

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 See the **SUPPLEMENTARY INFORMATION** section for electronic access to the draft guidance document.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:** Richard (Rik) Lostritto, Center for Drug Evaluation and Research, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 51, Rm. 4148, Silver Spring, MD 20993-0002, 301-796-1697.

**SUPPLEMENTARY INFORMATION:**

**I. Background**

FDA is announcing the availability of a draft guidance for industry entitled "Regulatory Classification of Pharmaceutical Co-Crystals." This guidance provides NDA and ANDA applicants with information on the appropriate regulatory classification of pharmaceutical co-crystal solid-state forms.

Co-crystals are crystalline materials composed of two or more different molecules, typically drug and co-crystal formers ("coformers"), in the same crystal lattice. Pharmaceutical co-crystals have opened up opportunities for engineering solid-state forms beyond conventional solid-state forms of an active pharmaceutical ingredient (API), such as salts and polymorphs. Co-crystals can be tailored to enhance drug product bioavailability and stability and to enhance the processability of APIs during drug product manufacture. Another advantage of co-crystals is that they generate a diverse array of solid-state forms for APIs that lack ionizable functional groups, which is a prerequisite for salt formation.

This guidance revises the guidance for industry "Regulatory Classification of Pharmaceutical Co-Crystals" issued in April 2013, which classifies co-crystals as a drug product intermediate (or as an in-process material). This classification has contributed to uncertainty regarding the interpretation of the guidance because in a commercial setting, co-crystals are typically manufactured in drug substance facilities, yet when classified as a drug product intermediate, additional current good manufacturing practice requirements apply. Therefore, the guidance has not been conducive to the development of co-crystals. In response to this and other feedback from stakeholders, FDA has reconsidered the appropriate classification of co-crystals. This revision addresses the concern by providing information on the appropriate classification of co-crystal

solid-state forms, the data that should be submitted to support the classification, and the regulatory implications of such a classification.

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 regulatory classification of pharmaceutical co-crystals. 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. The Paperwork Reduction Act of 1995**

This guidance refers to previously approved collections of information found in FDA regulations. This guidance refers to information collection provisions that are subject to review by the Office of Management and Budget (OMB) under the Paperwork Reduction Act of 1995 (44 U.S.C. 3501-3520). The collections of information in 21 CFR 314.50(d)(1) and 314.94(a)(5) and (a)(9) have been approved under OMB control number 0910-0001.

**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 <http://www.regulations.gov>.

Dated: August 11, 2016.

**Jeremy Sharp,**

*Deputy Commissioner for Policy, Planning, Legislation, and Analysis.*

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**DEPARTMENT OF HEALTH AND HUMAN SERVICES**

**Food and Drug Administration**

[Docket No. FDA-2011-N-0144]

**Agency Information Collection Activities; Submission for Office of Management and Budget Review Comment Request; Voluntary Qualified Importer Program Guidance for Industry**

**AGENCY:** Food and Drug Administration, HHS.

**ACTION:** Notice.

**SUMMARY:** The Food and Drug Administration (FDA) is announcing that a proposed collection of information has been submitted to the Office of Management and Budget

(OMB) for review and clearance under the Paperwork Reduction Act of 1995.

**DATES:** Fax written comments on the collection of information by September 16, 2016.

**ADDRESSES:** To ensure that comments on the information collection are received, OMB recommends that written comments be faxed to the Office of Information and Regulatory Affairs, OMB, Attn: FDA Desk Officer, FAX: 202-395-7285, or emailed to [oir\\_submission@omb.eop.gov](mailto:oir_submission@omb.eop.gov). All comments should be identified with the OMB control number 0910-NEW and title, "Voluntary Qualified Importer Program Guidance for Industry." Also include the FDA docket number found in brackets in the heading of this document.

**FOR FURTHER INFORMATION CONTACT:** FDA PRA Staff, Office of Operations, Food and Drug Administration, Three White Flint North, 11601 Landsdown St., 10A63, North Bethesda, MD 20852, [PRAStaff@fda.hhs.gov](mailto:PRAStaff@fda.hhs.gov).

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

**FDA's Voluntary Qualified Importer Program (VQIP); Guidance for Industry OMB Control Number 0910-NEW**

The FDA Food Safety Modernization Act (FSMA) (Pub. L. 111-353) enables FDA to better protect public health by helping to ensure the safety and security of the food supply. It enables FDA to focus more on preventing food safety problems rather than relying primarily on reacting to problems after they occur. FSMA recognizes the important role industry plays in ensuring the safety of the food supply, including the adoption of modern systems of preventive controls in food production. Under FSMA, those that import food have a responsibility to ensure that their suppliers produce food that meets U.S. safety standards.

