidance, FDA has suggested a process by which vitamin compositions of the test and reference diets can be matched to within ±20 percent. We invite comments on whether this approach is reasonable and ask you to explain your thinking. If you do not believe the approach is reasonable, please explain your reasoning and suggest an alternative approach.

Question 11. We invite comments on whether the matching of the vitamin compositions between the test and reference diets should be eliminated because, for example, vitamins such as vitamin K and vitamin B12, among others, do not impact the growth of rats during the 28-day PER study. If your answer is ''yes, the matching of vitamin compositions between test and reference diets should be eliminated,'' what do you propose as the vitamin composition for the reference diet? Please explain your reasoning. If your answer is ''no,'' please explain your reasoning.

E. Question for Section IV.B.1.g. Fiber

Question 12. We invite comment on whether fiber should be added to the PER study test and matched casein reference diets under all conditions, under specified conditions, or not added at all. If your answer is ''yes, under all conditions,'' what is your proposed level of addition (*e.g.,* to match the concentrations of non-digestible fiber in the infant formula at its rate of addition)? If your answer is ''yes, under specified conditions,'' what are the specific conditions under which fiber should be added and at what concentration? If your answer is ''no, fiber should not be added,'' please explain your reasoning.

F. Question for Section IV.B.1.h. Sulfur Amino Acids (Methionine, Cystine)

Question 13. In the draft guidance, we recommend that the concentration of inorganic sulfur (*e.g.,* as sulfate salts) in the PER study casein reference control diet be adjusted to 0.964 g/kilograms diet, the content calculated from the mineral composition set forth in the AOAC Method as originally described. We also provide a procedure for matching the (methionine + cystine) concentrations in the casein reference control and test diets, and for use of this sulfur amino acid-matched group as a second casein reference control group in PER studies. This approach will reduce the risk of a failure of the PER study control group. If you think the approach is needed, please explain your reasoning. If you think that such an approach is not necessary, please explain why not. If you think that other approaches might be more helpful in reducing the risk of a failure of the reference control group, please describe such approaches and explain their advantages.

Dated: February 6, 2023.

Lauren K. Roth,

Associate Commissioner for Policy.

[FR Doc. 2023–02836 Filed 2–9–23; 8:45 am]

BILLING CODE 4164–01–P

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. FDA–2020–D–1136]

Temporary Policy on Repackaging or Combining Propofol Drug Products During the COVID–19 Public Health Emergency; Withdrawal of Guidance

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice; withdrawal.

SUMMARY: The Food and Drug Administration (FDA or Agency) is announcing the withdrawal of the guidance for industry entitled ''Temporary Policy on Repackaging or Combining Propofol Drug Products During the COVID–19 Public Health Emergency,'' which was issued in April 2020 to communicate a temporary policy regarding the repackaging or combining of propofol drug products. FDA is withdrawing this guidance document because the conditions that created the need for this policy described in the document have evolved and the policy is no longer needed.

DATES: The withdrawal date is March 13, 2023.

FOR FURTHER INFORMATION CONTACT: Kimberly Thomas, Office of Regulatory Policy, Center for Drug Evaluation and Research, Food and Drug Administration, 10903 New Hampshire Ave., Silver Spring, MD 20993, 301–796–2357.

SUPPLEMENTARY INFORMATION:

I. Background

As part of FDA's commitment to providing timely guidance to support response efforts to the Coronavirus Disease 2019 (COVID–19) [1] pandemic, in April 2020, the Agency published the guidance for industry entitled ''Temporary Policy on Repackaging or Combining Propofol Drug Products During the COVID–19 Public Health Emergency.'' This guidance communicated the Agency's temporary policy regarding the repackaging or combining of propofol drug products by licensed pharmacists in State licensed pharmacies, Federal facilities, and outsourcing facilities registered pursuant to section 503B of the Federal Food, Drug, and Cosmetic Act (FD&C Act) (21 U.S.C. 353b).[2] FDA had received reports from some hospitals that they were having difficulty obtaining adequate supplies of FDA-approved propofol injectable emulsion (propofol) products, 10 milligrams (mg) per milliliter (mL), in the presentations used to support COVID–19 patients who had been sedated and intubated, or for other procedures involved in the care of such patients. At the time the guidance was published, propofol was on FDA's drug shortage list, with several presentations on backorder or on allocation. FDA recognized that pharmacies and outsourcing facilities that had access to certain presentations of propofol drug products wanted to repackage or combine units of a finished, FDA-approved drug product to provide hospitals with presentations needed for patients with COVID–19. The guidance stated that as a temporary measure during the public health emergency related to COVID–19, or for such shorter time as FDA may announce by updating or withdrawing the guidance based on evolving needs and circumstances, FDA intended to extend, under certain circumstances described in the guidance, its existing enforcement discretion policy described in the

[1] The virus has been named ''SARS–CoV–2'' and the disease it causes has been named ''Coronavirus Disease 2019'' (COVID–19).

[2] As explained in the guidance, provided that circumstances described in the guidance were present, FDA did not intend to take action for violations of section 505 (concerning new drug applications), section 502(f)(1) (concerning labeling with adequate directions for use), and section 582 (concerning drug supply chain security) of the FD&C Act (21 U.S.C. 355, 352(f)(1), and 360eee-1) if a State-licensed pharmacy, a Federal facility, or an outsourcing facility prepared drug products as described in this guidance and met other applicable requirements. Applicable requirements included, for example, the requirement that manufacturers not adulterate a drug product by preparing, packing, or holding the drug product under insanitary conditions. See section 501(a)(2)(A) of the FD&C Act (21 U.S.C. 351(a)(2)(A)). In addition, FDA did not intend to take action for violations of section 501(a)(2)(B) of the FD&C Act if the drug product was repackaged by a State-licensed pharmacy or a Federal facility in accordance with the conditions described in the guidance, and any applicable requirements. Finally, with respect to entities that did not qualify for the exemptions from registration under section 510 of the FD&C Act (21 U.S.C. 360), FDA did not intend to take action for violations of section 502(o) of the FD&C Act.