IMPLEMENTING QUALITY METRICS IN BIOPHARMACEUTICAL COMPANIES

For Taiwan PDA

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TOPICS

- Introduction
- Purpose
- Ten Quality Metrics that FDA Intends to Calculate
- Meeting with FDA
- Example: Quality Scorecard
- Quality List Discussed Between PDA and FDA in 2013

INTRODUCTION

Quality Metrics **are a key component of an effective Quality Management System (QMS) and are the measurements used in ensuring patients receive acceptable products or deliverables.**

Quality Metrics **are used to directly translate patient needs into acceptable performance measures in both products and processes.**

It is important to note that *Quality Metrics* must be established in an effort to directly improve the product or processes within Quality Systems.

PURPOSE

- **FDA intends to use quality metrics to support its understanding of the inherent risk of manufacturing establishments and products and as the basis for criteria it deems necessary and appropriate for purposes of allocating inspection resources.**

- **FDA intends to use quality metrics data to further develop FDA's risk-based inspection scheduling, to identify situations in which there may be a risk for drug supply disruption, to improve the efficiency and effectiveness of establishment inspections, and to improve FDA's evaluation of drug manufacturing and control operations.**

Refer to FDA Draft Guidance for Industry: Request for Quality Metrics

TEN QUALITY METRICS THAT FDA INTENDS TO CALCULATE

- **Lot Acceptance Rate**

  = 1 – x (x = the number of specification-related rejected lots in a timeframe divided by the number of lots attempted by the same establishment in the same timeframe).

- **Product Quality Complaint Rate**

  = the number of product quality complaints received for the product divided by the total number of lots of the product released in the same timeframe.

- **Invalidated Out-of-Specification (OOS) Rate**

  = the number of OOS test results for the finished product invalidated by the establishment divided by the total number of OOS test results divided by the total number of tests performed by the establishment in the same timeframe.

- **Annual Product Review (APR) or Product Quality Review (PQR) on Time Rate**

  = the number of APRs or PQRs completed within 30 days of annual due date at the establishment divided by the number of products produced at the establishment.

Refer to FDA Draft Guidance for Industry: Request for Quality Metrics

TEN QUALITY METRICS THAT FDA INTENDS TO CALCULATE

(continued)

- **The number of lots attempted of the product.**
- **The number of specification-related rejected lots of the product, rejected during or after manufacturing.**
- **The number of attempted lots pending disposition for more than 30 days.**
- **The number of OOS results for the product, including stability testing.**
- **The number of lot release and stability tests conducted for the product.**
- **The number of OOS results for lot release and stability tests for the product which are invalidated due to lab error.**

Refer to FDA Draft Guidance for Industry: Request for Quality Metrics

MEETING WITH FDA

August 24, 2015

Introductory Remarks
by Janet Woodcock, Director, CDER and Acting Director, OPQ

- **The Quality Metrics (in J.W. mind) are straight forward**
- **FDA is recognizing issues:**
  - Standardization between sectors
  - Manufacturers may have to change the way they collect/report metrics
  - There is some burden
- **Manufactures would want to know if they are failing to meet specifications**
- **Customer complaints – paying attention to them and prompt investigation is very important**
- **Quality Management is all about meeting the expectations of customers**
- **The guidance is a draft:**
  - FDA hopes to get comments to the docket and be able to move ahead and finalize a program
  - FDA does not consider that this program will immediately lead to sending out the troops
  - FDA does not want to have unintended consequences from these metrics
  - This is a part of whole FDA goal of moving in the post-market period
  - FDA expects to have a time period, during which they will be able to process what collected information means and also industry will be able to learn

MEETING WITH FDA

August 24, 2015

Quality Metrics Overview

by Asley Boam, Acting Director, OPPQ, OPQ, CDER

- **Why Quality Metrics?**
  - Industry
  - FDA
  - Patients
- **Who would report? Reporting Establishment**
  - One report for each API or FDF
  - FDF (market authorization holders, OTC, marketed unapproved drug product)
  - API manufacturers
- **What would be reported?**
  - Ten metrics listed in the draft guidance (FDA assumes that industry already possess or have access to all needed data per cGMP)
- **Data vs. Metrics**
  - FDA would use data to calculate metrics (Lot acceptance rate, Complaints, Invalidated OOS rate, APR/PQR on time rate)
  - Public comments requested on optional metrics (senior management engagement, CAPA effectiveness, process capability/performance)

