submit payments. The draft guidance also explains how respondents can request discontinuation from the BPD program as well as how respondents can request to move products to the discontinued section of the biosimilar list. Finally, the draft guidance provides information on the consequences of failing to pay BsUFA II fees, as well as processes for submitting reconsideration and appeal requests. The draft guidance is available on our website at *https://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM584984.pdf.*

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

TABLE 1—ESTIMATED ANNUAL REPORTING BURDEN [1]

Information collection title	Number of respondents	Number of responses per respondent	Total annual responses	Average burden per response (hours)	Total hours
Biosimilar User Fee Cover Sheet; Form FDA 3792	35	1	35	0.5 (30 minutes)	17.5
Annual Survey	35	1	35	1	35
Request for discontinuation from BPD program	2	1	2	1	2
Request to move products to discontinued section of the biosimilar list.	5	1	5	0.5 (30 minutes)	2.5
Total					57

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

We have increased our estimate by an additional 15 respondents since last OMB approval of the information collection. This estimated increase is based on our expectation that participation in the BPD program will continue to grow, consistent with our experience since establishment of the information collection in 2012.

Dated: June 26, 2018.

Leslie Kux,

Associate Commissioner for Policy.

[FR Doc. 2018–14057 Filed 6–28–18; 8:45 am]

BILLING CODE 4164–01–P

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. FDA–2018–N–1903]

Modernizing Pharmaceutical Quality Systems; Studying Quality Metrics and Quality Culture; Quality Metrics Feedback Program

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice.

SUMMARY: The Food and Drug Administration (FDA, Agency, or we) Center for Drug Evaluation and Research (CDER) is announcing two new efforts to gather feedback on the use of quality metrics to modernize pharmaceutical quality systems and advance innovation based on stakeholder feedback. These efforts include Type C formal meeting requests and pre-abbreviated new drug application (pre-ANDA) meeting requests, and a pilot study to gain feedback from those establishments for which Type C formal meetings or pre-ANDA meetings do not apply (*e.g.,* active pharmaceutical ingredients (API) establishments, contract manufacturing organizations, over-the-counter (OTC) monograph products establishments, or marketed unapproved finished drug products establishments). Participation in either of these efforts is voluntary and the programs are intended to foster the joint efforts of FDA and stakeholders to further develop an FDA Quality Metrics Program. The FDA Quality Metrics Program aims to evaluate a new approach for regulatory oversight of pharmaceutical products through the collection of certain quality information developed and maintained in the course of manufacturing drugs under current good manufacturing practices. FDA intends to use quality metrics data to further develop the Agency's risk-based inspection scheduling (*e.g.,* decreased surveillance inspection frequency for certain establishments) to improve the efficiency and effectiveness of establishment inspections, improve FDA's evaluation of drug manufacturing and control operations, and identify situations in which there may be a risk for drug supply disruption.

DATES: Submit a written request to participate in the program by July 29, 2019. See sections II and III.B of this notice for information to include in such requests. FDA will start accepting requests beginning July 30, 2018.

FOR FURTHER INFORMATION CONTACT: Tara Gooen Bizjak, Center for Drug Evaluation and Research, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 51, Rm. 2109, Silver Spring, MD 20993, 301–796–3257, *Tara.Gooen@fda.hhs.gov.*

SUPPLEMENTARY INFORMATION:

I. Background

More than a decade ago, FDA launched an initiative to encourage the implementation of a modern, risk-based pharmaceutical quality assessment system. As part of this initiative, and in recognition of the increasing complexity of pharmaceutical manufacturing, FDA developed a 21st century vision for manufacturing and quality with input from academia and industry. The desired state was described as follows: ''A maximally efficient, agile, flexible pharmaceutical manufacturing sector that reliably produces high-quality drug products without extensive regulatory oversight.'' [1]

There has been significant progress toward this vision in the intervening years, as evidenced by programs and guidance from FDA around major initiatives such as pharmaceutical development and quality by design, quality risk management and pharmaceutical quality systems, process validation, and process analytical technology, among other initiatives. These programs and guidances are intended to promote effective use of the most current pharmaceutical science and engineering principles and knowledge throughout the life cycle of a product.

