organization. Registrants will receive confirmation when they have been accepted. If time and space permit, onsite registration on the day of the public meeting will be provided beginning at 8:30 a.m. We will post information at *https://www.fda.gov/Drugs/NewsEvents/ucm132703.htm* if registration closes before the day of the public meeting.

If you need special accommodations due to a disability, please contact *CompoundingPublicMeeting@fda.hhs.gov* no later than May 14, 2019.

Requests for Oral Presentations: During online registration you may indicate if you wish to present during a public comment session and which topic(s) you wish to address. All requests to make oral presentations must be received by March 1, 2019. You will also be asked to send *CompoundingPublicMeeting@fda.hhs.gov* a brief summary your comments by March 1, 2019. Individuals and organizations with common interests are urged to consolidate or coordinate their presentations, and request time for a joint presentation, or submit requests for designated representatives to present. For more information on oral presentation requests, visit *https://www.fda.gov/Drugs/NewsEvents/ucm132703.htm.* Following the close of registration, we will determine the amount of time allotted to each presenter and the approximate time each oral presentation is to begin. We will do our best to accommodate all stakeholders who wish to speak; however, the duration of comments may be limited by time constraints, including time allowances for each topic. Presenters will be notified of their selection no later than May 7, 2019. If selected for presentation, any presentation materials must be emailed to the *CompoundingPublicMeeting@fda.hhs.gov* no later than May 14, 2019. No commercial or promotional material will be permitted to be presented or distributed at the public meeting.

Streaming Webcast of the Public Meeting: This public meeting will also be webcast. Further information regarding the webcast, including the address for the webcast, will be made available at least 2 days in advance of the meeting on the public meeting website. More information regarding the meeting, including the public meeting website address, will be posted at: *https://www.fda.gov/Drugs/NewsEvents/ucm132703.htm.* FDA has verified the website addresses in this document, as of the date this document publishes in the **Federal Register**, but websites are subject to change over time.

Dated: December 4, 2018.

Leslie Kux,

Associate Commissioner for Policy.

[FR Doc. 2018–26725 Filed 12–10–18; 8:45 am]

BILLING CODE 4164–01–P

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. FDA–2014–D–0779]

Current Good Manufacturing Practice—Guidance for Human Drug Compounding Outsourcing Facilities Under Section 503B of the FD&C Act; Draft Guidance for Industry; Availability

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice of availability.

SUMMARY: The Food and Drug Administration (FDA or the Agency) is announcing the availability of a revised draft guidance entitled ''Current Good Manufacturing Practice—Guidance for Human Drug Compounding Outsourcing Facilities Under Section 503B of the FD&C Act.'' This revised draft guidance describes FDA's policies regarding compounders registered under section 503B of the Federal Food, Drug, and Cosmetic Act (FD&C Act) as outsourcing facilities and the current good manufacturing practice (CGMP) requirements in FDA regulations. Based on feedback from stakeholders and comments received on the initial draft guidance, the guidance is being revised, in part, to reflect further consideration of how CGMP requirements should be applied in light of the size and scope of an outsourcing facility's operations.

DATES: Submit either electronic or written comments on the revised draft guidance by February 11, 2019 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 concerning the collection of information under the Paperwork Reduction Act of 1995 (PRA) proposed in the revised draft guidance by February 11, 2019.

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–2014–D–0779 for ''Current Good Manufacturing Practice—Guidance for Human Drug Compounding Outsourcing Facilities Under Section 503B of the FD&C Act.'' 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.

- 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.gpo.gov/fdsys/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.

Submit comments on information collection issues under the PRA to the Office of Management and Budget (OMB) in the following ways:

- Fax to the Office of Information and Regulatory Affairs, OMB, Attn: FDA Desk Officer, Fax: 202–395–7285, or email to *oira_submission@omb.eop.gov.* All comments should be identified with the title ''Current Good Manufacturing Practice—Guidance for Human Drug Compounding Outsourcing Facilities Under Section 503B of the FD&C Act.''

