QUALITY METRICS
TECHNICAL CONFORMANCE GUIDE

Technical Specifications Document

This Document is incorporated by reference into the following Guidance Document(s):

Draft Guidance for Industry *Request for Quality Metrics*, published July 28, 2015

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Food and Drug Administration
Center for Drug Evaluation and Research (CDER)
Center for Biologics Evaluation and Research (CBER)

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Revision History

Date	Version	Summary of Revisions
June 2016	1.0	Initial version

TABLE OF CONTENTS

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1. INTRODUCTION

1.1 Background

This Quality Metrics Technical Conformance Guide (Guide) serves as the technical reference for implementation of the draft FDA guidance for industry on *Request for Quality Metrics.*[1] Since publication of the Pharmaceutical CGMPs for the 21st Century in 2004,[2] CDER has continued to promote its vision of "a maximally efficient, agile, flexible manufacturing sector that reliably produces high-quality drug products without extensive regulatory oversight." The draft guidance for industry on *Request for Quality Metrics* and this technical reference document continue FDA's policy efforts to ensure successful implementation of CDER's objectives outlined in the 21st Century publication. FDA expects that quality metrics calculated from data that it collects will provide objective measures that, when used with additional internal data, will provide the Agency with indicators of the effectiveness of pharmaceutical manufacturing quality systems. The goal of these measures is to assure quality drug products are available to patients. The objectives of CDER's quality metrics program can best be achieved through collaboration and a shared understanding of standards for metric indicators and data exchange/reporting.

This Guide supplements the draft FDA guidance for industry on *Request for Quality Metrics* and provides recommendations about submission of information that will support the FDA's calculation of quality metrics.

1.2 Purpose

This Guide provides technical recommendations for the submission of quality metric data. It is intended to ensure clear expectations for industry on the submission of quality metric data as described in the *Request for Quality Metrics* draft guidance.

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[1] See http://www.fda.gov/ucm/groups/fdagov-public/@fdagov-drugs-gen/documents/document/ucm455957.pdf. We update guidances periodically. To make sure you have the most recent version of a guidance, check the FDA Drugs guidance Web page at http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/ucm310704.htm.

[2] See Pharmaceutical cGMP's for the 21st Century: A Risk- Based Approach at http://www.fda.gov/Drugs/DevelopmentApprovalProcess/Manufacturing/QuestionsandAnswersonCurrentGoodManufacturingPracticescGMPforDrugs/ucm137175.htm.

1.3 Document Revision and Control

This document is incorporated by reference into the draft FDA guidance for industry on *Request for Quality Metrics*. Please refer to the draft guidance at http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM455957.pdf for ongoing changes to the guidance or submission processes before final adoption.

1.4 Relationship to Other Documents

For resources on data standards, please also refer to the Study Data Technical Conformance Guide located on the FDA Study Standards Resources Web page at http://www.fda.gov/forindustry/datastandards/studydatastandards/default.htm.

2. EXCHANGE FORMAT – ELECTRONIC SUBMISSIONS

2.1 File Transport Format

Currently, FDA receives, processes, and archives electronic dataset files in several formats. The FDA is committed to open dialog about best practices which includes a review of various formats. Extensible Markup Language (XML) shall be the recommended format for Drug Quality Metrics submission.

2.1.1 Extensible Mark-up Language

Extensible Mark-up Language (XML), as defined by the World Wide Web Consortium (W3C), specifies a set of rules for encoding documents in a format that is both human-readable and machine-readable.[3] XML's primary purpose is to facilitate the sharing of structured data across different information systems.

3. FILE FORMAT – ELECTRONIC SUBMISSIONS

3.1 Variable and Dataset Descriptor Length

The length of variable names, descriptive labels, and dataset labels should not exceed the maximum permissible number of characters described in Table 1:

Table 1: Maximum Length of Variables and Dataset Elements

Element	Maximum Length in Characters
Variable Name	8
Variable Descriptive Label	40
Dataset Label	40

[3] See http://www.w3.org/XML.

