

Annual Meeting 2015
Philadelphia, PA



New Paradigms for
Manufacturing Excellence

Measuring Effectiveness of Data Integrity Programs: Metrics for Excellence



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Outline

- Complex, Global Challenge of Data Integrity
- Foundational Elements of a Data Integrity Governance Program
- Possible Framework & Measures of Success
- Key Dependencies for Program Effectiveness
- Q&A



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“Entering a period of profound change...”

“Where is the business headed?...”

“We have to ride the wave...”

Be an “Innovative Disrupter”...!



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Compared with the Industrial Revolution, we estimate that this change is happening ten times faster and at 300 times the scale, or roughly 3,000 times the impact. Although we all know that these disruptions are happening, most of us fail to comprehend their full magnitude and the second and third order effects that will result. Much as waves can amplify one another, these trends are gaining strength, magnitude, and influence as they interact with, coincide with, and feed upon one another. Together, these four fundamental disruptive trends are producing monumental change. McKinsey Global Institute, “The four global forces breaking all the trends”, April 2015



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Emerging Markets
Global Inter-Connectedness
Aging Population
Technological Change
Sharing Economy... 'As-a-Service' Economy
'Data Revolution'
'Democratization of Knowledge'



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There is an urgent imperative to adjust to these new realities. Yet, for all the ingenuity, inventiveness, and imagination of the human race, we tend to be slow to adapt to change. There is a powerful human tendency to want the future to look much like the recent past.

McKinsey Global Institute, "The four global forces breaking all the trends", April 2015



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Is 'Data Integrity' a 'New' Regulatory Expectation?

NO

- Evolving Business Models
- Increasing Globalization
- Evolving Documentation Practices



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Current Environment--Risk Factors for Data Integrity Issues

- Overseas Testing and Manufacturing
- Supply Chain
- Out-sourcing of Operations (e.g., QC Labs, Manufacturing)
- Economic Stressors—*cutting corners*
- Data Review Practices