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: Marci Kiester, Center for Drug Evaluation and Research, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 51, Rm. 2258, Silver Spring, MD 20993–0002, 301–796–0600.

SUPPLEMENTARY INFORMATION:

I. Background

FDA is announcing the availability of a revised draft guidance for industry entitled ''Current Good Manufacturing Practice—Guidance for Human Drug Compounding Outsourcing Facilities Under Section 503B of the FD&C Act.'' Under section 503B(b) of the FD&C Act (21 U.S.C. 353b(b)), a compounder can register as an outsourcing facility with FDA. Drug products compounded in an outsourcing facility can qualify for exemptions from FDA approval requirements in section 505 of the FD&C Act (21 U.S.C. 355), the requirement to label products with adequate directions for use under section 502(f)(1) of the FD&C Act (21 U.S.C. 352(f)(1)), and the drug supply chain security requirements in section 582 of the FD&C Act (21 U.S.C. 360eee–1), if the requirements in section 503B are met. Outsourcing facilities are inspected by FDA according to a risk-based schedule and must comply with other provisions of the FD&C Act, including CGMP requirements under section 501(a)(2)(B) (21 U.S.C. 351(a)(2)(B)). FDA intends to issue CGMP regulations specific to outsourcing facilities. Until final regulations are issued, this draft guidance describes FDA's policies regarding outsourcing facilities and the CGMP requirements in 21 CFR parts 210 and 211.

This draft guidance revises the draft guidance for industry entitled ''Current Good Manufacturing Practice—Interim Guidance for Human Drug Compounding Outsourcing Facilities Under Section 503B of the FD&C Act,'' which published in July 2014 (79 FR 37743). This revised draft guidance applies to drugs compounded in accordance with section 503B. In addition, this guidance generally applies to drugs that outsourcing facilities repackage and biological products that outsourcing facilities mix, dilute, or repackage in accordance with relevant guidance for outsourcing facilities. This revised draft guidance reflects FDA's intent to recognize the differences between outsourcing facilities and conventional drug manufacturers and to tailor CGMP requirements to the nature of the specific compounding operations conducted by outsourcing facilities while maintaining the minimum standards necessary to protect patients from the risks of contaminated or otherwise substandard drug products.

The comment period on the initial draft guidance ended on September 2, 2014. FDA received 26 comments on the draft guidance. In response to received comments or on its own initiative, FDA made changes and updates in the revised draft guidance as follows.

FDA received a number of comments regarding the requirements in FDA regulations applicable to nonsterile drug products because the draft guidance focused primarily on sterile compounding. To address these comments, the revised draft guidance differentiates between requirements applicable to sterile drug products and nonsterile drug products where appropriate. The revised draft guidance also distinguishes the risks presented by using sterile and nonsterile components in producing sterile drug products and offers recommendations and policies on quality control commensurate with the risk. Further, the revised draft guidance addresses concerns raised regarding FDA's policies in several other areas. FDA made significant revisions to address comments on (1) stability testing, including the assignment of a beyond use date (BUD) as an expiration date; (2) release testing; (3) the potential use of a drug master file to address contract laboratory testing arrangements and testing of component quality before use in compounding; (4) the use of accredited third-party laboratories to perform testing; (5) a clear definition of ''in-use time,'' distinguishing it from ''BUD'' and ''expiration date''; and (6) reserve samples.

We note that the default BUDs and storage conditions associated with nonsterile drug products described in this revised draft guidance differ from those described for nonsterile repackaged drug products in FDA's guidance for industry entitled ''Repackaging of Certain Human Drug Products by Pharmacies and Outsourcing Facilities'' (Repackaging guidance). FDA believes that the BUDs described in this revised draft CGMP guidance are also relevant to nonsterile drug products repackaged by outsourcing facilities. When this guidance is finalized, we intend to make conforming revisions to the BUDs for repackaged nonsterile drug products in the Repackaging guidance, as appropriate.