3.2 Special Characters: Variables and Datasets

Variable names, as well as variable and dataset labels, should include only American Standard Code for Information Interchange (ASCII) text codes.

3.3 Variable and Dataset Names

Variable and dataset names should not contain punctuation, dashes, spaces, or other non-alphanumeric symbols. In addition, the variable and dataset names should not contain special characters, including:

\ / * ,? < > | “ ‘ : % # + ( ) { } [ ]

3.4 Variable and Dataset Labels

Variable and dataset labels can include punctuation characters. However, special characters should not be used, such as:

1. Unbalanced apostrophe, e.g., Parkinson's.
2. Unbalanced single and double quotation marks.
3. Unbalanced parentheses, braces, or brackets, e.g., ‘(‘, ‘{‘and ‘[‘.
4. ‘<’ less than sign and ‘>’ greater than sign.

3.5 Data Definition File

The data definition file is a human and machine-readable dataset that contains a list of the datasets included in the submission along with a detailed description (i.e., metadata) of the contents of each data set.

4. GENERAL CONTENT AND FORMAT OF A SUBMISSION

4.1 Data Element Specifications

Below are product data elements which correlate to column product names described in Appendix-A of the draft FDA guidance for industry on *Request for Quality Metrics*.

4.2 Data Elements - Descriptions

4.2.1 Drug Product Name

For drugs that are subject to approved applications under section 505 of the FD&C Act or under section 351 of the PHS Act, and for drugs that are described in a drug master file (DMF) that is intended to support an application, the API/drug substance or FDF/drug product name provided in the application should be used.

For drugs that are not subject to an approved application under section 505 of the FD&C Act or under section 351 of the PHS Act, the API or FDF drug product name should be used. If the drug product name is included as part of registration, the same name included in registration should be used.

4.2.2 Drug Designation

Indicate if the drug referenced in the completed data table is prescription (Rx) or over-the-counter (OTC). This element is not required to be reported for an API intended for use in the manufacture of a drug product**.**

4.2.3 Applicable Monograph

The applicable monograph, if any, for the drug referenced. This element is not required to be reported for products that are subject to an application under either section 505 of the FD&C Act or under section 351 of the PHS Act, or covered by a submission to a DMF that is intended to support such an application.

4.2.4 Drug Product Type

The drug product type – Active Pharmaceutical Ingredient (API) or Finished Dosage Form (FDF). This field is restricted to two options; only one option can be selected.

4.2.5 Applicant Name

The name of the application holder.

4.2.6 Final Labeler Name

The name of the labeler listed in the NDC code.

4.2.7 Final Labeler Codes

The name of the labeler listed in the NDC code (for validation of text entered as “final labeler name”).

4.2.8 Application Type

The application type is New Drug Application (NDA), Abbreviated NDA (ANDA), Biologics License Application (BLA), Drug Master File (DMF), or Non-application product (NA).

4.2.9 Application Number

The NDA, ANDA, BLA number for an approved product or the applicable DMF number. Leave blank for non-application products.

4.2.10 NDC Product Code

The final labeled NDC product code.

4.2.11 Time Period Start

The beginning of the time period within which the data being reported were collected.

4.2.12 Time Period End

The end of the time period within which the data being reported were collected.

4.2.13 Lots Attempted

The number of lots attempted for the drug referenced above in 4.2.1 for each establishment.[4]

4.2.14 Lots Rejected

The number of specification-related lots rejected for the drug referenced above in 4.2.1 for each establishment.

4.2.15 Attempted Lots Pending Disposition

The number of lots attempted pending disposition for more than 30 days on the last day of the time period within which the data being reported was collected.

4.2.16 Out of Specification (OOS) Results – Finished Drug Product or API

The number of test results that fall outside the specifications or acceptance criteria for the drug referenced above in 4.2.1 for each establishment.

4.2.17 Number of Lot Release and Stability Tests – Commercial Use

The number of lot release and stability tests conducted for the drug referenced above in 4.2.1 for each establishment.