While much progress has been made, we have not fully realized our 21st century vision for manufacturing and quality. Rather than focusing on use of science- and risk-based principles as described in current good manufacturing practices, many establishments continue to focus on minimum requirements (*e.g.,* check-box approach). Recalls and drug shortages, which are often indications of serious product quality defects caused by drug

[1] See ''FDA Pharmaceutical Quality Oversight: One Quality Voice'' at *https://www.fda.gov/downloads/AboutFDA/CentersOffices/OfficeofMedicalProductsandTobacco/CDER/UCM442666.pdf.*

manufacturing issues, continue to occur.[2] [3] The Agency has found that most drug shortages stem from quality issues (*e.g.,* substandard manufacturing facilities or processes, or significant quality defects are identified in the finished product). These situations necessitate remediation efforts to fix the issue, which in turn may interrupt production and cause a shortage of drugs. Taking action to reduce drug shortages remains a top priority for FDA.

FDA sought input from industry on the establishment of an FDA Quality Metrics Program as another mechanism to promote continual improvement in manufacturing quality. FDA has also consulted with other stakeholders to identify mutually useful and objective quality metrics. The Agency learned that it should perform further studies of the FDA Quality Metrics Program through a pilot program and additional discussions with stakeholders. Based on this input, FDA is initiating this Quality Metrics Feedback Program to assist the Agency in the development of a Quality Metrics Program. Stakeholders are encouraged to participate in these efforts by using the two feedback procedures described below. Additional references may be found at the FDA web page, Quality Metrics for Drug Manufacturing, *https://www.fda.gov/Drugs/DevelopmentApprovalProcess/Manufacturing/ucm526869.htm.*

Based on stakeholder feedback, FDA is presenting two new methods for engaging industry. The approaches announced in this notice provide industry stakeholders with an opportunity to provide information to further the development of the Quality Metrics Program. CDER will also continue to engage with trade associations to gather feedback for industry subsectors.

FDA does not intend to publicly disclose information submitted to the Agency as part of this Quality Metrics Feedback Program that is exempt from disclosure under disclosure laws and regulations. The following types of information may be exempt from public disclosure if not made public by the owner: (1) Commercial relationships; (2) production and sales volume; (3) business plans; and (4) unapproved applications.

II. Type C Formal Meetings and Pre-ANDA Meetings

Applicants who have an interest in participating in this method of the FDA Quality Metrics Feedback Program should submit a written request. New drug application (NDA) applicants or sponsors should follow the procedures for submitting Type C meeting requests as described in the draft guidance for industry entitled ''Formal Meetings Between the FDA and Sponsors or Applicants of PDUFA Products (December 2017).'' [4] The requests should be labeled as ''Type C Meeting—Request to Participate in the Quality Metrics Feedback Program.'' Pre-ANDA applicants or sponsors planning to submit an original or supplemental pre-ANDA should submit a pre-ANDA meeting request to *OPQ-OS-QualityMetrics@fda.hhs.gov* and label it as ''Pre-ANDA Meeting—Request to Participate in the Quality Metrics Feedback Program.''

In addition to the procedures and items outlined in the referenced guidances, a request for a meeting should include the following items:

1. A description of the quality metrics currently used for the product and process in the facility(ies) that are specific to the risks of the facility(ies), products, manufacturing processes, supply chain, and current business decisions (*e.g.,* amount of product held in inventory or days on hand). That is, the metrics which have been determined by the applicant to be most meaningful to product quality and for patient impact.

2. A statement on whether the following quality metrics are measured using consistent definitions: Lot acceptance rate per product or rejection rate, invalidated out-of-specification rate per product, product quality complaint rate, process performance and process capability per product, corrective action and preventive action effectiveness, quality system timeliness, and on-time-in-full fulfillment of orders.

3. A statement that suitably detailed technical definitions for the quality metrics data elements in the previously mentioned items (1) and (2) are established to enable consistent measurement and comparison.

4. A description of the routine assessment and management oversight of quality culture. This assessment should include all levels of staff, from senior management to base level employees, to gauge and shape the behaviors, beliefs, values, morals, conventions, goals, and practices that characterize or are associated with manufacturing at the facility(ies).

5. A description of the ongoing site management and senior management review of the quality metrics program, including identification of areas for continual improvement.