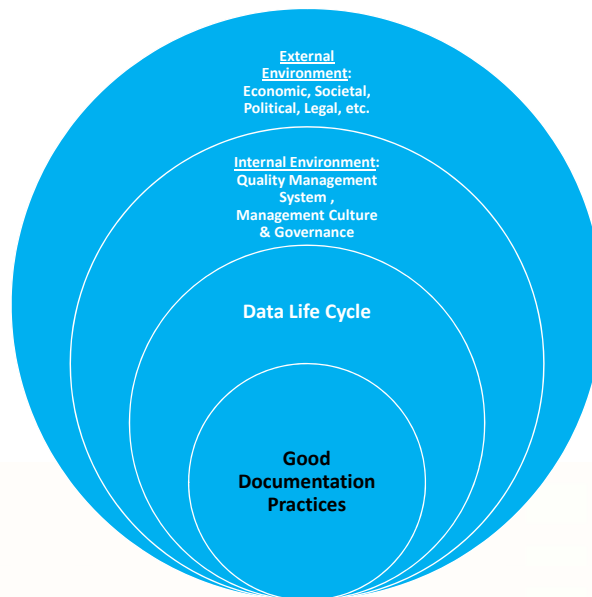


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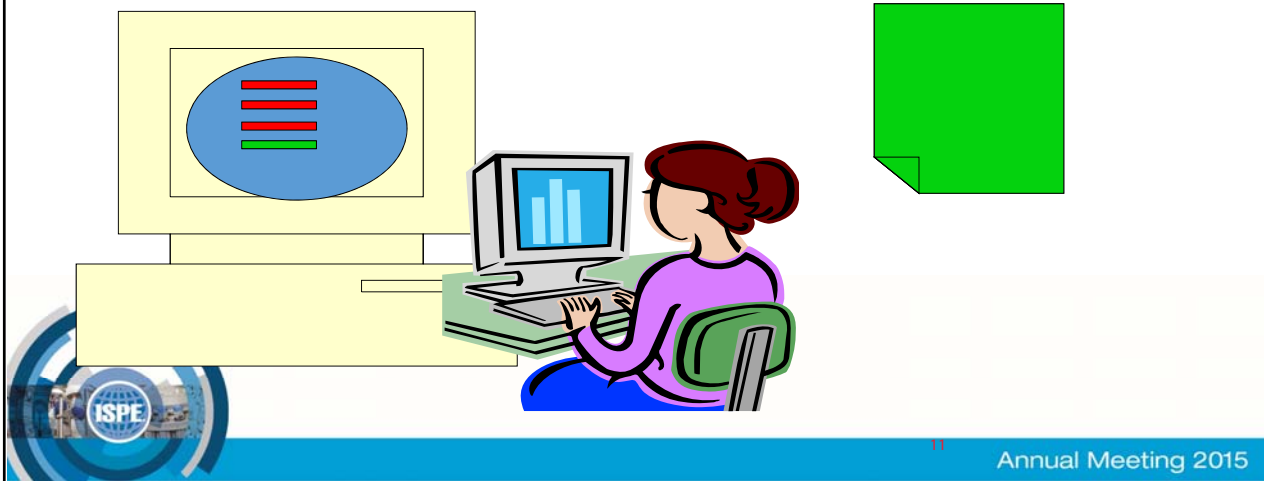
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Current Environment--Risk Factors for Data Integrity Issues

- Increasing use of Electronic Systems without commensurate understanding and implementation of risk-based controls for Electronic Data Integrity
 - Controls to Prevent Data Integrity Issues
 - Controls to Detect Data Integrity Issues



Potential Pitfall: “We Consider Printouts to be the “Raw Data” / the ‘Official Record’”



Part 11 Paradigm Shift



Applying the “GxP Predicate Rule” to Electronic Data: *Inside the “Black Box”*



Good Documentation Practices

- Legible
- Contemporaneous
- Permanent
 - Ink, preferably black
 - No pencil or white out
- Attributable
- Traceable
- Date Stamped
- Changes with single line cross-out to retain original entry, reason, initials, date
- Accurate



13

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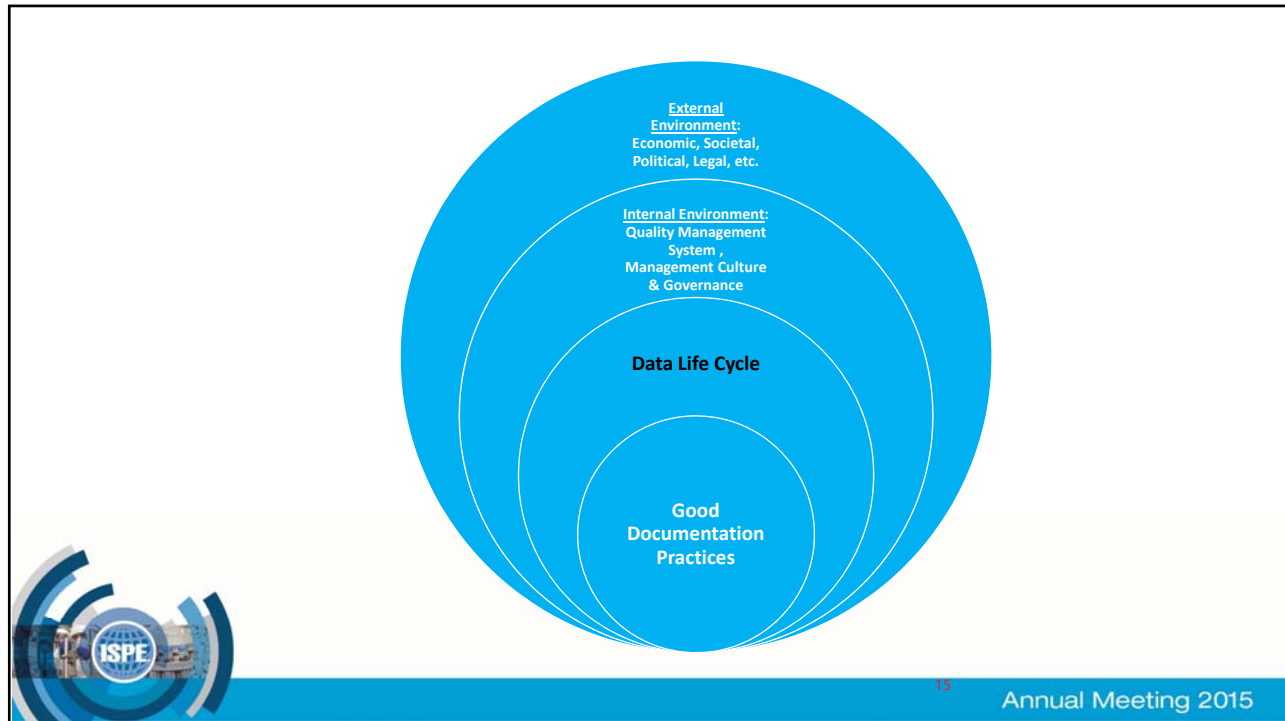
21 CFR Part 11 / EU Annex 11 / ICH E6 = Good Documentation Practices for Electronic Data