4.2.18 Out of Specification (OOS) Results Invalidated

The number of invalidated OOS results for finished drug product or API and stability tests due to laboratory error for the drug referenced above in 4.2.1 for each establishment.

[4] In this section of the guidance, "establishment" means "covered establishment" as defined in the FDA guidance for industry on *Request for Quality Metrics*.

4.2.19 Product Quality Complaints

The sum of product quality complaints received for product distributed in the United States for the drug product referenced above in 4.2.1 across all establishments.

4.2.20 Lots Attempted and Released

The number of lots attempted which are released for distribution or for the next stage of manufacturing for the finished drug product or API referenced above in 4.2.1 for each establishment.

4.2.21 Annual Product Review (APR) / Product Quality Review (PQR) Completed

Indication (yes/no) of whether the APR or PQR was performed within 30 days of the annual due date.

4.2.22 Annual Product Review (APR) / Product Quality Review (PQR) Required

Number of APRs or PQRs required.

4.2.23 DUNS Number

The DUNS number for each establishment listed in the quality metrics data submission.

4.2.24 Dosage Form

The dosage form for the drug product referenced above in 4.2.1.

4.2.25 Facility Establishment Inventory Number (FEI)

The FEI for each establishment listed in the quality metrics data submission.

4.2.26 Establishment Activity Classification

List the activity classification (e.g., Direct Product Manufacturing) for all establishments listed in the quality metrics data submission.

4.3 Mandatory Data Elements – Formats

Table 2: Mandatory Data Element Formats

Data Element Name	Data Element Label	Data Element Type	Data Element Description
PRODNAME	Drug Product Name	Text	
RXSTATUS	RX OTC Status	Text	RXSTATUS = RX or OTC

Data Element Name	Data Element Label	Data Element Type	Data Element Description
MONOGRPH	Applicable Monograph	Text	
PRODTYPE	Drug Product Type	Text	PRODTYPE = API, FDF
APPLICNT	Applicant Name	Text	
FINLBLER	Final Labeler Name	Text	
LABELER	Final Labeler Codes	Num	
APPLTYPE	Application Type	Text	APPTYPE = NDA, ANDA, BLA DMF, or NA
APPNUM	Application Number	Text	
NDCCODE	NDC Product Code	Num	
TIMEPRD	Time Period Start	Date	
TIMEPRD	Time Period End	Date	
LTSATT	Lots Attempted	Num	Number of lots attempted of the product
LTSREJ	Lots Rejected	Num	Number of specification-related rejected lots of the product
APRWIDD	Attempted Lots	Num	Number of attempted lots pending disposition (more than 30 days)
OOSRES	Out-of-Specification Results	Num	Number of OOS results - Finished product (including stability testing)
LTRELTST	Lot Release Tests	Num	Number of lot release tests conducted for commercial use
OOSRESIN	Out-of-Specification Results Invalidated	Num	Number of OOS results for finished product and stability tests for the product that are invalidated due to lab error
PRODQCMP	Product Quality Complaints	Num	Number of product quality complaints received for the product distributed in the United States
LTSREL	Lots Attempted and Released	Num	Number of lots attempted that are released for distribution or for the next stage of manufacturing the product
APRWIDD	APR/PQR Completed	Text	Have associated APRs or PQRs been completed within 30 days of annual due date for the product? APRWIDD = Y or N
APRPQRS	APR or PQR Required	Num	Number of APRs or PQRs required for the product
DUNSNUM	DUNS Number	Num	A unique nine-digit identification number for each physical facility

Data Element Name	Data Element Label	Data Element Type	Data Element Description
			location
DOSAGE FORMS	Dosage Form	Text	Associated finished dosage form
FEINUM	Facility Establishment Inventory Number	Num	Facility Establishment Inventory Number
ACTIVITY	Establishment Activity	Text	Subset of Business Operations: Analytical testing, Pack, Manufacture, Other
QUARTER	Reporting Quarter	Text	QUARTER= 1, 2, 3, or 4

4.4 Optional Data Elements - Descriptions

4.4.1 APR Approval

Indicate Yes/No to indicate whether each associated APR/PQR was reviewed and approved.

