4164-01-P

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. FDA-2020-N-2018]

Quality Management Maturity for Active Pharmaceutical Ingredients Pilot Program for Foreign Facilities; Program Announcement

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice.

SUMMARY: The Food and Drug Administration (FDA or Agency), Center for Drug Evaluation and Research (CDER) is announcing its Quality Management Maturity for Active Pharmaceutical Ingredients Pilot Program (QMM API Pilot Program) for foreign facilities manufacturing active pharmaceutical ingredients (APIs), including facilities manufacturing drug substance intermediates used to produce APIs, that are used in FDA-regulated prescription and over-the-counter (OTC) drug products. The purpose of the QMM API Pilot Program is to gain insight from third-party assessments of a facility's quality management system to inform future development of an FDA rating system to characterize quality management maturity (QMM). Such a rating system would allow a cross-sectional comparison of facilities. Facilities that choose to disclose their facility ratings to drug product manufacturers could benefit from a competitive advantage, as knowledge of QMM ratings would enable drug product manufacturers to differentiate among facilities when purchasing APIs. This notice invites foreign facilities that are interested in participating in the QMM API Pilot Program to submit a request to participate.

DATES: FDA will accept requests to participate in the QMM API Pilot Program through November 30, 2020, and the QMM API Pilot Program will run through December 31, 2021. See

the "Participation" section for selection criteria and instructions on how to submit a request to participate.

FOR FURTHER INFORMATION CONTACT: *For general questions about the QMM API Pilot Program*: Jennifer Maguire, Center for Drug Evaluation and Research (CDER), 10903 New Hampshire Ave., Bldg. 51, Rm. 4134, Silver Spring, MD 20993, 240-402-4817, Jennifer.Maguire@fda.hhs.gov.

To submit a request to participate in the QMM API Pilot Program: Seongjin (Cindy) Pak, CDER, 10903 New Hampshire Ave., Bldg. 51, Rm. 4220, 301-796-1673, Seongjin.Pak@fda.hhs.gov.

SUPPLEMENTARY INFORMATION:

I. Background

In 2002, FDA launched an initiative "Pharmaceutical CGMPs for the 21st Century--A Risk-Based Approach," to enhance and modernize the regulation of pharmaceutical manufacturing and product quality.[1] One objective, among others, was to facilitate the implementation of a modern, risk-based pharmaceutical quality assessment system. The desired goal has been described as a maximally efficient, agile, flexible pharmaceutical manufacturing sector that reliably produces high-quality drug products without extensive regulatory oversight.

There has been significant progress toward this vision as evidenced by FDA programs and initiatives in such areas as pharmaceutical development and quality by design, quality risk management and pharmaceutical quality systems, process validation, and emerging technologies. These programs and initiatives promote use of the best pharmaceutical science and engineering principles throughout the product life cycle.

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[1] See FDA's final report: "Pharmaceuticals CGMPs for the 21st Century--A Risk-Based Approach" (September 2004) at https://www.fda.gov/media/77391/download.

Another example is the FDA Quality Metrics Program, described in the November 2016 revised draft guidance for industry, "Submission of Quality Metrics Data" (81 FR 85226). When final, this guidance will represent FDA's current thinking on this issue. In June 2018, FDA initiated two voluntary programs that sought additional industry input on quality metrics. FDA solicited industry participation for a Site Visit Program (83 FR 30751) for manufacturing establishments to present the advantages and challenges associated with implementing and managing a quality metrics program and for a Quality Metrics Feedback Program (83 FR 30748) to engage stakeholders in identifying mutually useful and objective quality metrics.

The Agency continues to develop the FDA Quality Metrics Program but recognizes that quality metrics are only one element within a manufacturer's larger effort to increase the maturity of their quality management system. Manufacturers that demonstrate QMM[2] operate under an enhanced quality management system that exceeds the minimum standards specified in current good manufacturing practice regulations and focuses on continual improvement. Characteristics of a mature quality management system include, for example, the ability to consistently and reliably deliver quality product over time, operational stability, and a strong quality culture. Additionally, for manufacturers with a mature quality management system, FDA can exercise a more flexible regulatory approach, leading toward the goal of producing high-quality drug products without extensive regulatory oversight.

