• Federal eRulemaking Portal: http://www.regulations.gov. Follow the instructions for submitting comments.
• Mail: Division of Healthcare Quality Promotion, National Center for Emerging and Zoonotic Infectious Diseases, Centers for Disease Control and Prevention, 1600 Clifton Road NE., MS–A07, Atlanta, GA 30329. Attn: Docket No. CDC–2016–0110.

Instructions: All submissions received must include the agency name and Docket Number. All relevant comments received will be posted without change to http://regulations.gov, including any personal information provided. For access to the docket to read background documents or comments received, go to http://www.regulations.gov.

Written materials identified by Docket No. CDC–2016–0110, will be available for public inspection Monday through Friday, except for legal holidays, 9 a.m. until 4:30 p.m. Eastern Standard Time, at CDC Library, 1600 Clifton Road NE., Atlanta, Georgia 30329. Please call ahead to (404) 639–7177 and request a Library representative to schedule your visit. All public comments will be reviewed and considered prior to finalizing the Draft Recommendation Update.

For Further Information Contact:
Contact Erin Stone, Division of Healthcare Quality Promotion, National Center for Emerging and Zoonotic Infectious Diseases, Centers for Disease Control and Prevention, 1600 Clifton Road NE., Mailstop A–31, Atlanta, Georgia 30329; Telephone: (404) 639–1717 and request a Library representative to schedule your visit. All public comments will be reviewed and considered prior to finalizing the Draft Recommendation Update.

Supplementary Information:
Since 2014 CDC has collaborated with national partners, academicians, public and private health professionals, and other partners to create this Draft Recommendation Update. CDC received input from the Healthcare Infection Control Practices Advisory Committee (HICPAC) throughout the development of the Draft Recommendation Update. HICPAC includes representatives from public health, infectious diseases, regulatory and other federal agencies, professional societies, and other stakeholders. This Draft Recommendation Update is not a federal rule or regulation.

The Draft Recommendation Update is designed for use by infection prevention staff, healthcare epidemiologists, administrators, nurses, and personnel responsible for developing, implementing, and evaluating infection prevention and control programs for healthcare settings across the continuum of care. The recommendations contained in the Draft Recommendation Update are based on a targeted systematic review of the best available evidence for a specific topic related to the prevention of intravascular catheter-related infections. Dated: November 21, 2016.

Sandra Cashman, Executive Secretary, Centers for Disease Control and Prevention

[FR Doc. 2016–28385 Filed 11–23–16; 8:45 am] BILLING CODE 4163–18–P

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration


Submission of Quality Metrics Data; Draft Guidance for Industry; Availability; Request for Comments

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice of availability; request for comments.

SUMMARY: The Food and Drug Administration (FDA or Agency) is announcing the availability of a revised draft guidance for industry entitled “Submission of Quality Metrics Data.” In order to help develop compliance and inspection policies and practices, improve the Agency’s ability to predict, and therefore possibly mitigate, future drug shortages, and to encourage the pharmaceutical industry to implement state-of-the-art, innovative quality management and pharmaceutical manufacturing, FDA intends to initiate a quality metrics reporting program. The revised draft guidance describes FDA’s plans for an initial, voluntary phase of this program. FDA expects that this voluntary phase will allow the Agency to learn more about a limited set of quality metrics and associated analytics, and to help inform future FDA decisionmaking about its quality metrics program. This revised draft also provides an opportunity to gain additional perspectives from industry participants on the future use of quality metrics data.

DATES: Although you can comment on any guidance at any time (see 21 CFR 10.115(g)(5)), 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 on the draft guidance by January 24, 2017.

ADDRESSES: You may submit comments 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): Division of Dockets Management (HFA–305), Food and Drug Administration, 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852.
• For written/paper comments submitted to the Division of Dockets Management, 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–2015–D–2537 for “Submission of Quality Metrics Data.” 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 Division of Dockets Management 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 Division of Dockets
Management. 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: http://www.fda.gov/
regulatoryinformation/dockets/
default.htm.

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 Division of Dockets
Management, 5630 Fishers Lane, Rm.
1061, Rockville, MD 20852. Submit
written requests for single
copies of the draft guidance to the
Division of Drug Information, Center for
Drug Evaluation and Research (CDER),
Food and Drug Administration, 10001
New Hampshire Ave., Hillandale
Building, 4th Floor, Silver Spring, MD
20993–0002 or to the Office of
Communication, Outreach and
Development, Center for Biologics
Evaluation and Research (CBER), Food
and Drug Administration, 10903 New
Hampshire Ave., Bldg. 71, Rm. 7301,
Silver Spring, MD 20993–0002, 240–402–7911.