Finally, this revised draft contains revisions to the conditions under which the Agency generally would not intend to take regulatory action regarding the requirement to test the finished product before release (see § 211.165 (21 CFR 211.165)). These revisions make a broader range of production volumes eligible for the relevant enforcement policy, which we believe would encourage additional compounders to register as outsourcing facilities. Compared to compounders that are not registered under section 503B of the

FD&C Act, outsourcing facilities are subject to increased Federal oversight through FDA inspection on a risk-based schedule, as well as to additional standards that help to assure the quality of their compounded drug products. Outsourcing facilities produce drug products for hospitals, clinics, or healthcare practitioners to keep on hand as ''office stock'' for patients who present with an immediate need for them. The revised draft guidance addresses standards critical to reducing the risk of patient harm while balancing appropriate flexibility. FDA is seeking public comment on whether the conditions outlined in the revised draft appropriately balance the risks and needs associated with drugs produced for office stock, including comments on the production volumes specified in the guidance.

This revised 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 ''Current Good Manufacturing Practice—Guidance for Human Drug Compounding Outsourcing Facilities Under Section 503B of the FD&C Act.'' 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. This guidance is not subject to Executive Order 12866.

II. Paperwork Reduction Act of 1995

Under the PRA (44 U.S.C. 3501–3520), Federal Agencies must obtain approval from OMB for each collection of information that 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** for 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 collection of information associated with this document, FDA invites comments on these topics: (1) Whether the proposed information collected 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 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.

1. Quality Assurance Activities

A quality control unit must be established by outsourcing facilities to oversee various aspects of drug production and to monitor quality assurance (see, *e.g.,* § 211.22 (21 CFR 211.22)). The responsibilities of the quality control unit must be established in procedures (§ 211.22(d)) and should include investigations and development and oversight of appropriate corrective and preventive actions regarding results of tests and examinations, unexpected results or trends, failures that occur during validation or revalidation of sterilization or depyrogenation processes, stability failures, environmental and personnel monitoring results that exceed alert or action limits, process deviations or equipment malfunctions that involve critical equipment, and complaints that indicate possible drug product contamination or other risks to patients. The quality control unit must periodically (at least annually) review records of compounding operations to evaluate the quality standards for each drug product to determine the need for changes in specifications or control procedures (21 CFR 211.180(e)).

FDA estimates that annually approximately 74 outsourcing facilities [1] (''No. of Recordkeepers'' in table 1, row 1) will individually establish approximately 13 procedures on the responsibilities of the quality control unit (''No. of Records per Recordkeeper'' in table 1, row 1) as described in section III.A of the guidance. FDA also estimates that preparing and maintaining these procedures will take approximately 3 hours for each record (''Average Burden per Recordkeeping'' in table 1, row 1).

2. Facility Design

The revised draft guidance describes those elements of facility design of outsourcing facilities that are considered critical to assuring the quality of sterile drug products at those facilities. For example, the draft guidance states that sterile drugs should be produced only in ISO 5 (International Organization for Standardization) or better air quality and that the ISO 5 zone or critical area must be qualified (*i.e.,* shown to meet the specifications) (see §§ 211.42 and 211.113(b) (21 CFR 211.42 and 211.113(b))). The revised draft guidance lists certain studies and tests that should be successfully performed for outsourcing facilities and states that the results of these studies and tests should be documented.

FDA estimates that annually approximately 74 outsourcing facilities (''No. of Recordkeepers'' in table 1, row 2) will individually document approximately 20 studies and tests (''No. of Records per Recordkeeper'' in table 1, row 2) that are critical to assuring the quality of sterile drug products. FDA also estimates that preparing and maintaining each record as described in the guidance will take on average approximately 1.5 hours for each record (''Average Burden per Recordkeeping'' in table 1, row 2).