- Legible ➡ *No over-writing, Enforce saving of each step and event*
- Contemporaneous ➡ *Time-date stamps, Enforce saving at time of event*
- Permanent ➡ *Enforce saving of processing*
 - Ink, preferably black
 - No pencil or white out ➡ *Annotation tools*
- Attributable ➡ *Log-on (e.g., User ID / password), E-Sigs*
- Traceable ➡ *Metadata, Corroborating Paper Records, etc.*
- Time/Date Stamped ➡ *Time-date stamps synchronization and control*
- Changes with single line cross-out to retain original entry, reason, initials, time/date ➡ *Audit Trails*
- Accurate ➡ *Validation*



14

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Data Life Cycle

- Do I have all my data?
 - *Design of data collection: protocol, process, method*
 - *Data Life Cycle controls for data + metadata*
- Has my data been objectively processed?
 - *Controls to Prevent & Detect Testing Toward Outcome*
- Am I reviewing all my data?
 - *Printouts versus Source Electronic Records*
 - *Review of Audit Trails*
- Am I reporting all my data?
 - *Controls to Prevent & Detect Selective Reporting*



What is the relevance of Data Integrity?

Impact on:

- Patient Safety
- Product Quality



17

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Risk Management Methodology

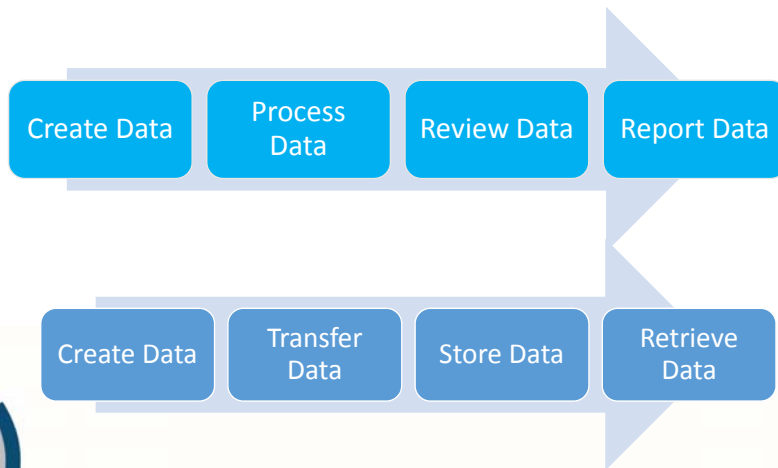
- Risk Management Programs—ICH Q9
 - Risk Assessment
 - Risk Mitigation and Control
 - Risk Communication
 - Risk Review