SUPPLEMENTARY INFORMATION:

I. Background
FDA is announcing the availability of
a revised draft guidance for industry
titled “Submission of Quality Metrics
Data.” 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 product quality with
input from academia and industry. FDA
articulated its vision as “a maximally
efficient, agile, flexible pharmaceutical
manufacturing sector that reliably
produces high-quality drug products
without extensive regulatory oversight.”

Significant progress toward achieving
this vision has occurred 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
others. These programs and guidances
are intended to promote effective use of
the most current pharmaceutical science
and engineering principles, and
knowledge throughout a product’s life
cycle.

Despite these achievements, however,
we have not fully realized our 21st
century vision for manufacturing and
quality, and indicators of serious
product quality defects persist. The
Agency has found that the majority of
drug shortages stem from quality
issues—the discovery of substandard
manufacturing facilities or processes, or
identification of significant quality
defects in finished products,
necessitating remediation efforts, which
in turn, may interrupt production, and
cause a shortage of drugs. Taking action
to reduce drug shortages remains a top
priority for FDA.

The continued existence of product
quality issues may point to increased
complexities in the supply chain,
limited innovation in manufacturing,
inadequate adoption of modern
manufacturing technologies and robust
quality management systems, or other
factors. As described in the revised
draft guidance, FDA is proposing a voluntary
phase of a quality metrics reporting
program to learn more about a limited
set of quality metrics and associated
analytics. Under this program,

beginning in early 2018, FDA
anticipates accepting the voluntary
submission of data from owners and
operators of certain human drugs
establishments, especially
manufacturers of covered drug products
and active pharmaceutical ingredients
(API) used in covered drug products. A
covered drug product is: (1) Subject to
an approved application under section
505 of the Federal Food, Drug, and
Cosmetic (the FD&C Act) (21 U.S.C. 355)
or under section 351 of the Public
Health Service Act (the PHS Act) (42
U.S.C. 262); (2) marketed pursuant to an
over-the-counter (OTC) monograph, or
(3) a marketed unapproved finished
drug product. Other types of
establishments may also choose to
submit quality metrics data as explained
in the revised draft guidance. FDA
expects to use information about
participating establishments in our risk-
based decisionmaking, and to evaluate
our planned analytics as we further
develop the quality metrics program as
a subject of future rulemaking.

Under Title VII section 706 of the
Food and Drug Administration Safety
and Innovation Act (FDASIA) (Pub. L.
112–144), FDA may require the
submission of any records or other
information that FDA may inspect
under section 704 of the FD&C Act (21
U.S.C. 374), in advance or in lieu of an
inspection by requesting the records or
information from a person that owns or
operates an establishment that is
engaged in the manufacture,
preparation, propagation, compounding,
or processing of a drug. The quality
metrics data described in the revised
draft guidance is information of the type
that FDA may inspect under section 704
of the FD&C Act. However, FDA does
not intend to require the submission of
information pursuant to section
704(a)(4) of the FD&C Act in
implementing the voluntary phase of
the quality metrics reporting program.
FDA does not intend to take
enforcement action based on errors in a
quality metrics data submission made to
this voluntary phase of the reporting
program, provided the submission is
made in good faith.

Current good manufacturing practice
(CGMP) for human drugs requires
manufacturers to have an ongoing
program to maintain and evaluate
product and process data that relate to
product quality (21 CFR 211.180(e) and
21 U.S.C. 351(a)(2)(B)). Manufacturers
are expected to use a quality program to
support process validation, and
manufacturers may include the metrics
described in this guidance in their
quality program. As discussed in the
revised draft guidance, FDA encourages
manufacturers to routinely use additional quality metrics beyond the metrics described in this guidance in performing product and establishment specific evaluations.

FDA envisions information collected from a fully implemented quality metrics reporting program will be an important factor in further focusing the use of FDA resources on the areas of highest risk to public health, which may include: (1) Establishing a signal detection program as one factor in identifying establishments and products that may pose significant risk to consumers; (2) identifying situations in which there may be a risk for drug supply disruption; (3) improving the effectiveness of establishment inspections; and (4) improving FDA’s evaluation of drug manufacturing and control operations.

FDA has engaged with stakeholders in several ways to develop mutually useful and objective quality metrics. On July 28, 2015, FDA published a draft guidance entitled “Request for Quality Metrics” (80 FR 44973). On August 24, 2015, FDA conducted a public meeting to discuss the draft guidance at the Agency’s campus in Silver Spring, MD. FDA has also consulted stakeholders at various trade and professional association meetings, and published a prior request for comment in the Federal Register on February 12, 2013 (78 FR 9928). On July 28, 2015, FDA announced the Federal Register on February 12, 2013 (78 FR 9928), that concerned manufacturing quality metrics as they relate to drug shortages. These efforts identified several categories of quality-related information that CDER and CBER considered in developing the quality metrics discussed in the guidance. The revised draft guidance announced in this notice replaces the currently published draft guidance.