To maximize the benefits of an in-person meeting, FDA prefers that the applicant or sponsor provide a statement of willingness for one or more of the following: (1) To provide access to certain current and historical product-specific measures and the data supporting the measures, including lot acceptance rate or rejection rate, product quality complaint rate, and invalidated out-of-specification rate; (2) to share available information supporting the categories (product specific measurements), where applicable, of process performance and process capability (product specific), corrective and preventive actions (CAPA) effectiveness, quality culture, quality system metrics (*e.g.,* periodic product report on-time rate), and on-time-in-full fulfillment of orders (product specific); and (3) to discuss details of their quality metrics program, including quality metrics data definitions and methods of analyzing available data.

We intend to accept as many meeting requests as Agency resources allow and to focus on establishments that show an interest in engaging in robust discussions regarding their quality metrics programs. FDA expects to notify companies in writing of its decision regarding meeting acceptance within 60 days of receipt of their requests. Although incomplete and/or unclear requests will generally be denied, FDA may contact the applicant to request additional information. Once a meeting is granted, the participant can engage with the Quality Metrics Program team in accordance with existing meeting procedures and guidance(s). FDA anticipates that discussions with stakeholders will help to further develop the Quality Metrics Program and will provide the Agency with information on existing industry practices using modern pharmaceutical quality systems.

III. Pilot Program

A. Participation

Establishments eligible to participate in this voluntary Quality Metrics Pilot

[2] Refer to *https://www.fda.gov/Drugs/DrugSafety/DrugRecalls/default.htm* for more information on drug recalls.

[3] In 2012, for example, based on information collected from manufacturers, FDA determined that 66 percent of disruptions in drug manufacturing were the result of either efforts to address product-specific quality failures or broader efforts to remediate or improve an unsafe manufacturing facility. FDA's ''Strategic Plan for Preventing and Mitigating Drug Shortages,'' see figure 2, at *https://www.fda.gov/downloads/drugs/drugsafety/drugshortages/ucm372566.pdf.*

[4] We update guidances periodically. To make sure you have the most recent version of a guidance, check the FDA Drugs guidance web page at *https://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/default.htm.*

Program are limited to nine or fewer firms that follow the procedures set forth in section III.B and meet the following selection criteria:

1. The company must be a covered establishment. A covered establishment is an owner or operator of an establishment that is engaged in the manufacture, preparation, propagation, compounding, or processing of a covered drug product, or an API used in the manufacture of a covered drug product. A covered drug product is: (1) Subject to an approved application under section 505 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355) or under section 351 of the Public Health Service Act (42 U.S.C. 262); (2) marketed pursuant to an OTC monograph; or (3) a marketed unapproved finished drug product. A covered establishment does not need to be involved in the physical manipulation of a drug.

2. The company must have a quality metrics program that has been developed and implemented by the quality unit and that is used to support product and process quality improvement. The established quality metrics program must include product-specific measurements and include at a minimum: (1) Lot acceptance rate or rejection rate, (2) invalidated out-of-specification rate, and (3) product quality complaint rate. If a product is manufactured at more than one location, these product specific metrics could be limited to operations at the participating covered establishment. To provide feedback on recommended changes in the metrics definitions, send an email to *OPQ-OS-QualityMetrics@fda.hhs.gov.*

The ideal participant in the Quality Metrics Pilot Program will have the following elements in their quality metrics program:

1. Quantitative measurement of quality metrics for the products and processes in the facility(ies) that are specific to the risks of the facility(ies), products, manufacturing processes, supply chain, and current business decisions (*e.g.,* amount of product held in inventory or days on hand);

2. Certain quality metrics measured, such as lot acceptance rate or rejection rate per product, invalidated out-of-specification rate per product, product quality complaint rate, process performance and process capability per product, CAPA effectiveness, quality system timeliness, and on-time-in-full fulfillment of orders;

3. Suitably detailed technical definitions for the quality metrics data elements to enable consistent measurement and comparison;

4. routine assessment and management oversight of quality culture at multiple levels of staff, such as senior management to base level employees, to assess and shape the behaviors, beliefs, values, morals, conventions, goals, and practices that characterize or are associated with manufacturing at the facility(ies); and

5. Ongoing site management and senior management review of the quality metrics with identification of areas for continual improvement.