18

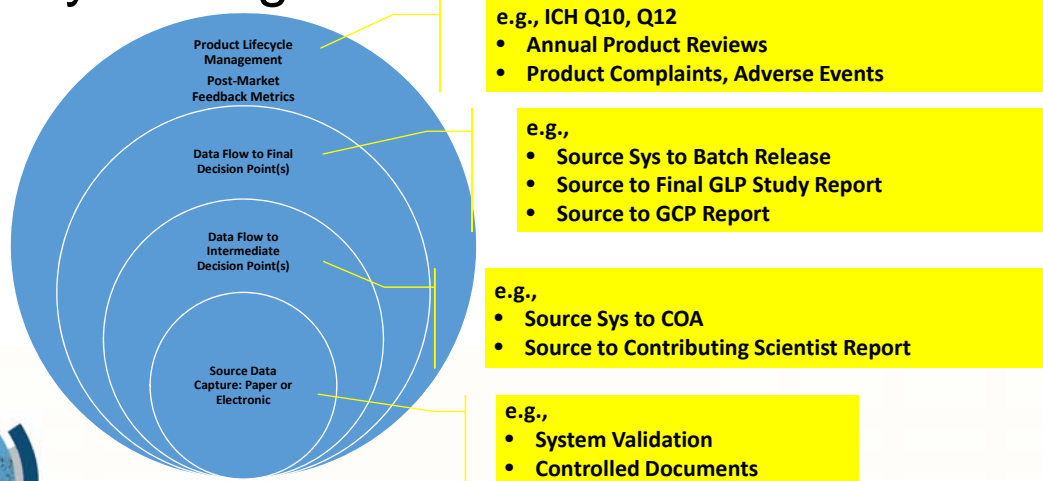
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Data Life Cycle = Business Process + Data Flow



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Where might Data Life Cycle fit into my Quality Management System?



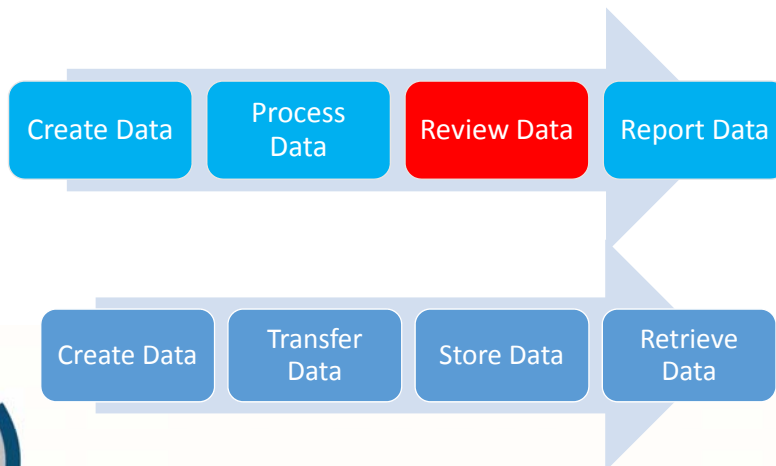
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Photo courtesy of Ian Thrussell, WHO



Data Life Cycle = Business Process + Data Flow



Critical Thinking: Mindfulness of 'Blind Spots' and 'Biases'



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Risk-Based Approach to Data Review

- “Critical” Thinking Skills for Data Reviewer
 - What are the reviewer’s “blind spots” and assumptions?
 - Focus only on what I expect to see? Or what could have, or did, go wrong?
 - Understand the significance of source data and processing of data and aberrant events relative to ‘results’?



²⁴Confidential and Proprietary to GMCA
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Risk-Based Approach to Data Review

- “Critical” Thinking Skills for Data Reviewer
 - What about ERROR PATTERNS?
 - Frequency
 - Pattern
 - Determinate or Indeterminate
 - Failure Mode
 - Failure Effect



25

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What is Goal of Data Process Mapping?