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 the submission of quality metrics data. It does not establish any rights for any person and is not binding on FDA or the public in an alternative approach if it satisfies the requirements of the applicable statutes and regulations.

II. Revisions to the 2015 Draft Guidance

On July 28, 2015, FDA announced the availability of the draft guidance entitled “Request for Quality Metrics” (80 FR 44973). The revised draft guidance includes the following changes from the earlier draft guidance: Adoption of phased-in (voluntary) approach, reduction in the number of data elements requested (i.e., reduction in reporting burden), support for both product reports and site reports, modifications to the quality metrics data definitions, addition of clarifying examples for the definitions, addition of comment fields, and clarification of special considerations for non-application and OTC product reporting. FDA recognizes that a voluntary phase of the program would give participants an opportunity to demonstrate transparency and a willingness to proactively engage with the Agency in pursuit of the goals described in the revised draft guidance. FDA also expects that it will be able to use information submitted during a voluntary phase of the program to inform risk-based decisionmaking, and to help evaluate our planned analytics as we further develop the quality metrics reporting program as a subject of future rulemaking.

A voluntary program would also allow all types of drug manufacturing establishments to report information. For example, active ingredient manufacturers, including those manufacturing atypical active ingredients, and excipient manufacturers, may participate in the voluntary phase of the reporting program. While the program is geared towards finished drug products and API manufacturing, all manufacturers may report quality metrics data. FDA may not be able to accomplish the overall goals of an FDA quality metrics reporting program, as described in the draft guidance, from voluntary reporting alone. If FDA does not receive a large body of data from reporting establishments, the ways in which the Agency can use the information may be limited. For example, the data received may not constitute a representative sample of the industry. Further, a self-selection bias may increase the risk of signaling an outlier where none exists. For these reasons, we expect to use the information collected during this voluntary phase of the program to specifically focus on: (1) Working with establishments towards early resolution of potential problems and to reduce the likelihood that the establishment’s operations will be disrupted and impact the drug supply, (2) helping to prepare for and direct our inspections, and (3) use of the calculated metrics as an element of the post-approval manufacturing change reporting program with an emphasis on encouraging lifecycle manufacturing improvement.

We intend to include the reporting of quality metrics as a factor in our surveillance inspection risk-based model, publish a list of reporters who provide a certain amount of information, share publicly the measured impact on inspection frequency reduction, and provide an opportunity for participants to submit feedback.

In the revised draft guidance, FDA has reduced the proposed footprint of the program from four primary metrics and three optional metrics to three primary metric areas (i.e., lot acceptance rate, invalidated out-of-specification rate, and product quality complaint rate). FDA continues to recognize the importance of measuring an establishment’s pharmaceutical quality system robustness and quality culture (e.g., senior management engagement, Corrective Action and Preventive Action effectiveness and continual improvement, and process capability/ performance). Furthermore, these areas continue to be covered on FDA drug establishment manufacturing inspections, and concomitant metrics may be added as the program matures. FDA revised the guidance to clarify the technical definitions and provide illustrative examples for specific scenarios (see Appendix B of the revised draft guidance). FDA revised the draft guidance to contemplate submission of either product reports segmented by site, or site reports segmented by product. FDA intends to publicly recognize both product reporting and site reporting establishments on a quality metrics reporters list. The Agency intends to encourage product reporting because it demonstrates a certain level of oversight and controls over the manufacturing of drug products across the supply chain. In addition, we believe that a product report is better suited to identify potential drug supply disruptions. As described in the revised draft guidance, FDA intends to publish a quality metrics reporters list that includes product reporters that provide a list of the establishments in their product supply chain and some or all of the quality metrics data identifying them as “Product Reporter Top Tier” or “Product Reporter Mid Tier”, respectively. The proposed quality metrics reporter list would also identify reporters who provide only the list of the establishments in their product supply chain.

In the approach described in the revised draft guidance, site reporting establishments would also be included on the quality metrics reporters list, as there may be scenarios where product reporting establishments do not have access to this information or may choose not to report for covered establishments. FDA intends to provide an opportunity
for both types of establishments to benefit from this incentive.

In order to implement a phased-in approach, FDA intends to begin collecting quality metrics data as part of a voluntary phase of the program. The first phase of the quality metrics program outlined in the revised draft guidance would be fully voluntary. After evaluating the results of the voluntary phase of the quality metrics program in 2018, FDA intends to initiate notice and comment rulemaking under existing statutory authority to develop a mandatory quality metrics reporting program.

