Quality Metrics for better Quality Compliance

Dr. Raghunandan H.V.| JSS University

Agenda

- How does industry use Metrics?
- FDA Challenges and Requirements and Use
- Complexities of Implementation (Industry Feedback)
- What does it all mean???

Industry use of Metrics

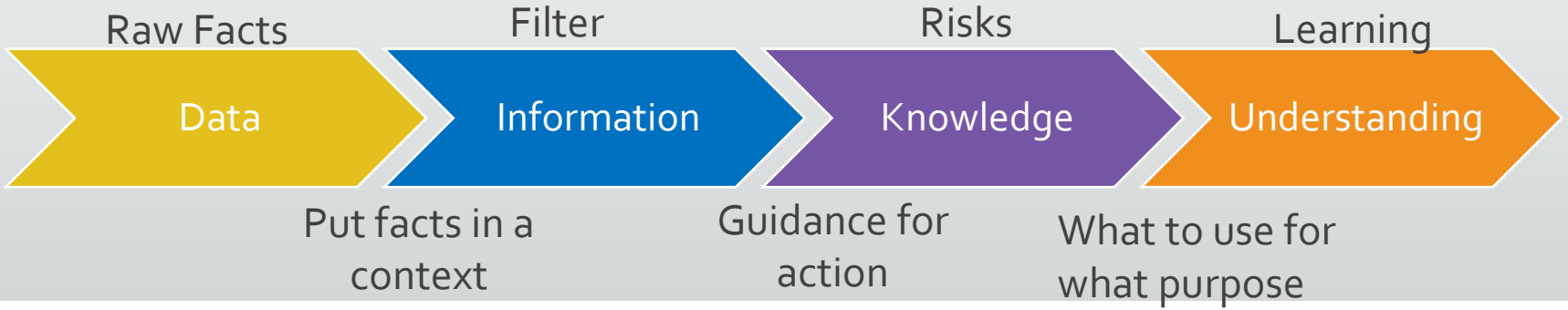
ICH Q8
Knowledge Management

Support

- Development,
- Manufacturing,
- Compliance and
- Flexibility

Application

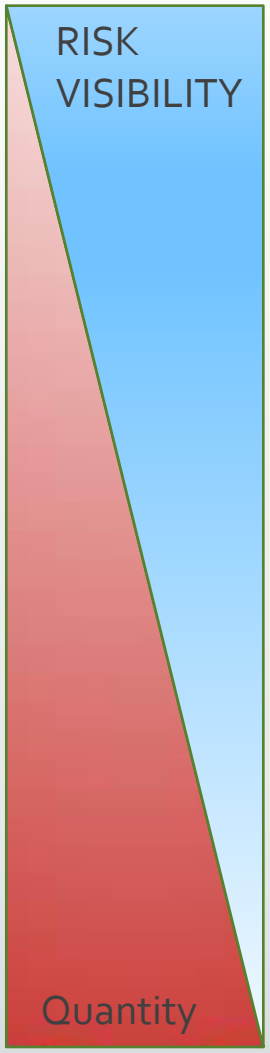
- Integrate QRM into process
- Make Use of data and use QRM to convert data to information
- Know what comes next
- Predict what will happen
- Document rationale
- Create Understanding



Metrics and Trending

- Key in **Risk identification** – systematic use of information to identify potential sources of harm (hazards) referring to the risk question or problem description [ICH Q9 / Definitions]
- Enables the detection of potential problems as early as possible to plan corrective and preventive actions
- Provides indication that controls are losing effectiveness
- Important in achieving problem resolution and problem prevention
- Another important concept of modern quality systems is the use of trending to examine processes as a whole.

