Quality Metrics

Why are we going…
Where are we going…

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QUALITY AND OPQ

Vision for 21st 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 → **Leverage Expertise**
- Silos → **Integration**
- Issues of quality → **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?

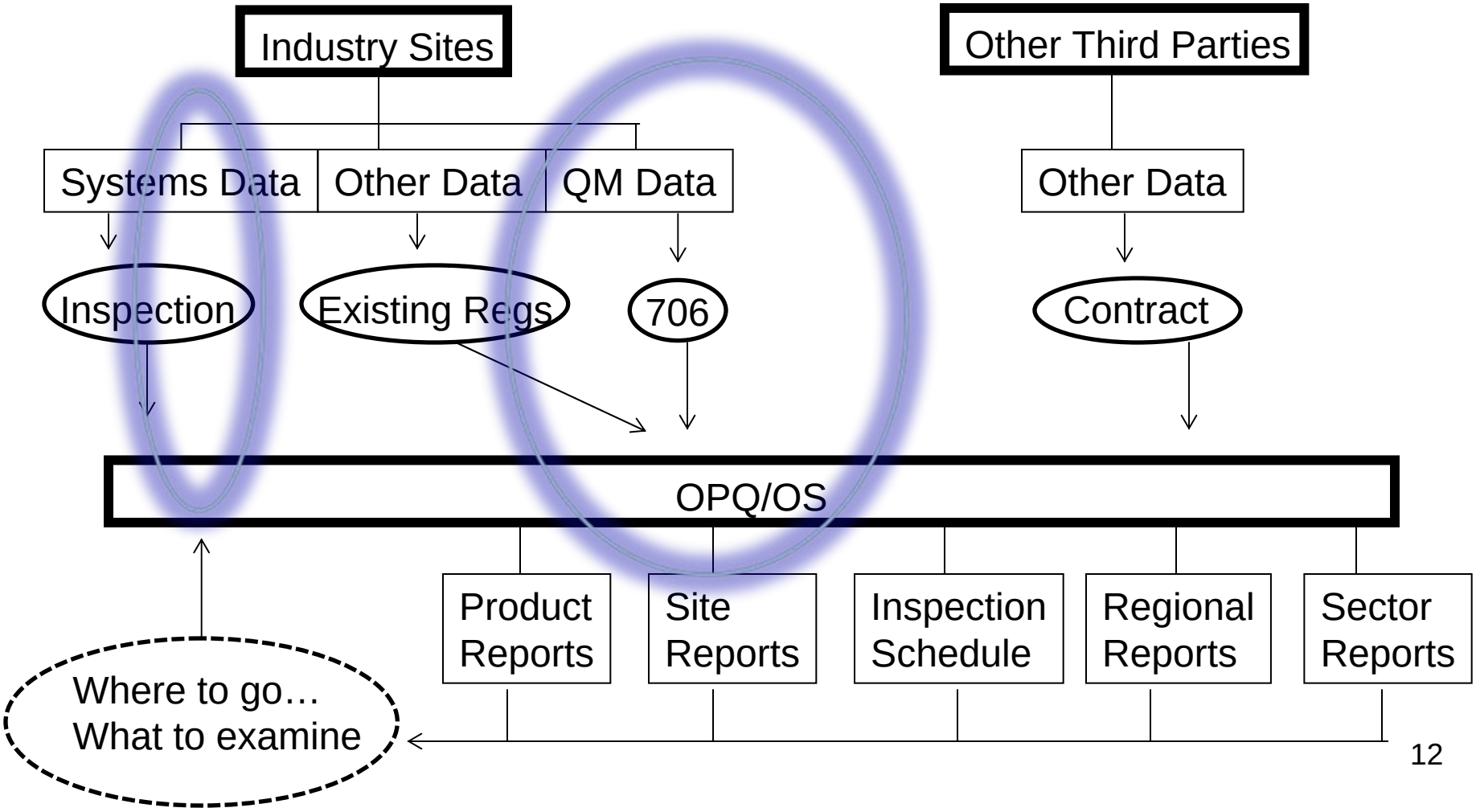
- Common language to gauge progress around quality
- Potential useful to reduce shortages
- Objective measures provide clarity to all
- Path to achieve regulatory flexibility and reduced post market change control burden