FDA carefully considered supporting flexible data collection timeframes for the purposes of reporting. In the context of a program that required product-based reporting, such flexibility would be feasible. However, in the context of the voluntary phase of the reporting program, FDA is proposing a common timeframe to facilitate publication of the quality metrics reporters list, and given the need to identify duplicate data if both the product reporting establishment and site reporting establishment submit data.

A Technical Specifications Document entitled “Quality Metrics Technical Conformance Guide, Version 1.0” was published on June 27, 2016 (81 FR 41545). This guide provides technical recommendations for the submission of quality metrics data. It is intended to serve as the technical reference for implementation of the quality metrics program. FDA intends to publish Version 2.0 of the Technical Conformance Guide soon after publication of the revised draft guidance. We anticipate that the electronic submission platform will be available to test in 2017.

Reporting establishments will be able to submit 300 word text comments to provide an explanation of submitted data or report plans for improvement. FDA may refer to the comments if unusual data or trends are identified or as preparation for an onsite inspection. The submission of comments is optional. In the future, FDA may consider establishing a set of codes to standardize the comments.

FDA also revised the draft guidance to address the special complexities for grouping non-application drug products. Defining a “product” for the purpose of grouping non-application drugs for the submission of quality metrics data proved challenging without an application number. Using one segment to group products, such as active pharmaceutical ingredient(s), manufacturing process, minor formulation changes, or stock-keeping unit, is an imperfect solution. For the purpose of this revised draft guidance, FDA has defined a product family for finished drug products as any combination of National Drug Code (NDC) product code segments where the active pharmaceutical ingredient and dose form is the same (i.e., a product family could be multiple strengths or only a single strength). For APIs, the product family is defined by the NDC product code segment. Our intent is to define product family in a way that was likely consistent with how products are grouped for the Periodic Product Review per 21 CFR 211.180(e) (e.g., Annual Product Review). We expect that this approach will group similar products with similar manufacturing operations together.

There are also special considerations with respect to product quality complaints for OTC products. Manufacturers of OTC products typically receive much more frequent communications from customers than manufacturers of prescription drug products, and the nature of these communications are quite different. The definition of a product quality complaint is intended to cover any possible or actual quality issue, while excluding preferential complaints. We anticipate that our analytics will account for this imbalance in reporting type between prescription and OTC drug products.

III. How To Report Quality Metrics Data to FDA

FDA expects to encourage reporting establishments to submit quality metrics data reports where the data is segmented on a quarterly basis throughout a single calendar year. At present, FDA intends to open the electronic portal in January 2018 to receive voluntary submissions of data. FDA expects to publish a Federal Register notice providing instructions on the submission of voluntary reports and specifying the dates that we intend to open the portal, published no fewer than 30 days before the portal is opened (e.g., before December 1, 2017). FDA expects to begin the data analysis once the portal is closed and then publish initial findings and the quality metric reporters list on the FDA Web site.

To reduce discrepancies between site and product reporting, FDA is proposing a defined, uniform reporting period. In the rare instance that a reporting establishment or covered establishment discovers an error in its submission, an amendment may be made with an associated explanation via email to OPQ-OS-QualityMetrics@fda.hhs.gov.

The amendment process is specified in the Technical Conformance Guide.

IV. Paperwork Reduction Act of 1995

This revised draft guidance contains 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 collection of some of the information requested in the revised draft guidance is covered under FDA regulations at 21 CFR parts 210 and 211 and approved under OMB control number 0910–0139. In accordance with the PRA, FDA intends to solicit public comment and obtain OMB approval for any information collections recommended in this guidance that are new or that would represent material modifications to those previously approved collections of information found in FDA regulations or guidances. Subject to OMB approval, FDA anticipates that it will begin collecting quality metrics data in January 2018.

V. Electronic Access


Dated: November 18, 2016.

Leslie Kux,
Associate Commissioner for Policy.

[FR Doc. 2016–28332 Filed 11–23–16; 8:45 am]
BILLING CODE 4164–01–P

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. FDA–2007–D–0369]

Bioequivalence Recommendations for Cyclobenzaprine Hydrochloride; Revised Draft Guidance for Industry; Availability

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice of availability.

SUMMARY: The Food and Drug Administration (FDA, the Agency, or we) is announcing the availability of a revised draft guidance for industry on generic cyclobenzaprine hydrochloride extended release capsules, entitled “Draft Guidance on Cyclobenzaprine Hydrochloride.” The recommendations provide specific guidance on the design