A transparent method of evaluating and communicating QMM is needed to fully realize the 21st century pharmaceutical quality vision. Toward that end, FDA is announcing the start of the QMM API Pilot Program. Through this pilot program, a third-party contractor identified by the FDA will conduct an assessment of a facility's quality management system, accompanied by

[2] For additional information on quality management maturity, see FDA's Report: "Drug Shortages: Root Causes and Potential Solutions" (October 2019) at https://www.fda.gov/media/131130/download.

FDA staff. The Agency will gain insight from the results of the QMM assessments to inform the development of a rating system to measure and rate QMM. Assessments under the QMM API Pilot Program will cover multiple topics. Examples include but are not limited to:

1. supply chain management;
2. manufacturing strategy and operations;
3. safety, environmental, and regulatory compliance;
4. inventory management;
5. performance management and continual improvement;
6. risk management;
7. management review and responsibility;
8. planning;
9. workforce management;
10. quality culture; and
11. customer experience.

In the same timeframe as the QMM API Pilot Program, FDA will conduct a QMM pilot program for domestic manufacturers of finished dosage forms (FDF). These pilot programs are funded separately and are intended to provide FDA with representative information about QMM from different types of drug manufacturers (API and FDF). Elsewhere in this issue of the *Federal Register*, FDA is publishing "Quality Management Maturity for Finished Dosage Forms Pilot Program for Domestic Drug Product Manufacturers; Program Announcement."

II. Participation

Facilities located outside the United States that manufacture APIs or drug substance intermediates used to produce APIs and are interested in participating in the QMM API Pilot

Program should submit a written request directly to Seongjin (Cindy) Pak (see FOR FURTHER INFORMATION CONTACT). Participation is voluntary. Participants in the Quality Metrics Feedback Program are encouraged to participate in the QMM API Pilot Program. FDA will select up to nine participants for the QMM API Pilot Program. Participation in the QMM API Pilot Program is limited to foreign manufacturing facilities since FDA's funding source for this program is specific to activities related to the surveillance of foreign sites.

A. Selection Criteria

To be considered for the QMM API Pilot Program, participants must meet the following selection criteria:

1. Participant is a facility located outside the United States that manufactures APIs or drug substance intermediates used to produce APIs for FDA-regulated prescription and OTC drug products. Facilities located in Puerto Rico or other U.S. territories are not considered to be foreign facilities and thus are not eligible to participate in the QMM API Pilot Program.
2. All FDA inspection(s) of the manufacturing facility conducted within the 5 years prior to September 15, 2020, received a final classification of "No Action Indicated" or "Voluntary Action Indicated."
3. Participant agrees to:
    a. Permit a third-party contractor to conduct a QMM assessment, whether the assessment is conducted on-site or remotely. FDA will identify an external contractor having the expertise to assess QMM, and FDA staff will join the contractor for the assessment.

b. Collect and submit metric data to FDA and the contractor by an agreed upon date, prior to the assessment. As part of the scoping discussions for the assessment, FDA will provide the facility with templates and additional details about the data collection.

c. Be available for consultations with the contractor and FDA prior to and after the assessment, including discussions regarding the participant's established QMM-related activities and the contractor's post-assessment recommendations regarding these activities.

During this QMM API Pilot Program, the contractor and FDA staff will be available to answer questions and address concerns that arise.

B. Information to Include in the Request

When submitting a request to participate in the QMM API Pilot Program, include the information below to aid in FDA's selection and planning. FDA will not consider requests submitted without the following minimal information:

1. a contact person (name and email);
2 facility location;
3. facility FDA Establishment Identifier and Data Universal Numbering System numbers;
4. a brief description of the manufacturing operations conducted at the facility;
5. preferred dates for the assessment;
6. written confirmation that the facility meets the selection criteria in section II.A, including agreement to items 3a-c;
7. written confirmation that the facility can handle a visit of up to 10 FDA staff and contractors; and

8. a brief description of prior experiences undergoing an assessment related to the maturity of the facility's quality culture, including the name of the organization that conducted the assessment and date of the assessment.

Dated: October 13, 2020.

Lauren K. Roth,

Acting Principal Associate Commissioner for Policy.

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