- 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



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

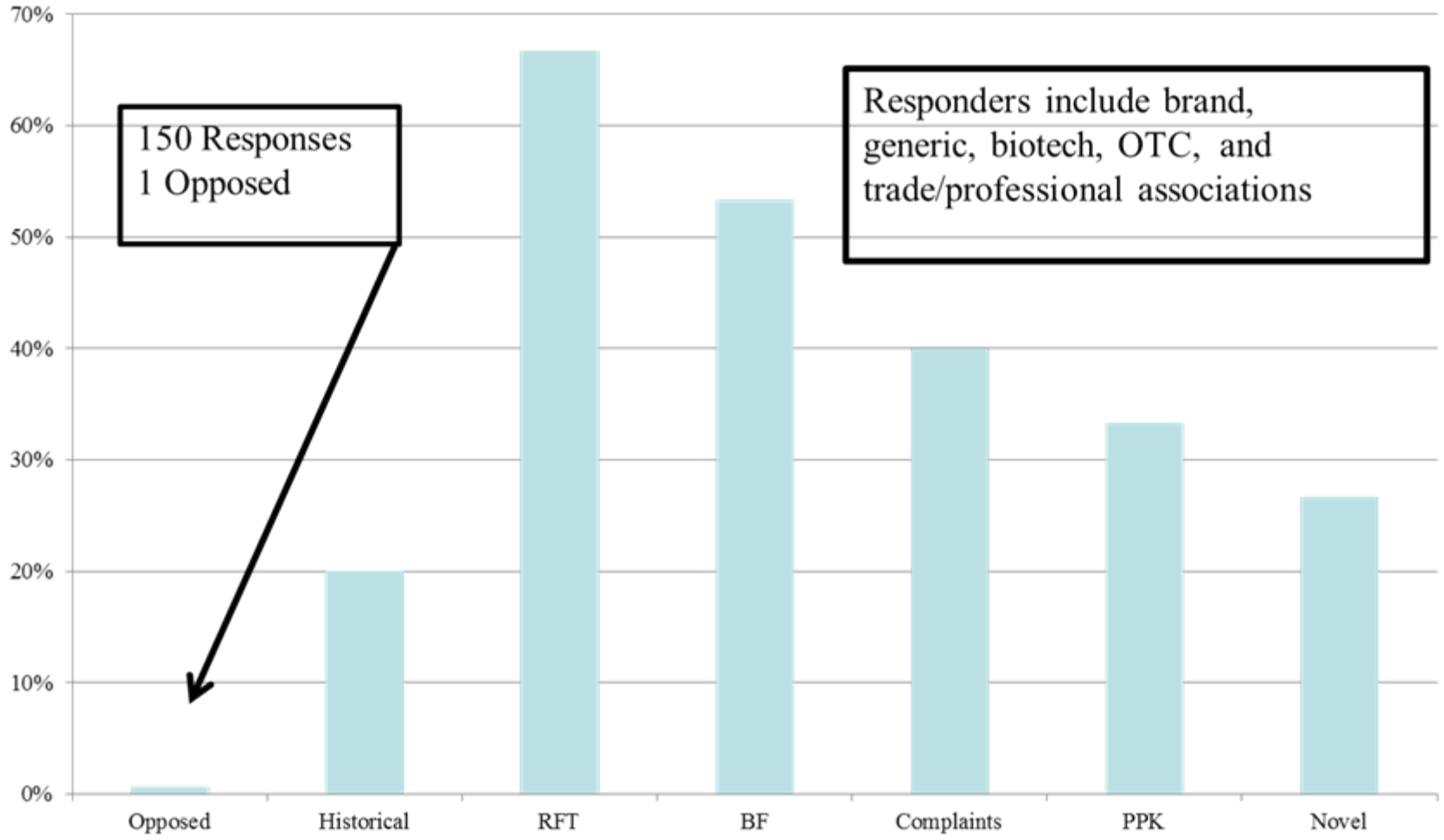
- Potential "Dear industry" letter to communicate specific metric(s) request