4.4.2 APR Approval by Quality Unit and/or Operations Unit

If response to 4.4.1 is Y, indicate whether the approving entity was: 1. Head of the quality unit; 2. Head of the operations unit; 3. Both; or 4. Other.

4.4.3 Percentage of Corrective Actions and Preventive Actions (CAPA) Involving Re-training

Indicate the estimated percentage of your corrective actions plans that involved re-training of personnel (i.e., a root cause of the deviation is lack of adequate training).

4.4.4 Process Capability (PC) or Process Performance (PP) Index Calculation

Indicate Yes/No if PC or PP Index was calculated for each critical quality attribute as part of that product’s APR or PQR.

4.4.5 CAPA Trigger Policy

Indicate Yes/No if establishment management has a policy requiring CAPA at some lower process capability or performance index.

4.4.6 Triggers for CAPA

Related to 4.4.5, indicate what PC or PP index value triggers a CAPA.

4.5 Optional Data Elements – Formats

Table 3: Optional Data Element Formats

Data Element Name	Data Element Label	Data Element Type	Data Element Description
APRAPPVD	APR/PQR Approved	Text	Was each APR/PQR reviewed and approved? APRAPPVD = Y or N
APRAPPVDY	APR/PQR Approved by Quality and/or Operations Unit	Text	1. Head of the quality unit; 2. Head of the operations unit; 3. Both; or 4. Other.
CAIRTP	CAPAs Requiring Re-Training	NUM	What percentage of CAPA required re-training of personnel?
PCPPCALC	PC/PP Index Calculation	Text	Is a PC or PP Index calculated for all CQA? PCPICALC = Y or N
REQCAPA	CAPA Trigger Policy	Text	Are CAPAs triggered at some lower PC or PP Index? REQCAPA = Y or N
PCPPCAPA	Triggers for CAPA	Num	What PC or PP index value triggers a CAPA?

5.0 DATA VALIDATION RULES

For purposes of this Guide, data validation is a process that attempts to ensure that submitted data are both compliant and useful. Compliant means the data conform to the applicable and required data standards. Useful means that the data support the intended use (i.e., regulatory review and analysis). Data validation is one method used to assess submission data quality. Standardized data do not ensure quality data, but they do make it easier to assess some aspects of data quality by facilitating the automation of various data checks. Data validation relies on a set of validation rules that are used to verify that the data conform to a minimum set of quality standards. The data validation process can identify data issues early in the review that may adversely affect the use of the data. FDA recognizes that it is impossible or impractical to define a priori all the relevant validation rules for any given submission. Sometimes serious issues in the submitted data are only evident through manual inspection of the data and may only become evident once the review is well under way. Often these issues are due to problems in data content (i.e., what was or was not submitted, or issues with the collection of original source data), and not necessarily how the data were standardized.

When the FDA guidance for industry on *Request for Quality Metrics* is published in final, the validation rules will be posted to the external FDA Web page. Establishments should validate their metric data before submission using the posted validation rules and correct any validation errors.

6.0 Glossary

The following is a list of acronyms and terms used in this technical specifications document:

API:	Active Pharmaceutical Ingredient
APR:	Annual Product Review
ASCII:	American Standard Code for Information Interchange
BLA:	Biologics License Application
CAPA:	Corrective Action and Preventive Action
CBER:	Center for Biologics Evaluation and Research
CDER:	Center for Drug Evaluation and Research
DMF:	Drug Master File
DUNS:	Data Universal Numbering System
ESG:	Electronic Submissions Gateway
FD&C Act:	Federal Food, Drug, and Cosmetic Act
FDF:	Finished Dosage Form
FEI:	Facility Establishment Identifier Number
NDA:	New Drug Application
NDC:	National Drug Code
OOS:	Out-of-Specification
OPQ:	Office of Pharmaceutical Quality
OTC:	Over the Counter
PQR:	Product Quality Review
PQS:	Pharmaceutical Quality System
Rx:	Prescription
W3C:	World Wide Web Consortium
XML:	Extensible Markup Language