FSMA also requires FDA to establish a voluntary, fee-based program for the expedited review and importation of foods by importers who achieve and maintain a high level of control over the safety and security of their supply chains. This control includes importation of food from facilities that have been certified under FDA's accredited third-party audit program, as well as other measures that support a high level of confidence in the safety and security of the food they import. Expedited entry incentivizes importers to adopt a robust system of supply chain management and further benefits public

health by allowing FDA to focus its resources on food entries that pose a higher risk to public health.

Section 302 of FSMA amended the Federal Food, Drug, and Cosmetic Act (the FD&C Act) by adding new section 806, Voluntary Qualified Importer Program (21 U.S.C. 384b). Section 806(a)(1) of the FD&C Act directs FDA to establish this voluntary program for the expedited review and importation of food, and to establish a process for the issuance of a facility certification to accompany food offered for importation by importers participating in VQIP. Section 806(a)(2) directs FDA to issue a guidance document related to participation in, revocation of such participation in, reinstatement in, and compliance with VQIP.

Accordingly, in the **Federal Register** of June 5, 2015 (80 FR 32136), FDA published a notice announcing the

availability of a draft guidance entitled “FDA’s Voluntary Qualified Importer Program,” and invited public comment regarding the guidance as well as the information collection provisions associated with the guidance (80 FR 32136 at 32138). In response to the solicitation of comments regarding the information collection provisions, the Agency received multiple comments. Two comments suggested that FDA’s recordkeeping and reporting estimates were too low. Because neither comment provided justification for why the burden calculation might be too low or offered alternative calculations, we have retained our original estimates noting that, upon implementation of the program, we will again invite public comment on the information collection burden and make adjustments to our estimates accordingly. One comment attributed costs to the information

collection but did not provide a basis for the calculations provided. We therefore have not adopted the comment, but again note that public input will be solicited on the information collection upon implementation of the program.

Finally, one comment objected to the provision regarding respondents obtaining a Dun & Bradstreet (D&B) Data Universal Numbering System (DUNS) number and providing it to the Agency. We have determined that the DUNS number is an appropriate unique facility identifier during Foreign Supplier Verification Program (FSVP) rulemaking. We expect that most VQIP importers will also be FSVP importers and will have obtained a DUNS number.

*Description of Respondents:* Respondents to the collection are importers of human or animal food.

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

TABLE 1—ESTIMATED ONE-TIME RECORDKEEPING BURDEN <sup>1</sup>

Information collection activity	Number of recordkeepers	Number of records per recordkeeper	Total one-time records	Average burden per recordkeeping	Total hours
Quality Assurance Program (QAP) preparation .....	200	1	200	160	32,000

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

We estimate it will take a VQIP applicant no longer than 10 hours to develop its QAP, including compiling its company profile, organizational structure, corporate quality policy statement, procedures for QAP implementation, food safety and food defense policies and procedures, and procedures for record retention. On average, the preparation of a QAP by a VQIP applicant is estimated at

approximately 160 hours (110 + 40 + 10). In estimation of the one-time recordkeeping burden to prepare a QAP manual, we assume that VQIP importers do not already have a similar manual in place (e.g., food safety plan under the Current Good Manufacturing Practice and Hazard Analysis and Risk-Based Preventive Controls for Human Food regulation (21 CFR part 117); food defense plan under the Focused

Mitigation Strategies to Protect Food Against Intentional Adulteration regulation (IA regulation) (21 CFR part 121)). The one-time recordkeeping burden for 200 VQIP applicants to prepare QAPs is estimated at 32,000 hours (200 applicants × 160 hours/ applicant) (see table 1). To the extent that some importers do have QAP manuals in place, the burden would be overestimated.

TABLE 2—ESTIMATED ANNUAL RECORDKEEPING BURDEN <sup>1</sup>

Information collection activity	Number of recordkeepers	Number of records per recordkeeper	Total annual records	Average burden per recordkeeping	Total hours
QAP modification .....	200	1	200	16	3,200

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

A VQIP importer is expected to update its QAP on an ongoing basis. We estimate it would take 10 percent of the effort to prepare the QAP, or 16 hours, to update the QAP each year. Therefore, we estimate the annual recordkeeping burden of modification of the QAP for 200 VQIP importers at 3,200 hours (200

importers × 16 hours/importer). The VQIP food defense security criterion is similar to the Food Defense Plan requirement under § 121.126 (21 CFR 121.126) in the IA regulation. Under the IA regulation, the food defense plan must include the written identification of actionable process steps, focused

mitigation strategies, procedures for monitoring, corrective action procedures, and verification procedures. Therefore, we estimate that, on average, it would take 40 hours for an applicant to prepare the food defense portion of the VQIP QAP.