3. Control Systems and Procedures for Maintaining Suitable Facilities

The revised draft guidance describes procedures that should be established and followed that assign responsibility for sanitation and describe the cleaning schedules, methods, equipment, and materials to be used in cleaning buildings and facilities. For multiuse facilities and nondedicated equipment, changeover and cleaning procedures for equipment and utensils must be established and followed to prevent contamination (see §§ 211.42 and 211.67). Procedures for cleaning and disinfecting must also be established (see §§ 211.42, 211.56, and 211.67). If powder drugs are handled, procedures must be established and followed to appropriately manage cross-contamination risk (§ 211.100 (21 CFR 211.100)). Processes and procedures should minimize contamination risks posed by the number and complexity of manipulations, number of simultaneous operations and workstations, and staging of materials used in the process. Temperature and humidity must be maintained in cleanrooms; such controls are critical to reduce microbial growth (see 21 CFR 211.46). In addition, the guidance describes that procedures should ensure recording of instances when there is a loss of positive pressure in the cleanroom during production.

FDA estimates that annually approximately 74 outsourcing facilities (''No. of Recordkeepers'' in table 1, row 3) will individually establish and maintain approximately 6 records (procedures and documentation) for

[1] This figure is based on the number of outsourcing facilities that were registered on July 27, 2018.

maintaining suitable outsourcing facilities (''No. of Records per Recordkeeper'' in table 1, row 3). FDA also estimates that preparing and maintaining each record as described in the guidance will take on average approximately 5 hours for each record (''Average Burden per Recordkeeping'' in table 1, row 3).

4. Environmental and Personnel Monitoring

The revised draft guidance states that operations and appropriate written procedures designed to prevent microbial contamination include a well-defined and documented program for environmental monitoring that evaluates the potential routes of microbial contamination of the human drug that could arise from the air, surfaces, process, operation, and personnel practices (see §§ 211.42(c)(10)(iv), 211.100, and 211.113(b)). Personnel monitoring should include a routine program for daily/shift monitoring of operators' gloves and an appropriate schedule for monitoring other critical sites of the gown (*e.g.,* gown sleeves for hood work) during or immediately after completion of aseptic operations; establish and justify limits that are based on the criticality of the operation relative to the contamination risk to the product; and call for an investigation of results that exceed the established levels or demonstrate an adverse trend, a determination of the impact on the sterility assurance of finished products intended to be sterile, and the development and execution of appropriate corrective actions. This monitoring should take place before planned disinfection so that actual operating conditions are being assessed. In addition, an outsourcing facility or its contract laboratory should establish procedures for establishing the validity of media if microbiological media used in performing tests, including environmental and personnel monitoring, are not purchased from a qualified supplier.

FDA estimates that annually approximately 74 outsourcing facilities (''No. of Recordkeepers'' in table 1, row 4) will individually establish approximately 1,200 environmental and personnel monitoring procedures and records to document test results (''No. of Records per Recordkeeper'' in table 1, row 4) for aseptic processing areas. FDA also estimates that preparing and maintaining the environmental and personnel monitoring procedures as described in the guidance will take on average approximately 0.25 hours for each record (''Average Burden per Recordkeeping'' in table 1, row 4).

5. Containers and Closures

Scientifically sound and appropriate criteria for containers and closures must be established to ensure that containers and closures used for drug products are suitable for each drug product for which they will be used (see § 211.160(b) (21 CFR 211.160(b))). Appropriate procedures must be established for testing the containers and closures to determine whether they meet the criteria for use, and the tests and results must be documented (see 21 CFR 211.84(d)(3) and 211.184). Procedures for storage, if appropriate, of sterilized containers or closures must be established in a manner to prevent contamination and to maintain sterility (see 21 CFR 211.80(a) and (b)).

FDA estimates that annually approximately 74 outsourcing facilities (''No. of Recordkeepers'' in table 1, row 5) will individually establish and maintain approximately 300 procedures and pieces of documentation for testing containers and closures (''No. of Records per Recordkeeper'' in table 1, row 5) in the aseptic processing areas. FDA also estimates that preparing and maintaining these procedures and documentation as described in the guidance will take on average approximately 0.25 hours for each record (''Average Burden per Recordkeeping'' in table 1, row 5).