MEETING WITH FDA

August 24, 2015

Quality Metrics Overview (continued)
by Asley Boam, Acting Director, OPPQ, OPQ, CDER

- **When/how would data be reported?**
  - Submit data for a 1-year period (after FDA issues a request)
  - Reports due within 60 days of end of reporting period
  - Public comments sought on frequency of reporting and data collection timeframe
  - Reporting through the FDA ESG

- **How does FDA intend to use quality metrics?**
  - Develop objective measures for quality of drug product and site, effectiveness of systems for manufacturing
  - Analysis of quality metrics – context matters – appropriate comparators may vary
  - Goals for use of quality metrics:
    - identify risk based factors that could impact inspection frequency,
    - improve detection of manufacturing conditions that may lead to shortages
  - Use in conjunction with other information: inspection results, recalls, FARs

EXAMPLE: QUALITY SCORECARD

Metric (%)	Definition	Baseline	Base Target	Stretch Target	MTD	YTD
Quality Events Completed On Time	Total number of events completed on time vs. total # of events closed. On-time completion for OOS, and Major investigations is 30 days.	77.3%	85.0%	90%	100.0%	83.7%
First Time Right	% of batches having no non-conforming events. This includes OOS, and Major investigations that have direct product impact. Number of batches vs. total # of batches released + rejected. Excludes non-commercial batches not for sale.	79.9%	80.0%	85%	60.0%	75.8%
Training Completion	Total number of training requirements completed on time vs. total number of active training requirements	94.6%	97.0%	99%	99.0%	99.0%
Audit Commitment Completion	Total number of Audits commitments completed vs. total number of commitments.	N/A	95.0%	97%	100.0%	99.5%
APR Completion	Total number of APRs completed vs total number scheduled	100.0%	100.0%	N/A	100.0%	100.0 %
Pass Regulatory Inspection	FDA, TFDA, EMA. No Critical Observations or OAI	100.0%	100.0%	100.0%	100.0%	100.0%

QUALITY LIST DISCUSSED BETWEEN PDA AND FDA IN 2013

- Adverse Event Rate (difficult to correlate to specific lots, quality issues and specific drug product)
- Batch Failure Rate
- Confirmed OOT Rates
- Deviations Rate
- Batch Yields Rate
- Major Change Initiated
- Potential Stock-out or Drug Shortage Rate
- Recall Rate
- Repeat CAPA Rate
- Distribution Excursion Rate (unfulfilled requests)
- Right the First Time Rate

QUALITY LIST DISCUSSED BETWEEN PDA AND FDA IN 2013

(continued)

- Confirmed OOT rates by site (exceeding an action level)
- Deviations Rate
- Environmental Monitoring Excursions Grade A & B areas Rate
- PIC/S Inspection Scoring. Number of PIC/S member inspections and number of critical & major observations
- Training Effectiveness/On-time Completion Rate
- Percentage of Overdue PM for Critical Equipment Rate
- Unplanned Downtime Rate–because of unplanned maintenance including utility failures
- "Right First Time" Rate
- Reject Rate (partial vs. full rejects, API vs. DP)
- Analytical invalid Rate
- Contamination Rate

QUALITY LIST DISCUSSED BETWEEN PDA AND FDA IN 2013

(continued)

- Recapitalization as % of the Asset Value Rate
- PM as % of Asset Value Rate
- Audit/Inspectional Commitment On-Time Completion Dates Rate
- Organizational Health Metric (percentage of temporary workforce, employee satisfaction %, safety, employee turnover rate)
- Risk Management & Mitigation Profile Changes
- Cycle Times (disposition and end to end) Rate
- Human Error Rates
- On-time Annual Product Review
- Repeat Deviations Rate
- Investigation Free Lots Rate
- Potential Stock-outs or Drug Shortages Rate

THANK YOU FOR YOUR ATTENTION!

Any Questions?

Please contact

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