RISK AND ESCALATION



FDA Challenges and Requirements

FDA 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

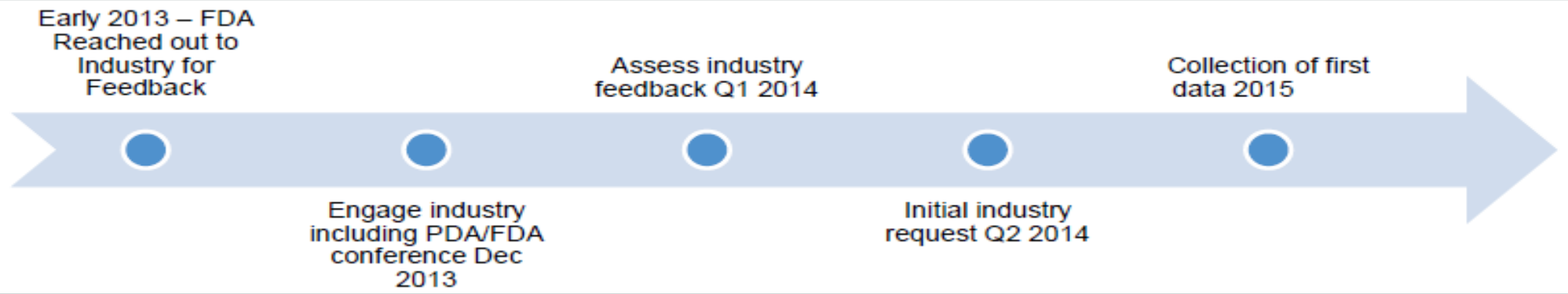
What about focus?

- More on review (predicting) than on post market surveillance
- Compliance or quality?

Potential Task 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 re-porcessed
- # of lot release tests conducted
- # of OOS results
- # of lot release results invalidated



How will FDA Use Metrics?

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

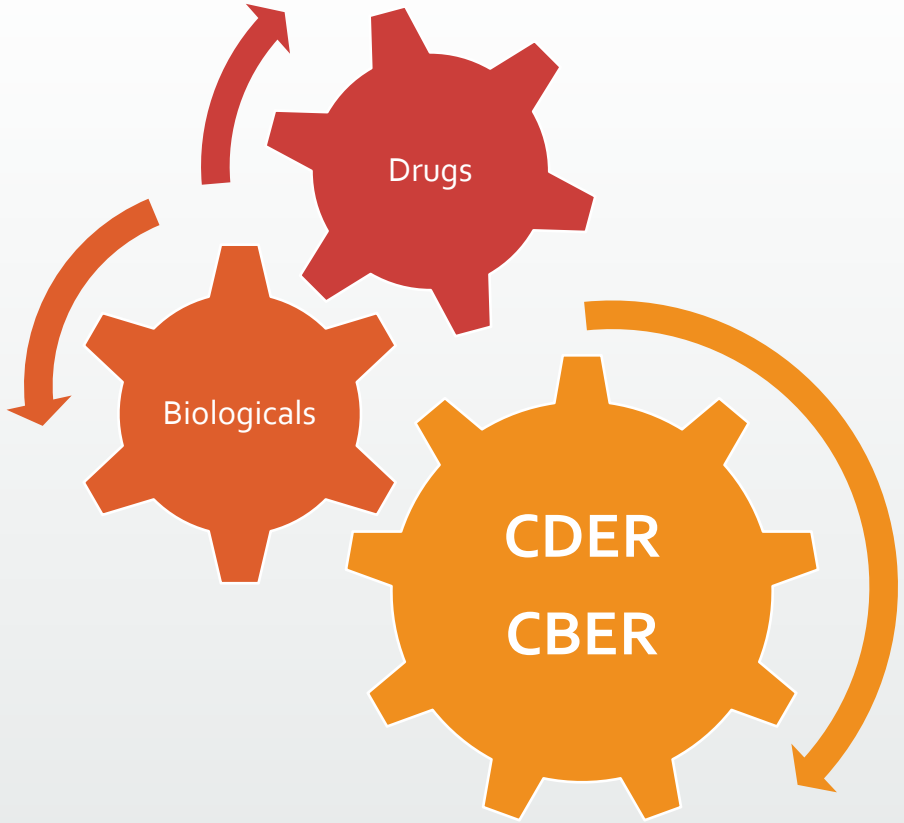
- Potentially predictive of future drug shortages

