U.S. Food and Drug Administration
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CDER /OPQ
Office of Surveillance

Quality Metrics in Surveillance

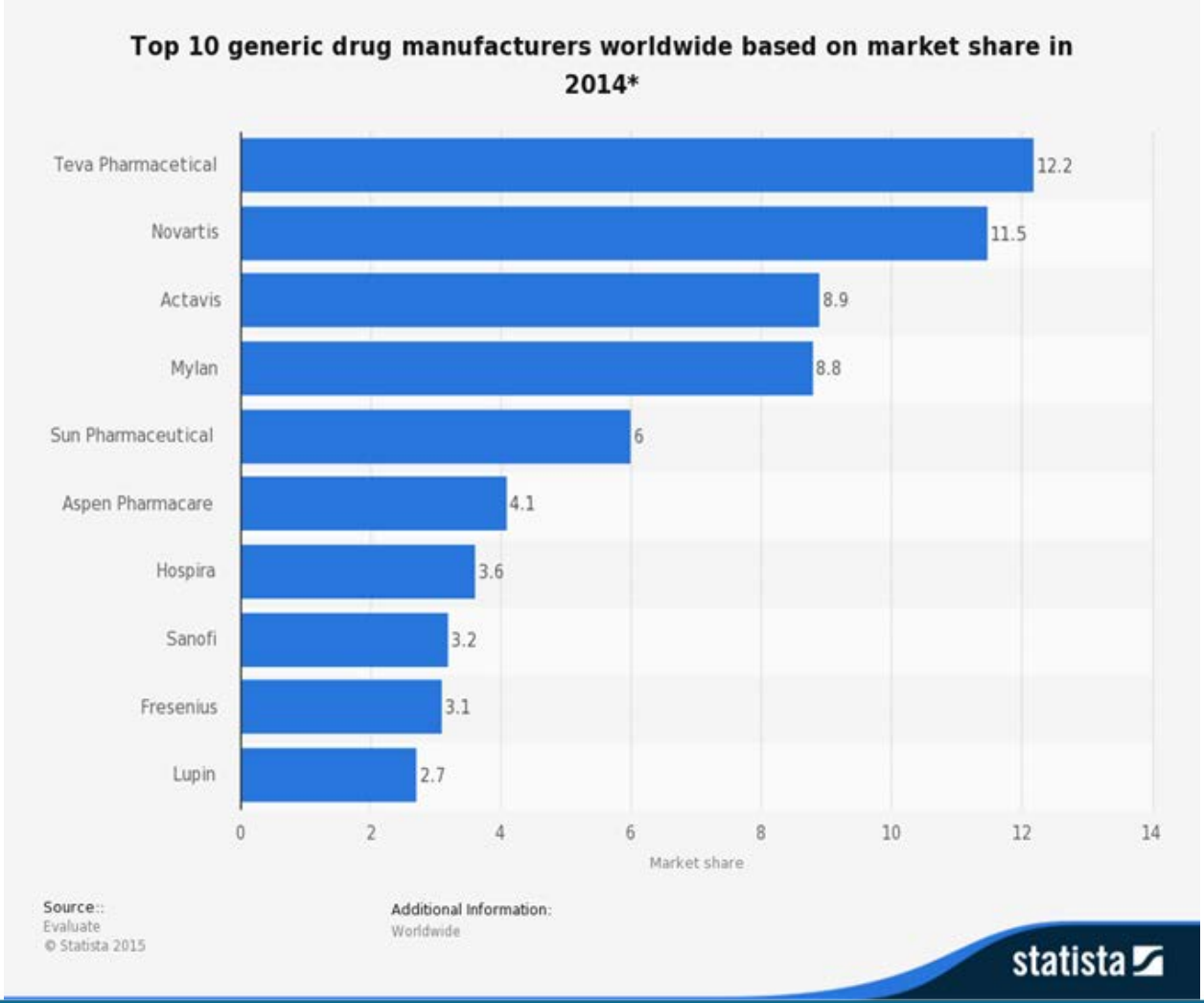
Russell Wesdyk
Acting Director
Office of Surveillance

Office of Surveillance Goals

- Builds from the shared vision
  - *A maximally efficient, agile, flexible pharmaceutical manufacturing sector that reliably produces high quality drug products without extensive regulatory oversight*