Quality Metrics – Industry Input

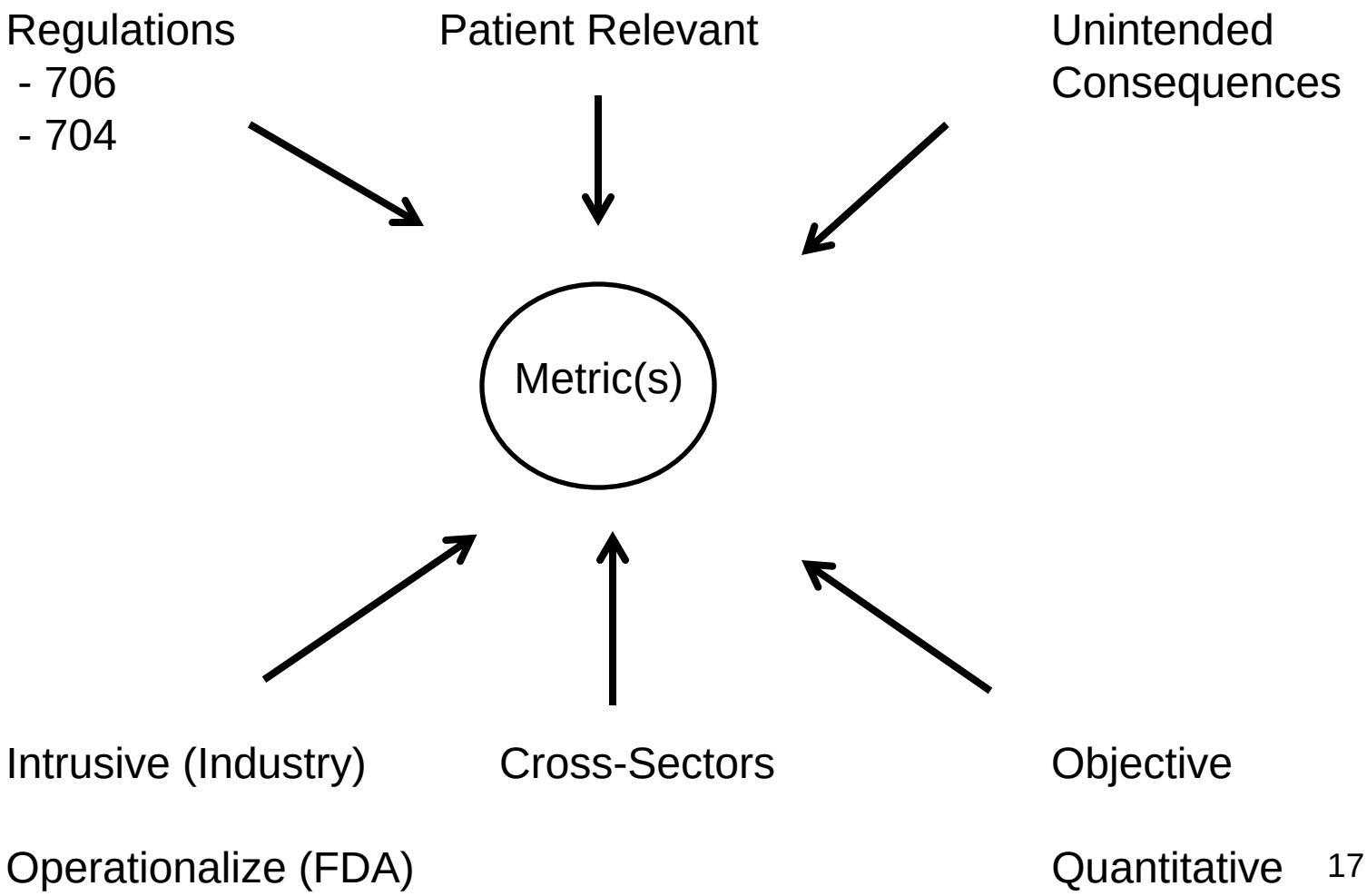
- Initial stakeholder feedback sought in drug shortage FRN
  - Positive feedback
    - BIO, GPHA, ISPE, PDA, PHRMA

- Broadly engaging industry and other stakeholders on details of program
  - What metrics, etc…
  - FDA in listening mode

Quality Metrics: Industry FRN Feedback



Metric Criteria



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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