6. Equipment

Procedures should be established and records maintained for routine calibration and maintenance of equipment (mechanical, electronic, or automated).

FDA estimates that annually approximately 74 outsourcing facilities (''No. of Recordkeepers'' in table 1, row 6) will individually establish and maintain approximately 150 procedures and pieces of documentation for the calibration and maintenance of equipment (''No. of Records per Recordkeeper'' in table 1, row 6). FDA also estimates that preparing and maintaining these records will take on average approximately 0.25 hours for each record (''Average Burden per Recordkeeping'' in table 1, row 6).

7. Components

Procedures should be established and records maintained concerning the source and quality of components such as raw materials or ingredients used in producing nonsterile and sterile drug products at outsourcing facilities. The revised draft guidance also states that FDA generally does not intend to take regulatory action against an outsourcing facility regarding testing components if an adequate supplier quality agreement is in place and maintained appropriately.

FDA estimates that annually approximately 74 outsourcing facilities (''No. of Recordkeepers'' in table 1, row 7) will individually establish and maintain approximately 150 records of testing to ensure the quality of components used in producing drug products, as recommended in the guidance (''No. of Records per Recordkeeper'' in table 1, row 7). FDA also estimates that preparing and maintaining these records will take on average approximately 4 hours for each record (''Average Burden per Recordkeeping'' in table 1, row 7).

8. Production and Process Controls

Production and process documentation and procedures, such as batch records, must be established to assure the quality of drug products at outsourcing facilities (see § 211.100). Training on aseptic technique, cleanroom behavior, gowning, and procedures covering aseptic manufacturing area operations must be established (see 21 CFR 211.25(a)). The validation of sterilization operations (*e.g.,* holding vessels, filling equipment, lyophilizers) and periodic verification activities and results must be documented (see § 211.113(b)).

FDA estimates that annually approximately 74 outsourcing facilities (''No. of Recordkeepers'' in table 1, row 8) will individually establish and maintain approximately 1,325 records pertaining to production and process controls, such as validation procedures and training, to ensure the quality of sterile drug products (''No. of Records per Recordkeeper'' in table 1, row 8). FDA also estimates that preparing and maintaining these records, as described in the guidance, will take on average approximately 0.25 hours for each record (''Average Burden per Recordkeeping'' in table 1, row 8).

9. Release Testing

Drug products produced at outsourcing facilities must be tested to determine whether they meet final product specifications before release for distribution, and procedures for final release testing must be established and followed (§§ 211.165 and 211.167).

FDA estimates that annually approximately 74 outsourcing facilities (''No. of Recordkeepers'' in table 1, row 9) will individually establish and maintain approximately 1,725 records pertaining to final release testing of drug products, including release testing

procedures and documentation (''No. of Records per Recordkeeper'' in table 1, row 9). FDA also estimates that preparing and maintaining these records, as described in the guidance, will take on average approximately 1.5 hours for each record (''Average Burden per Recordkeeping'' in table 1, row 9).

If sterility testing is not completed before release under certain conditions described in Appendix A of the guidance, procedures should be established that specify that if the product fails to meet a criterion for sterility, all healthcare and other facilities that received the product should be immediately notified of the test results and provided with any appropriate information and recommendations to aid in the treatment of patients; the notification should be documented; and FDA should be notified in writing.

FDA estimates that annually approximately 10 outsourcing facilities (''No. of Respondents'' in table 2, row 1) will individually send approximately 1 notification of test results to all healthcare and other facilities that received the drug product and provide them with any appropriate information and recommendations to aid in the treatment of patients (No. of Disclosures per Respondent'' in table 2, row 1). FDA also estimates that preparing and sending each notification will take approximately 5 hours (''Average Burden per Disclosure'' in table 2, row 1).