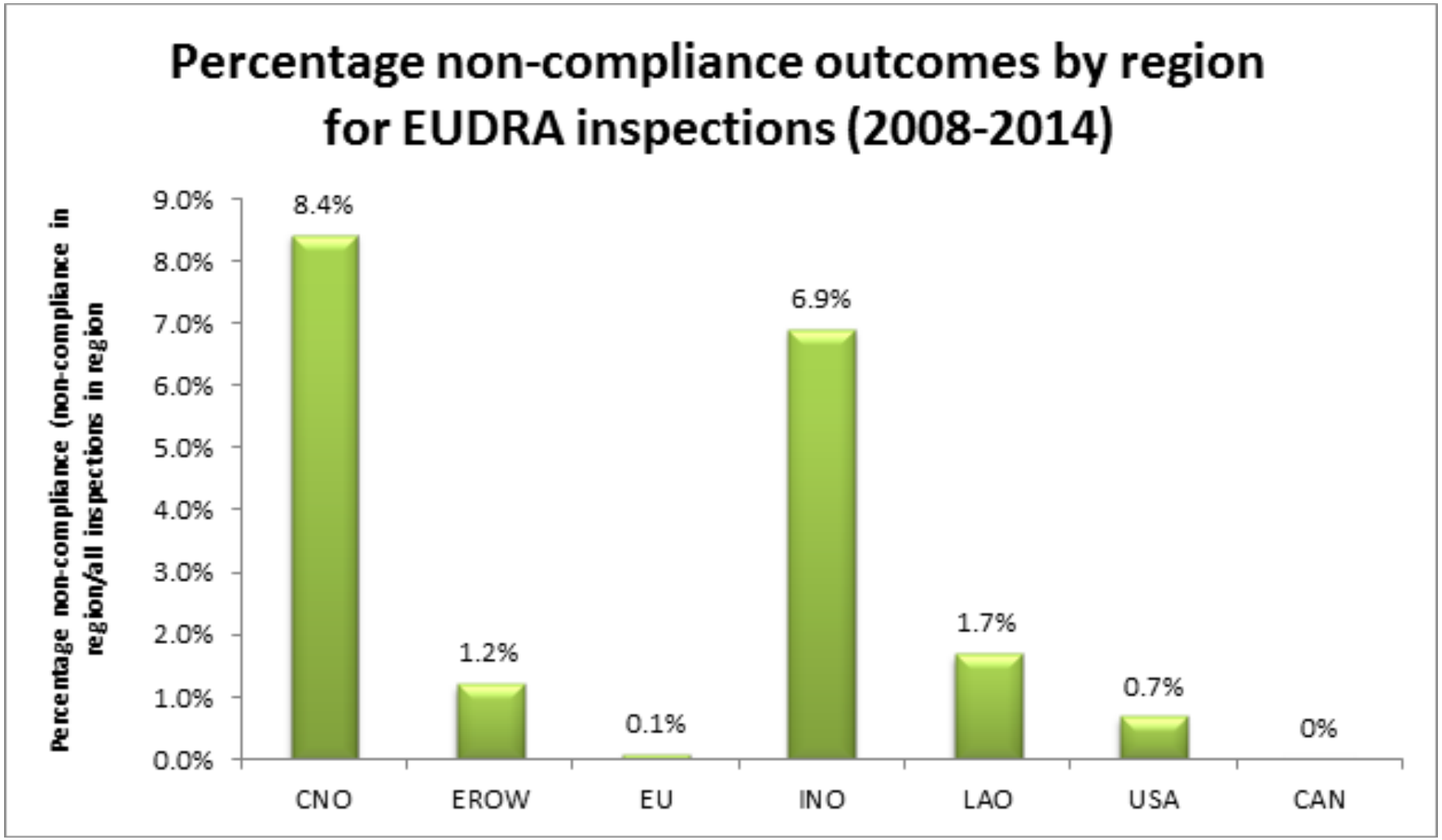
- Essentially to identify products, sites and firms that are performing above and below the requirements
  - Easier to identify those below
    - There is a mutual benefit in that
  - Identify those above to reduce regulatory oversight

India in The World



Indian Pharma Presence is Growing

But What Will Indian Pharma Be?



Do You Want To Compete With This?

- Do your customers/patients want you to?