The establishments that will likely benefit most from the Quality Metrics Pilot Program and discussions with FDA are those that are able to: (1) Provide access to certain current and historical product-specific measures and the data supporting the measures, including lot acceptance rate or rejection rate, product quality complaint rate, and invalidated out-of-specification rate; (2) share available information supporting the following categories (product specific measurements), where applicable, of process performance and process capability (product specific), CAPA effectiveness, quality culture, quality system metrics (*e.g.,* periodic product report on-time rate), and on-time-in-full fulfillment of orders (product-specific); (3) discuss details of their quality metrics program, including quality metrics data definitions and methods of analyzing available data (for comparison purposes, we are interested in establishments that are willing to provide data based on definitions in the draft guidance as well as their preferred definitions); (4) be available for real-time consultations with FDA; (5) provide information about the firm's quality management system related to the quality metrics program; and (6) comment on and discuss their experiences with this Quality Metrics Pilot process.

B. Procedures

To be considered for the voluntary Quality Metrics Pilot Program, a company should submit a statement of interest for participation to *OPQ-OS-QualityMetrics@fda.hhs.gov.* The statement of interest should include agreement to the selection qualities listed in section III.A.

The following captures the proposed process for the Quality Metrics Pilot Program selection:

1. FDA will collect statements of interest for participation in the pilot program beginning July 30, 2018.

2. FDA will select the first nine participants that submit a statement of interest in participation meeting the selection criteria in the first paragraph of section III.A. While any covered establishment meeting the criteria may request inclusion in the pilot program per the first paragraph of section III.A, FDA would prefer that establishments for which Type C formal meetings and pre-ANDA meetings are not applicable use this approach. Additionally, FDA is seeking participants that represent different sectors of the pharmaceutical industry, including companies that manufacture the following types of products: Brand, generics, biotechnology, APIs, and non-application products marketed under the OTC monograph system. Furthermore, we are looking for representation from contract development and manufacturing organizations, establishments with small and large portfolios, and establishments with past or current product availability issues (*e.g.,* history of a drug supply issue or recall).

3. Lessons learned from the initial participants in the pilot program (maximum of nine participants) will help inform FDA's thinking as it refines the Quality Metrics Program.

IV. Beginning Date of the Quality Metrics Pilot Program and Type C Formal Meetings and Pre-ANDA Meetings

FDA intends to accept requests for participation in the voluntary Quality Metrics Pilot Program and Type C formal meetings and Pre-ANDA meetings beginning July 30, 2018. The pilot program will begin July 30, 2018 and will close July 29, 2019. The Type C formal meetings and pre-ANDA meetings will be granted based on the schedules described in the associated guidance documents.

V. Paperwork Reduction Act of 1995

This notice refers to previously approved collections of information found in FDA regulations. These collections of information 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 part 505 have been approved under OMB control number 0910–0001 and the collections of information in 21 CFR parts 210 and 211 have been approved under OMB control number 0910–0139.

The collections of information to be included in a meeting request for a product submitted in an NDA is approved under OMB control number 0910–0429. The collections of information to be included in a meeting request for a product submitted in an ANDA is approved under OMB control number 0910–0797.

Dated: June 25, 2018.

Leslie Kux,

Associate Commissioner for Policy.

[FR Doc. 2018–14005 Filed 6–28–18; 8:45 am]

BILLING CODE 4164–01–P

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. FDA–2018–N–1896]

Quality Metrics Site Visit Program for Center for Drug Evaluation and Research and Center for Biologics Evaluation and Research Staff; Information Available to Industry

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice.

SUMMARY: The Center for Drug Evaluation and Research (CDER) and the Center for Biologics Evaluation and Research (CBER) in the Food and Drug Administration (FDA or Agency) are announcing a 2018 CDER and CBER staff experiential learning site visit program specific to FDA's Quality Metrics Program. FDA is proposing this program, in part, in response to input from a variety of stakeholders over the past couple of years. The purpose of this 2018 Quality Metrics Site Visit Program is to provide experiential and firsthand learning opportunities to FDA staff involved in the development of the FDA Quality Metrics Program and to provide stakeholders with an opportunity to explain the advantages and challenges associated with implementing and managing a robust Quality Metrics Program. This notice invites pharmaceutical companies interested in participating in this program to submit a Quality Metrics Site Visit proposal.