FDA also estimates that annually approximately 10 outsourcing facilities (''No. of Respondents'' in table 3) will individually submit to FDA 1 notification of the test results for any drug product that fails to meet a sterility criterion (''No. of Responses per Respondent'' in table 3). Preparing and submitting this information will take approximately 5 hours per notification (''Average Burden per Response'' in table 3).

10. Laboratory Controls

Each laboratory used to conduct testing of components, in-process materials, and finished drug products for outsourcing facilities must follow written procedures for the conduct of each test and must document the results; establish sampling and testing procedures to ensure that components, in-process materials, and drug products conform to the product specifications; keep complete records of all tests performed to ensure compliance with established specifications and standards, including examinations and assays; and, if using a validated or an established compendial test, verify and document that the test procedure works under the conditions of actual use (see §§ 211.160 and 211.194).

FDA estimates that annually approximately 74 outsourcing facilities (''No. of Recordkeepers'' in table 1, row 10) will individually establish and maintain approximately 200 laboratory records as described in the guidance (''No. of Records per Recordkeeper'' in table 1, row 10). FDA also estimates that preparing and maintaining these records will take on average approximately 0.5 hours for each record (''Average Burden per Recordkeeping'' in table 1, row 10).

11. Stability/Expiration Dating

Stability testing is used to ensure that a drug product will retain its quality (*e.g.,* strength) and remain sterile, if applicable, through the labeled expiration date. The draft guidance states that procedures established by outsourcing facilities for assessing the stability of drug products must include the following: Using stability-indicating test methods that are reliable, meaningful, and specific; evaluating samples of the drug product in the same container-closure system in which the drug product will be marketed; evaluating samples for stability that are representative of the lot or batch from which they were obtained and are stored under suitable conditions; and testing to evaluate antimicrobial effectiveness for drug products labeled or intended to be multiple dose (see §§ 211.122, 211.160, and 211.166). The guidance states that regardless of whether an expiration date or BUD to be used as an expiration date is used, container-closure integrity testing and antimicrobial effectiveness testing (for products labeled as multiple dose) are required to be completed before a batch is released (see §§ 211.166 and 211.167). Each of these studies only needs to be conducted once for each formulation and container-closure system, and a bracketing or matrixing approach can be considered to minimize the amount of testing needed. Outsourcing facilities are also responsible for including appropriate labeled directions for use for drug products, which may include in-use time if the product requires additional manipulation before administration. Appropriate studies, including stability studies, would need to support the stated in-use time.

FDA estimates that annually approximately 74 outsourcing facilities (''No. of Recordkeepers'' in table 1, row 11) will individually establish and maintain approximately 75 procedures for stability studies to determine an expiration date (''No. of Records per Recordkeeper'' in table 1, row 11) for drug products. FDA also estimates that preparing and maintaining these procedures as described in the guidance will take approximately 5 hours for each record (''Average Burden per Recordkeeping'' in table 1, row 11).

FDA also estimates that annually approximately 74 outsourcing facilities (''No. of Respondents'' in table 2, row 2) will add approximately 540 expiration dates to the labeling of drug products (''No. of Disclosures per Respondent'' in table 2, row 2). FDA also estimates that preparing the labeling will take approximately 0.25 hours (''Average Burden per Disclosure'' in table 2, row 2).

12. Packaging and Labels

Packaging of drugs must ensure the sterility, if applicable, and integrity of the product until it is administered to a patient, product labels must contain required information, and labeling operations must include controls to prevent mixups (see §§ 211.94, 211.122, 211.125, 211.130, and 211.134). The following must be implemented by outsourcing facilities for packaging and labeling operations to ensure the quality of drug products: The container, closure, and packaging systems adequately protect against foreseeable external factors in storage, shipment, and use that can cause contamination or deterioration; packaging records include specimens or copies of all labels used; adequate controls are established for issuing labels, examining issued labels, and reconciling used labels to prevent mixups; different labeling and packaging operations are adequately separated to prevent mixups; and controls are established that ensure proper identification of any filled containers of products that are stored unlabeled for any period of time (see §§ 211.94, 211.122, 211.125, 211.130, 211.134, and 211.188).