Basis of structured (objective) component of inspection and review

Only one element of risk assessment

Not to issue "restaurant style grades"

- Where do you stand relative to industry groupings



Quality Metrics – FDA Guidance (CDER & CBER)

Quality metrics are used throughout the drugs and biologics industry to monitor quality control systems and processes and drive continuous improvement efforts in drug manufacturing

Complexities of Implementation (Industry Feedback)

Complexities

- Many existing metrics are lagging indicators as opposed to leading indicators
- Clarity of Definitions among highly diverse contingent (API, small molecule, large molecule, etc..
- Concerns around cultural impacts of reporting metrics
- CMO Management (Product vs. Site)
- Virtual companies and expectations
- Global Implications (reporting requirements from other countries/language implications)

Quality Culture

Quality Culture plays a key role:

- Open and honest communication
- Clear vision and belief in quality
- Management leadership/sponsorship
- Listening
- Training and implementation of Continuous Improvement

Industry Recommended Metrics

PDA

- **Trend Metrics Collected per Product**
  - Confirmed Product Quality Complaint rate by Product
  - Batch Reject Rate by Product
  - Confirmed OOS Rate (DS and DP) by Product
- **Trend Metrics Collected per Site**
  - Confirmed OOS Rate (DS and DP) by Site
  - Batch Reject Rate by Site
- **Provide explanations/interpretations**
- **Focus on Trends and Variability**
- **Pilot Program to Start**

BIO

- **Error Rates**
  - % Critical Non Conformance Rate
  - Confirmed OOS Metric
- **Manufacturing Success Rate**
  - % Manufacturing Success Rate
- **Complaint Rate**
  - Critical and Confirmed complaints
- **Avoid public consumption of data**
- **Coordinate between CDER, CBER, CDRH, etc..**
- **Pilot Program to Start**

PhRMA

- **Site Information**
  - Products, size, change information
- **Quality Metrics**
  - Batch reject rate
  - Confirmed OOS
  - # media fill failures (for sterile facilities)
  - Product Quality Complaints
- Quality System
  - Inspection metrics from global authorities
- **Use metrics already reported (Recalls, FAR, BPD, drug shortage)**
- **Use a phase in approach with suggestions of other metrics**
- **Coordinate between CDER and other FDA Offices**
- **Global Implications should be considered**

ISPE

- **Identified Metrics**
  - Batch Rejection Rate
  - Rework and Reprocessing Rate
  - Confirmed OOS Rate
  - Unconfirmed OOS Rate
  - "Critical" Complaints
  - % APQRs complete on time
- **Includes clear definitions of each metric**
- **Provide raw numbers and rates**
- **Do not set any numerical targets**
- **Include a Pilot Program**

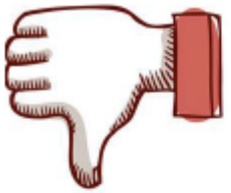
Other Metrics being considered

- Process Capability CpK, PpK, etc.
- Critical Investigations Rate
- CAPA Effectiveness Rate
- Quality System Effectiveness
- Environmental Monitoring Rate
- AE Rates
- Deviations Rates
- Recall Rate
- Repeat CAPA rate
- Right first Time rate
- Unplanned Downtime
- Indicators of ongoing investment/maintenance

Benefits and Risks

BENEFITS

- Greater visibility and transparency between industry and regulators
- Ability to identify drifts earlier to drive audit/inspection schedules
- Risk based approach to inspections
- Increasing consistency of metrics



RISKS

- Driving wrong behaviors and unintended consequence
- Establishing excessive or overly complex metrics
- Comparing data that is not consistently defined or comparison of single data values
- Using metrics as a quality “surrogate”