Can You Afford To?

Mfg Performance (Sigma)	Defects (ppm)	Yield	Cost of Quality	Estimated Cost of Quality on a base of $2B
2σ	308,537	69.2%	25–35%	$500M-$700M
3σ	66,807	93.3%	20–25%	$400M–$500M
4σ	6,210	99.4%	12–18%	$240M–$360M
5σ	223	99.98%	4–8%	$80M–$160M
6σ	3.4	99.99966%	1–3%	$20M–$60M

•Source: PriceWaterhouseCoopers Presentation, FDA Science Board Meeting November 16, 2001

Do We Not Have Mutual Goals?

- Remove those not meeting the standards from the marketplace
  - We are getting better at identifying those below the bar using existing tools
- Identify those performing above the requirements and reduce regulatory oversight
  - Identifying those above the bar is more challenging with existing tool
- Quality metrics is just another tool in the surveillance box
  - More aligned with identifying those firms, sites and products performing above the bar

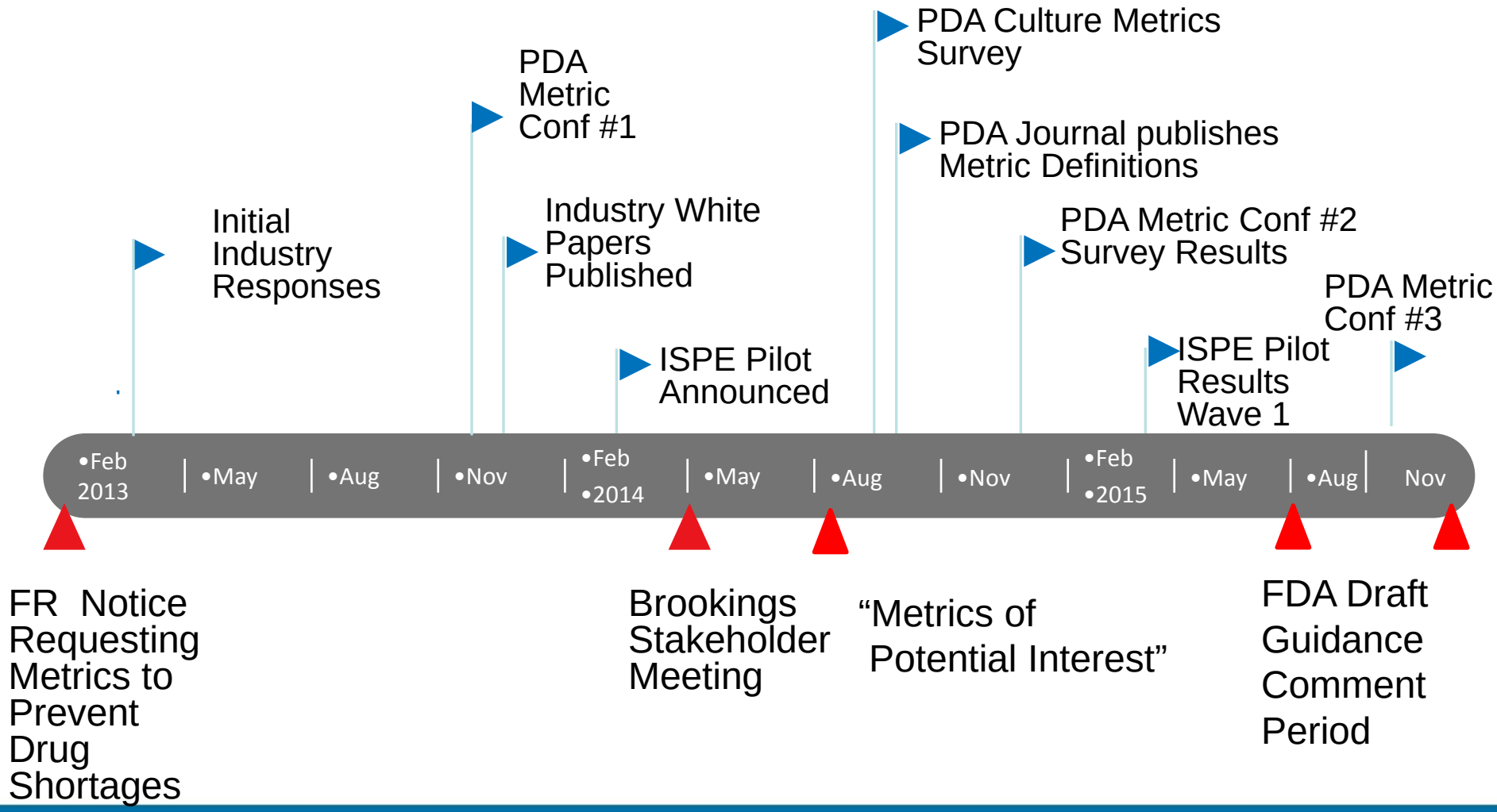
Quality Metrics

Another part of the quality intelligence picture…

Goals for Quality Metrics

- For industry
  - Promotes responsible practices and quality driven corporate culture
- For public:
  - Focus on quality leads to fewer recalls and quality related shortages
- For ~~FDA~~ All:
  - Industry achieves and is rewarded for quality, without extensive regulatory oversight

FDA Metrics Journey 2013- 2015



Request for Quality Metrics

Guidance for Industry

FDA Issues Draft Guidance

DRAFT GUIDANCE

This guidance document is being distributed for comment purposes only.

Comments and suggestions regarding this draft document should be submitted within 60 days of publication in the *Federal Register* of the notice announcing the availability of the draft guidance. Submit electronic comments to http://www.regulations.gov. Submit written comments to the Division of Dockets Management (HFA-305), Food and Drug Administration, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852. All comments should be identified with the docket number listed in the notice of availability that publishes in the *Federal Register*.