FDA estimates that annually approximately 74 outsourcing facilities (''No. of Recordkeepers'' in table 1, row 12) will individually establish and maintain approximately 20 procedures for packaging and labeling operations (''Records per Recordkeeper'' in table 1, row 12) for drug products. FDA also estimates that preparing and maintaining these procedures as described in the guidance will take approximately 5.5 hours for each record (''Average Burden per Recordkeeping'' in table 1, row 12).

13. Reserve Samples

An appropriately identified reserve sample that is representative of each lot or batch of drug product must be retained and stored under conditions

consistent with product labeling (21 CFR 211.170).

FDA estimates that annually approximately 74 outsourcing facilities (''No. of Recordkeepers'' in table 1, row 13) will individually establish and maintain approximately 12 procedures and records for reserve samples (''Records per Recordkeeper'' in table 1, row 13) for drug products. FDA also estimates that preparing and maintaining these procedures and records as described in the guidance will take approximately 0.5 hours for each record (''Average Burden per Recordkeeping'' in table 1, row 13).

FDA estimates the burden of this collection of information as follows:

TABLE 1—ESTIMATED ANNUAL RECORDKEEPING BURDEN [1]

Activity	Number of recordkeepers	Number of records per recordkeeper	Total annual records	Average burden per recordkeeping	Total hours
Quality assurance activities	74	13	962	3	2,886
Facility design	74	20	1,480	1.5	2,220
Control systems and procedures for maintaining suitable facilities.	74	6	444	5	2,220
Environmental and personnel monitoring	74	1,200	88,800	0.25 (15 minutes)	22,200
Containers and closures	74	300	22,200	0.25 (15 minutes)	5,550
Equipment	74	150	11,100	0.25 (15 minutes)	2,775
Components	74	150	11,100	4	44,400
Production and process controls	74	1,325	98,050	0.25 (15 minutes)	24,513
Release testing	74	1,725	127,650	1.5	191,475
Laboratory controls	74	200	14,800	0.5 (30 minutes)	7,400
Stability/Expiration dating	74	75	5,550	5	27,750
Packaging and labels	74	20	1,480	5.5	8,140
Reserve samples	74	12	888	0.5 (30 minutes)	444
Total					341,973

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

TABLE 2—ESTIMATED ANNUAL THIRD-PARTY DISCLOSURE BURDEN [1]

Type of disclosure	Number of respondents	Number of disclosures per respondent	Total annual disclosures	Average burden per disclosure	Total hours
Notification that a drug product fails to meet a sterility criterion.	10	1	10	5	50
An expiration date is added to the drug product's label.	74	540	39,960	0.25 (15 minutes)	9,990
Total					10,040

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

TABLE 3—ESTIMATED ANNUAL REPORTING BURDEN [1]

Type of reporting	Number of respondents	Number of responses per respondent	Total annual responses	Average burden per response	Total hours
Notification to FDA that a drug product fails to meet a sterility criterion	10	1	10	5	50

[1] 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 *https://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/default.htm* or *https://www.regulations.gov.*

Dated: December 4, 2018.

Leslie Kux,

Associate Commissioner for Policy.

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DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. FDA–2018–N–1990]

Su-Chiao Kuo: Debarment Order

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice.

SUMMARY: The Food and Drug Administration (FDA) is issuing an order under the Federal Food, Drug, and Cosmetic Act (FD&C Act) debarring Dr. Su-Chiao Kuo for a period of 3 years from providing services in any capacity to a person that has an approved or pending drug product application. FDA bases this order on a finding that Dr. Kuo was convicted of a misdemeanor under the FD&C Act for causing the introduction or delivery for introduction into interstate commerce of prescription drugs that were misbranded. In addition, FDA has determined that the type of conduct that served as the basis for the conviction undermines the process for the regulation of drugs. Dr. Kuo was given notice of the proposed