Quality Metrics

Why are we going…
Where are we going…

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QUALITY AND OPQ
Vision for 21\textsuperscript{st} Century Manufacturing

“A maximally efficient, agile, flexible pharmaceutical manufacturing sector that reliably produces high quality drugs without extensive regulatory oversight.”

Are we there yet?
Challenges

• What about quality?
  – FARS have increased
  – Recalls have increased
  – Shortages have increased
  – Lack of common measuring stick

• What about flexibility?
  – Supplement trends continue unabated

• What about workload?
  – Significant increases in application numbers
  – Increasingly complex
  – Increasingly global

• What about focus?
  – More on review (predicting) than on post market surveillance
  – Compliance or quality?
Concept of Operations - Structure

- Increasing complexity
- Silos
- Issues of quality

- Leverage Expertise
- Integration
- Surveillance and Metrics

Supported by holistic product quality IT data platform
Concept of Operations – Work Processes

• Individual opinion
  – Reactive; case specific

• Standards

• Discipline specific viewpoint

• Patients First
  – Incorporate QRM

Supported by holistic product quality IT data platform
SURVEILLANCE
&
QUALITY METRICS
What are Quality Metrics?

• An objective measure of the quality of a product or process
  – Quality is the fitness for intended use of the product, relevant to patients
  – Product (and/or process) segmentation

• An objective measure of the quality of a site
  – Quality is measure of site’s ability to manufacture products fit for intended use
  – Site segmentation (can include a build of product/process scores)

• An objective measure of the effectiveness of systems associated with the manufacture of pharmaceutical products, including the pharmaceutical quality system
  – On site evaluation of quality systems
More on Quality Metrics…

- Widely used in industry

- Components required under CGMPs
  - Annual Product Review
    - Manufacturing data, SPC charts, process capability output
  - Available to FDA Investigators during inspection

- Wide range of utility benefitting public health, industry and Agency stakeholders
Why Use Quality Metrics?

• Common language to gauge progress around quality

• Potential useful to reduce shortages

• Objective measures provide clarity to all

• Path to achieve regulatory flexibility and reduced post market change control burden

• Risk based inspection required under FDASIA
  – Always done
  – Reinvent and have meaningful input
How Will Quality Metrics Be Used?

- Assist to segment sites for risk based inspection schedule
  - Risk based inspection schedule required under FDASIA, Title VII, section 705

- Assist to segment products (and/or processes) and individual product manufacturers based on risk
  - Potentially predictive of future drug shortages
    - Possibly speeds preventative efforts

- Basis of structured (objective) component of inspection and review

- Not to issue “restaurant style grades”
  - Where do you stand relative to industry groupings
Quality Metrics Use in OPQ/OS

Industry Sites
- Systems Data
- Other Data
- QM Data
- Inspection
- Existing Regs
- 706

Other Third Parties
- Other Data
- Contract

Where to go...
What to examine
Initial Questions to Answer

• What are the right metrics?
  – How do we define them?
  – Which to collect and which to audit?

• How should the metrics collect be used?

• What regulatory mechanism to use to collect?
Potential Regulatory Mechanism

• FDASIA Title VII a useful tool
  – Sec. 705 requires FDA to do risk based inspection (i.e. site stratification schedule)
    • Currently have limited “practical” access to most meaningful data
  – Sec. 706 allows FDA to collect information that would have been available on inspection “in advance or in lieu of an inspection”

• Potential regulatory mechanism
  – Identify metric available on inspection
  – Collect it under 706
  – Utilize for 705 and 706, etc…

• Potential draft guidance on mechanism

• Potential “Dear industry” letter to communicate specific metric(s) request
Quality Metrics – Industry Input

• Initial stakeholder feedback sought in drug shortage FRN
  – Positive feedback
    – BIO, GPHA, ISPE, PDA, PHRMA

• Broadly engaging industry and other stakeholders on details of program
  – What metrics, etc…
  – FDA in listening mode
Quality Metrics: Industry FRN Feedback

150 Responses
1 Opposed

Responders include brand, generic, biotech, OTC, and trade/professional associations
Metric Criteria

- Regulations
- Patient Relevant
- Unintended Consequences
- Intrusive (Industry)
- Cross-Sectors
- Objective
- Operationalize (FDA)
- Quantitative
Questions to Consider

- What metrics are useful for stratification?
  - Products (and/or processes)
  - Sites

- What metrics are useful as objective measures of quality for inspection of the “6 systems” at the site?

- How do we define them?

- How do we use them?
Some Potential Metrics… Mentioned & Often Kept by Firms

• Batch Failure Rate

• Right First Time

• OOS / Laboratory Failure Investigation Rates

• Definitions matter!
  – Standards for sampling/acceptance plans
Message: Potential Ask of Industry

- Each FEI site reports the following (per CY) – stratify by product and/or application number.
  - # of lots attempted
  - # of lots rejected
  - # of lots reworked or reprocessed
  - # of lot release tests conducted
  - # of Out of Specification Results (# of lot release tests failed)
  - # of lot release results invalidated because of laboratory error/anomaly (# of lot release test outcomes reversed due to lab error)

- Data requirements from industry are minimal
Potential Next Steps

• Consider guidance on mechanism – 4Q13

• Engage industry and other stakeholders on metrics – 4Q13

• Assess industry feedback – 1Q14
  – Reaction to guidance
  – Industry white papers and proposed metrics

• Initial industry request – 2Q14
  – For collection in 2015
Quality Metrics – Key Points

• Keep it simple
  – Clearly within the context of inspection bounds for purposes of 705
  – Focus on definitions and foundation

• Improved objectivity
  – Site selection and product stratification
  – On-site inspection

• Segmenting sites/products, but also evaluating quality systems
Questions?

Note: This presentation may be dated by the time you are reading it as this is a fast evolving topic. Feel free to reach out for updated information.

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