For questions regarding this draft document contact (CDER) Tara Gooen Bizjak at 301-796-3257 or (CBER) Office of Communication, Outreach and Development at 1-800-835-4709 or 240-402-7800.

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research (CDER)
Center for Biologics Evaluation and Research (CBER)

July 2015
Pharmaceutical Quality/CMC
Current Good Manufacturing Practices (CGMPs)

QM Program – White Paper Metrics

Metric / Org.	Critical Deviation Rate	Confirmed OOS Rate	Batch Reject Rate	Product Quality Complaint Rate	Recall Rate	Stability Failure Rate	Rework / Reprocessing Rate	Unconfirmed OOS Rate	% APR completed On time	FAR/BPD Rate	Sterility Failure Rate	Drug Shortage Rate
Bio	X	X	X									
Genetech		X	X	X								
GPHA			X	X	X	X						
Mylan			X	X	X	X						
ISPE		X	X	X			X	X	X			
PDA		X	X	X	X							
PhRMA		X	X	X	X					X	X	X

What would be reported?

- Reporting establishments would report data; these data should already be available per CGMPs
  - Number of lots attempted
  - Number of specification-related rejected lots
  - Number of attempt lots pending disposition >30 days
  - Number of OOS results
  - Number of lot release and stability tests
  - Number of OOS results invalidated due to lab error
  - Number of product quality complaints for the product
  - Number of lots attempted which are released for distribution or for the next stage of manufacturing
  - Whether the associated APRs or PQRs were completed within 30 days of annual due date for the product
  - The number of APRs or PQRs required for the product

Data vs. Metrics

- FDA would use the data to calculate metrics:
  - Lot Acceptance rate
  - Product Quality Complaint rate
  - Invalidated Out-of-Specification (OOS) rate
  - Annual Product Review (APR) or Product Quality Review (PQR) On Time rate
- Public comment requested on several optional metrics
  - Senior management engagement
  - CAPA effectiveness
  - Process capability/performance