DATES: Submit either an electronic or written proposal to participate in this program by August 28, 2018. See section IV of this notice for information on what to include in such proposals.

FOR FURTHER INFORMATION CONTACT: Tara Gooen Bizjak, Center for Drug Evaluation and Research, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 51, Rm. 2109, Silver Spring, MD 20993–0002, 301–796–3257, email: *Tara.Gooen@fda.hhs.gov* or Stephen Ripley, Center for Biologics Evaluation and Research, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 71, Rm. 7268, Silver Spring, MD 20993–0002, 240–402–7911.

SUPPLEMENTARY INFORMATION:

I. Background

More than a decade ago, FDA launched an initiative to encourage the implementation of a modern, risk-based pharmaceutical quality assessment system. As part of this initiative, and in recognition of the increasing complexity of pharmaceutical manufacturing, FDA developed a 21st century vision for manufacturing and quality with input from academia and industry. The desired state was described as follows: ''A maximally efficient, agile, flexible pharmaceutical manufacturing sector that reliably produces high-quality drug products without extensive regulatory oversight.'' [1]

There has been significant progress toward this vision in the intervening years as evidenced by programs and guidances from FDA around major initiatives such as pharmaceutical development and quality by design, quality risk management and pharmaceutical quality systems, process validation, and emerging technology, among others. These programs and guidances are intended to promote effective use of the modern pharmaceutical science and engineering principles and knowledge throughout the life cycle of a product.

FDA sought input from industry on the establishment of an FDA Quality Metrics Program as another mechanism to promote continual improvement in manufacturing quality. FDA has also consulted with other stakeholders to identify mutually useful and objective quality metrics. The Agency heard that it should perform further studies of existing quality metrics programs and conduct additional discussions with stakeholders. Based on this input, CDER and CBER are initiating this 2018 Quality Metrics Site Visit Program to assist the Agency in understanding existing programs. This voluntary site visit program is designed to offer experiential and firsthand learning opportunities to CDER and CBER staff involved in the development of FDA's Quality Metrics Program and to provide stakeholders with an opportunity to explain the advantages and challenges associated with implementing and managing a robust quality metrics program. One goal of these visits is to provide CDER and CBER staff exposure to existing quality metrics programs through onsite visits, tour of operations, and discussions with establishments to assist staff in further developing FDA's Quality Metrics Program. Another goal is to provide a forum for industry to engage in the process and provide additional feedback into improving the FDA Quality Metrics Program.

[1] See ''FDA Pharmaceutical Quality Oversight: One Quality Voice'' at *https://www.fda.gov/downloads/AboutFDA/CentersOffices/OfficeofMedicalProductsandTobacco/CDER/UCM442666.pdf.*

II. The Site Visit Program

During a quality metrics site visit, CDER and CBER staff will observe how quality metrics data are gathered, collected, and reported to management. We anticipate 5 to 10 FDA representatives (involved in the development of FDA's Quality Metrics Program) would participate in a site visit taking place over a 1- to 2-day period. To facilitate the learning process, the host establishment may present overviews of the development and management of their quality metrics program. The presentation(s) will allow the participating establishments an opportunity to showcase technologies that support their program.

CDER and CBER encourage covered establishments, including establishments that do not perform physical manipulation of drugs, engaging in the development and manufacturing of both active pharmaceutical ingredients (small and large molecules) and drug products to submit quality metrics site visit proposals. A covered establishment is an owner or operator of an establishment that is engaged in the manufacture, preparation, propagation, compounding, or processing of a covered drug product, or an active pharmaceutical ingredient (API) used in the manufacture of a covered drug product. CDER and CBER staff participating in this program will benefit by gaining a better understanding of current industry practices, processes, and procedures for quality metrics programs.

CDER and CBER identified a number of establishment types that are of particular interest to their staff. The following list identifies some examples of these establishments but is not intended to be exhaustive, mutually exclusive, or to limit industry response to the notice:

- Manufacturer of brand, generic, biotechnology, APIs, and non-application product(s) marketed under the over-the-counter (OTC) monograph system, and any combination of these products;
- contract development and manufacturing organizations;
- establishments with small and large portfolios; and
- establishments with past or current product availability issues (*e.g.,* history of a drug supply issue, recall).