- Process Understanding.
- Knowledge Management.
- Quality Risk Management.
- Business Process Improvements:
 - Efficiencies, Effectiveness, Cost Reductions

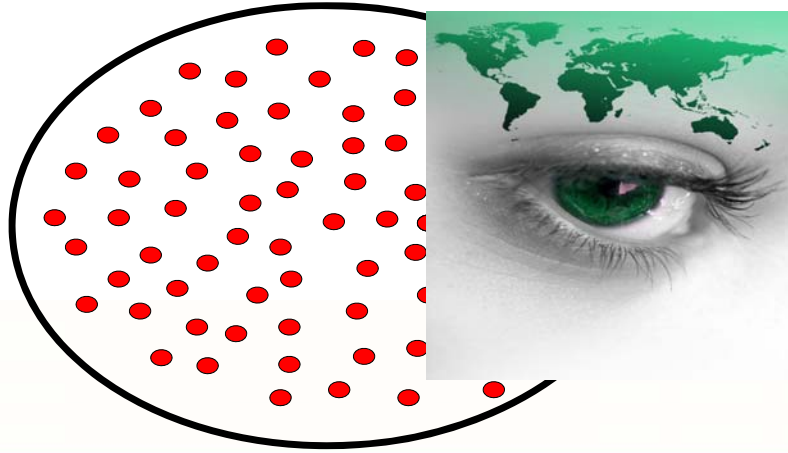
Deming: “Quality costs less not more.”



26

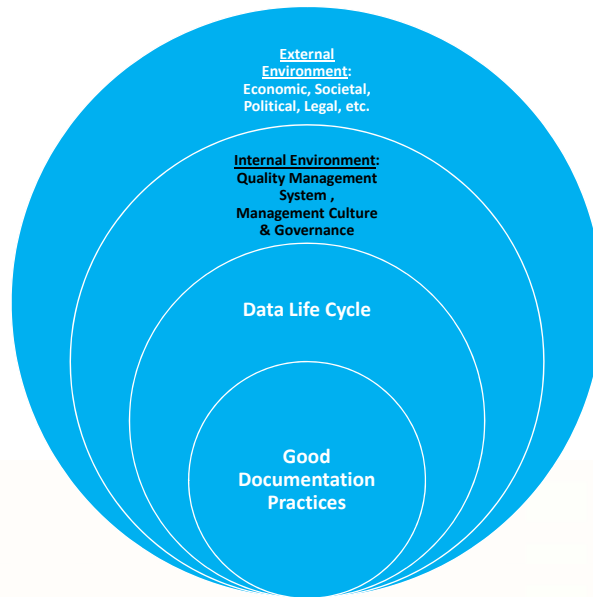
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Population of GxP Data: Meaningful Decision-Making



27

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28

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Quality Management Systems Key to Data Integrity

- Training Program
- Risk Assessment & Management
- Validation (*Computer, Method, Process*)
- Data Life Cycle
- Investigations Program
- Data Review Program
 - *Critical Thinking Skills*



29

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Quality Management Systems Key to Data Integrity

- Quality Audits & Inspections
- Vendor/Contractor Management
 - Agreements
 - Monitoring
- Management Culture & Controls
 - Transparency & Accountability
 - Tracking and Trending
 - Risk Profiling



30

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“The Fraud Triangle”*

*Source: *Occupational Fraud and Abuse*, by Joseph T. Wells, 1997; reference to work of Donald Cressey, *American Criminologist*

Incentive / Pressure

Incentives or pressures on management or other employees to materially misstate the truth

Attitude / Rationalization

An attitude, character or set of ethical values that allows one or more individuals to knowingly and intentionally commit a dishonest act, or a situation in which individuals are able to rationalize committing a dishonest act (e.g., the environment imposes sufficient pressure on them to meet certain goals or targets).

Opportunity

Circumstances that provide an opportunity to carry out a material misstatement



31

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Creating a Management Culture to Assure Data Integrity



- Transparency
- Accountability
- *Lead by Example*
- *Staying Continuously & Actively Involved*
- *Process Ownership / Personal Responsibility*
 - *Set Realistic Expectations*
- *Fair and Just Consequences & Rewards*
 - *Collaboration and Team Camaraderie*
- Staying “Current” with the “C” in CGxPs



32

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Possible Governance Framework

- Quality Risk Management
 - Defining Universe of Risk
 - Assigning Risk Rankings (e.g., capability & maturity measures)
 - Designing Risk Mitigation Controls
 - Focus on Remediation rather than Assessment
 - *With emphasis on Quick Wins!*
 - Communication & Monitoring of Residual Risk