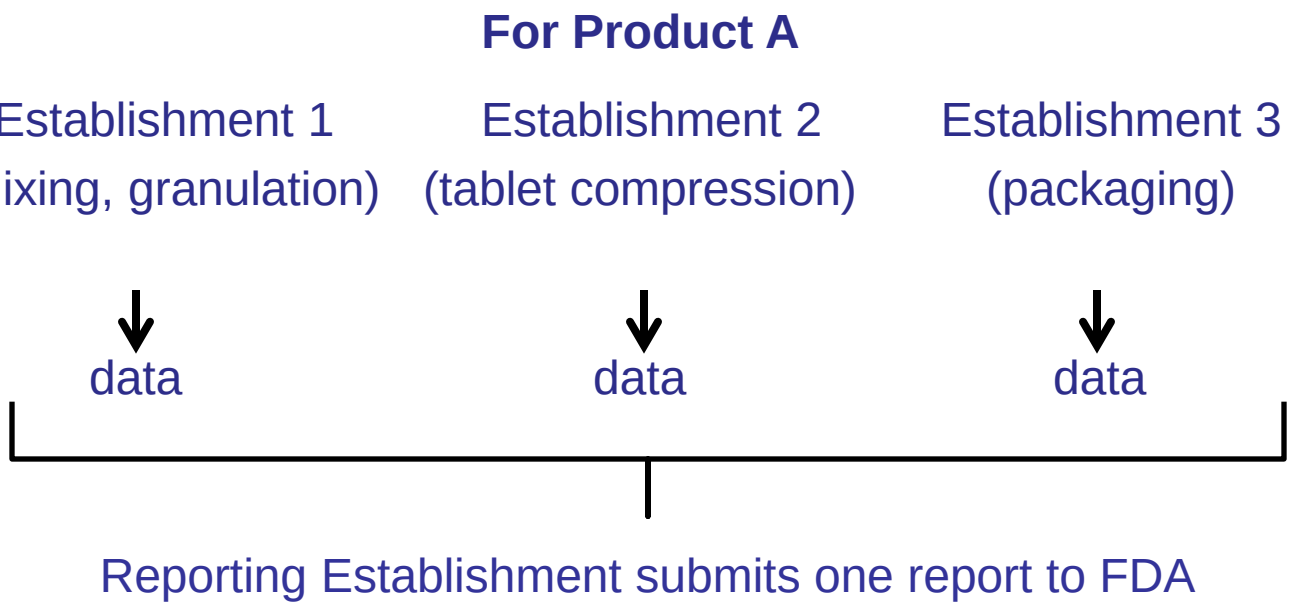
Who would report?

- Owners or operators of establishments that are engaged in the manufacture, preparation, propagation, compounding, or processing of a drug, specifically:
  - Finished dosage form (FDF) of a covered drug product, or
  - API used in the manufacture of a covered drug product.
- "Covered drug product"
  - subject to an approved application under section 505 of the FD&C Act or under section 351 of the PHS Act.
  - marketed pursuant to an OTC monograph.
  - a marketed unapproved drug product.
  - active pharmaceutical ingredients (API) used in the manufacture of a covered FDF.

Who would report?

- "Reporting Establishment"
  - Provides one report for each API or for each FDF
  - One establishment should already possess or have access to all of the data needed to submit such reports
  - Generally expect that the Quality Control Unit (Quality Unit) will be best positioned to provide these data

Example



Initial Implementation and Learning Period

Proposed Implementation of QM Program

- This is a surveillance program… not an enforcement program
- Submission of metrics would not result in
  - 483 observations or other enforcement actions
  - Fraud (vs. data quality issues) would be referred to OC
- Submission of metrics would initially result in
  - Diminished risk rank score in SSM (routine GMP inspection scheduling)
  - More metrics = greater reduction
  - Metric data itself would not influence reduction
    - Until learning period complete and relationships established… this will take time
- First principle… more information is better than less information
- Signal detection leads to OPQ engaging w the firm

Proposed Initial Learning Focus

- Correlations
  - Does not imply causation
  - Likely difficulty to establish
    - Outcomes data is very "dirty"
      - FARs, Recalls, EIR classification, even shortage
- Outlier Signal Detection
  - Can we identify best practices?
  - Can we identify potential issues and engage via OPQ rather than overlook and potentially face need for OC enforcement actions later?
- Data Quality Challenges and Solutions
  - What definitions need clarification
  - What data portal systems need refinement?

Test The Plumbing

- Informal Data Exchange
- Potential Date: Q2/Q3 2016
- Voluntary
- No benefit
- No disadvantage
- Data would not be used for any other purpose but to test the informatics capabilities

If interested, please send an email to:

gundeep.ahluwalia@fda.hhs.gov

More Information

For more information on this guidance, please see the CDER SBIA webinar at http://www.fda.gov/Drugs/DevelopmentApprovalProcess/SmallBusinessAssistance/ucm456059.htm

One Quality Voice

OPQ
OFFICE OF PHARMACEUTICAL QUALITY

Thank You