TABLE 3—ESTIMATED ONE-TIME REPORTING BURDEN <sup>1</sup>

Information collection activity	Number of respondents	Number of responses per respondent	Total one-time responses	Average burden per response	Total hours
Initial VQIP application .....	100	1	100	80	8,000
Initial VQIP application w/additional information .....	100	1	100	100	10,000
<b>Total .....</b>					<b>18,000</b>

<sup>1</sup> There are no capital or operating and maintenance costs associated with the collection of information.

The guidance will inform food importers of application procedures for VQIP. We estimate that up to 200 qualified importers will be accepted in the first year of VQIP. We estimate that it will take 80 person-hours to compile all the relevant information and complete the application for the VQIP

program. For the purpose of this analysis, we assume that 50 percent of all applications received will require additional information and it would take an additional 20 person-hours by the importer to provide that information. Therefore, we estimate that 100 importers will spend 8,000 hours

(80 hours/importer × 100 importers) and 100 importers will spend 10,000 hours (100 hours/importer × 100 importers) to submit their initial VQIP applications for a total one-time reporting burden of 18,000 hours (see table 3).

TABLE 4—ESTIMATED ANNUAL REPORTING BURDEN <sup>1</sup>

Information collection activity	Number of responses	Number of responses per respondent	Total annual responses	Average burden per response	Total hours
Subsequent year VQIP application .....	200	1	200	20	4,000
Request to reinstate participation .....	2	1	2	10	20
<b>Total .....</b>					<b>4,020</b>

<sup>1</sup> There are no capital or operating and maintenance costs associated with the collection of information.

The guidance states that each VQIP participant will submit to FDA a notice of intent to participate in VQIP on an annual basis. We expect that each of the expected 200 importers in VQIP would apply in the subsequent year to participate in VQIP. We expect that an application to participate in VQIP in a subsequent year will take significantly less time to prepare than the initial application. We use 25 percent of the amount of effort to prepare and submit the initial application for acceptance in VQIP. Therefore, it is expected that, on average, each VQIP importer will spend 20 hours to complete and submit a VQIP application for each subsequent year. The annual burden of completing a subsequent year application to participate in VQIP status by 200 importers is estimated at 4,000 hours (200 applications × 20 hours/application) (see table 4).

Finally, we have added to the VQIP estimated annual reporting burden an estimate of the burden associated with importers' requests to reinstate participation in VQIP after their participation is revoked. We believe most participants will not need to use this provision, and we have included an estimate that reflects this. Upon implementation of the VQIP, we will reevaluate our estimate for future OMB submission and revise it accordingly.

Dated: August 12, 2016.  
**Jeremy Sharp,**  
*Deputy Commissioner for Policy, Planning, Legislation, and Analysis.*  
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**DEPARTMENT OF HEALTH AND HUMAN SERVICES**

**Food and Drug Administration**

[Docket No. FDA-2015-D-5073]

**Use of Nucleic Acid Tests To Reduce the Risk of Transmission of Hepatitis B Virus From Donors of Human Cells, Tissues, and Cellular and Tissue-Based Products; 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 document entitled “Use of Nucleic Acid Tests to Reduce the Risk of Transmission of Hepatitis B Virus from Donors of Human Cells, Tissues, and Cellular and Tissue-Based Products; Guidance for Industry.” The guidance document provides establishments that make donor eligibility determinations

for donors of human cells, tissues, and cellular and tissue-based products (HCT/Ps), with recommendations concerning the use of FDA-licensed nucleic acid tests (NAT) in donor testing for hepatitis B virus (HBV) deoxyribonucleic acid (DNA). The guidance finalizes the draft guidance of the same title dated January 2016 and supplements previous FDA recommendations to HCT/P establishments concerning donor testing for hepatitis B surface antigen (HBsAg) and total antibody to hepatitis B core antigen (anti-HBc), in the document entitled “Guidance for Industry: Eligibility Determination for Donors of Human Cells, Tissues, and Cellular and Tissue-Based Products (HCT/Ps)” dated August 2007 (2007 Donor Eligibility Guidance).

**DATES:** Submit either electronic or written comments on Agency guidances at any time.

**ADDRESSES:** You may submit comments as follows:

*Electronic Submissions*

Submit electronic comments in the following way:

- *Federal eRulemaking Portal:* <http://www.regulations.gov>. Follow the instructions for submitting comments. Comments submitted electronically, including attachments, to