33

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Possible Governance Framework

- Management Development Program
 - ICH Q10
 - Tangible Measures of Alignment of Expectations (incentives & pressures) with Capability and Maturity (risk profile)
 - Behavioral Management—*Patient First*
 - Inspiring Positive Outcomes & Cultural Change
 - Code of Ethics & Ethics Program
 - Incentivizing 'Meaning' in Labor
 - Assessing & Reworking Employment Model



34

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Possible Governance Framework

- Data Integrity Compliance Officer (?)
 - Reporting to Quality Council, CEO, Board of Directors
- Other potential novel / adapted roles:
 - ‘Chief Data Officer’
 - ‘Data Process Owners’
 - ‘Data Analytics SMEs’
 - ‘Forensic Auditors’



35

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Possible Governance Framework

- Data Reviews, Quality Audits & Inspections
 - Assess Foundational Data & Remediate, as necessary
 - Assess Control Methodology & Practice
 - Investigations Program & CAPA
 - Enhancing ‘Critical Thinking’ Skills
 - Institute ‘Data Analytics’
 - Metrics, Tracking and Trending, & Feedback Loops—ICH Q12
 - *Beware of the potential dangers of metrics! Encourage balance and embrace ‘residual risk’*
 - Reporting to Management



36

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Possible Governance Framework

- Modernizing Quality Management Systems,
 - e.g., Training Program, CSV / Part 11, Data Review Practices, Vendor Management, etc.
- Introduce new Quality Systems controls, as needed:
 - e.g., *Data Life Cycle*
- Enhance existing systems, processes, organization, facilities, etc, per modernized QMS
 - Quick Wins!
 - Long-term continuous improvement



37

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Measures of Success—short term

A FEW EXAMPLES...

- Uptick in Discovery of Data Integrity Issues
- Resource investment
- Increasing engagement
 - E.g., Technology adoption, Skill development
- Modernized QMS:
 - Prospective personnel, systems, processes, methods, contract sites, suppliers introduced under modernized framework



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Strategic Plan for Preventing and Mitigating Drug Shortages

U.S. FOOD AND DRUG ADMINISTRATION, OCTOBER 2013

- *“Several indicators of historical quality, including a manufacturer’s history of inspection outcomes and classification, recalls, and shortages, are publicly available. Nevertheless, numerous comments to the Federal Register notice suggested that buyers (e.g., hospitals, health maintenance organizations, group purchasing organizations, and others) do not consider or value this potentially important information.”*



33

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Strategic Plan for Preventing and Mitigating Drug Shortages

U.S. FOOD AND DRUG ADMINISTRATION, OCTOBER 2013

- *“This decoupling of quality considerations from purchasing decisions makes cost the major factor in purchasing decisions, most likely intensifying price competition, leading manufacturers to focus more on reducing costs than on maintaining quality, and potentially contributing to shortages.”*



34

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Most Efficient Means to Incentivize Data Integrity and Management / Cultural Progress?

- Consumer Awareness—*incentivizing manufacturers by creating link between product quality and purchasing decisions*
- The ‘Uber Economics’ of Healthcare!
 - Commercial patient-reported outcomes & performance measures
 - Corresponding patient demographics



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Measures of Success—long term

A FEW EXAMPLES...

- Portfolio focus on end-to-end Value
- Optimized Consumer Outcomes
- Enhanced Consumer Trust
- Agile & flexible change management
- Rote thinking to Critical thinking
- Reduced costs through proper use of technology
- Innovation—e.g., personalized medicines



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Summary: Keys to a Successful Data Integrity Assurance Program

- Management Commitment & Governance
- Quality Risk Management
- Critical Thinking Skills
- Embracing Innovation
- Behavioral Change Management

Win-Win!



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Global Community for Healthcare: Medicines for All

- Safe
- Effective
- Quality
- Affordable
- Accessible
- Ethically Produced



44

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Questions / Comments



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45

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