

**Indian
Pharmaceutical
Alliance**



Building a Strong Quality Culture

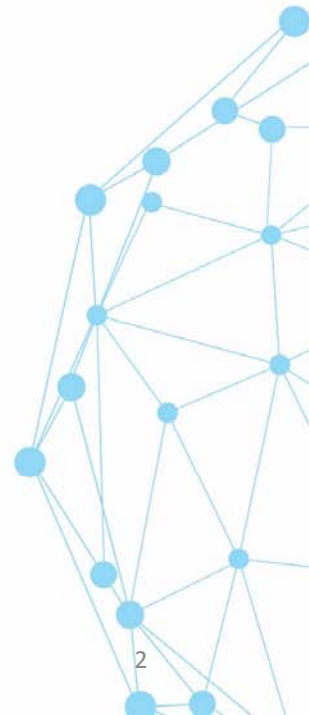
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Office of Pharmaceutical Quality





Agenda

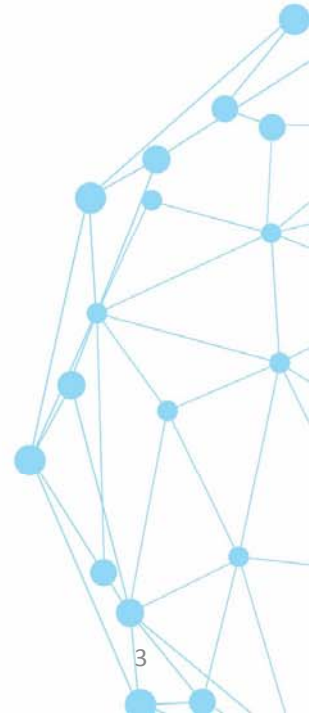
- Changing an Organization
- Cost of (Poor) Quality
- Implementing an Effective Quality System



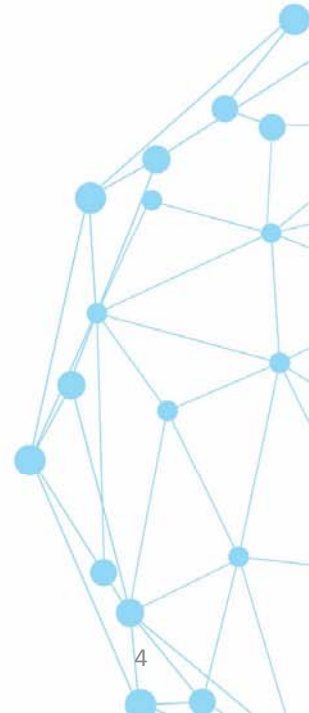
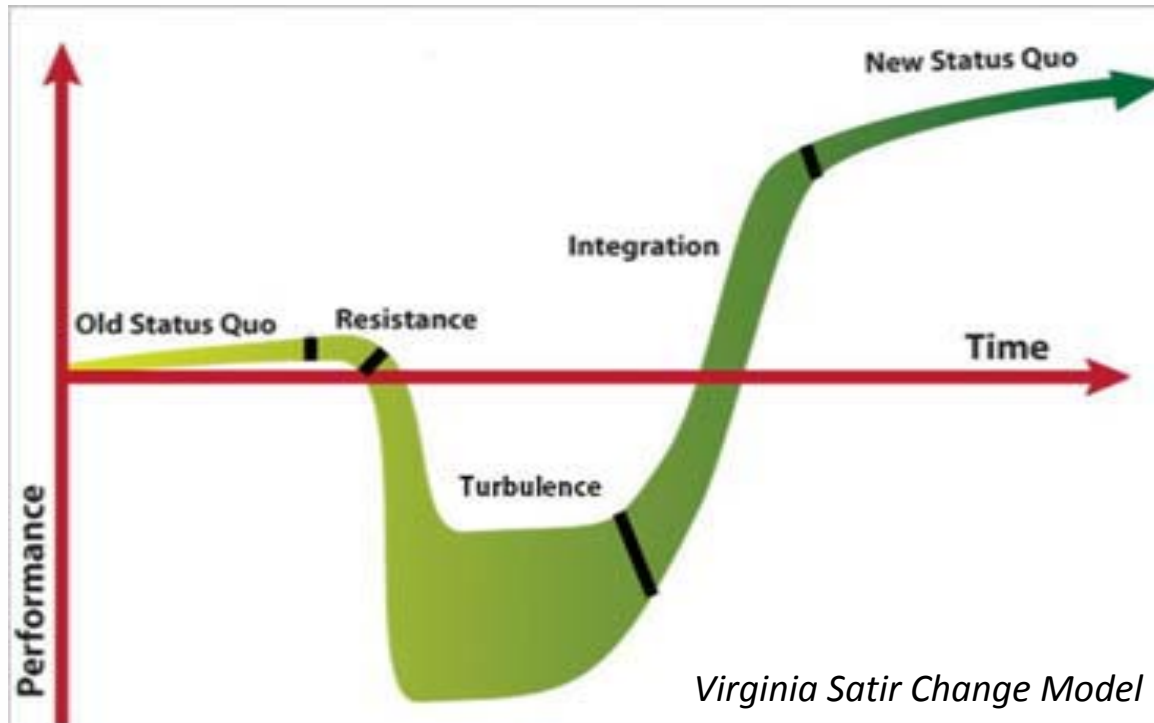


Traditional Role of QA / Compliance

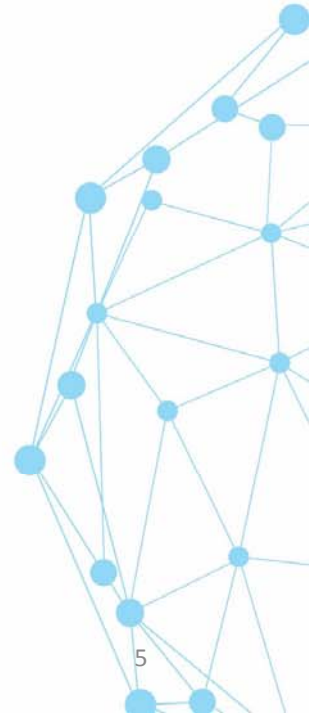
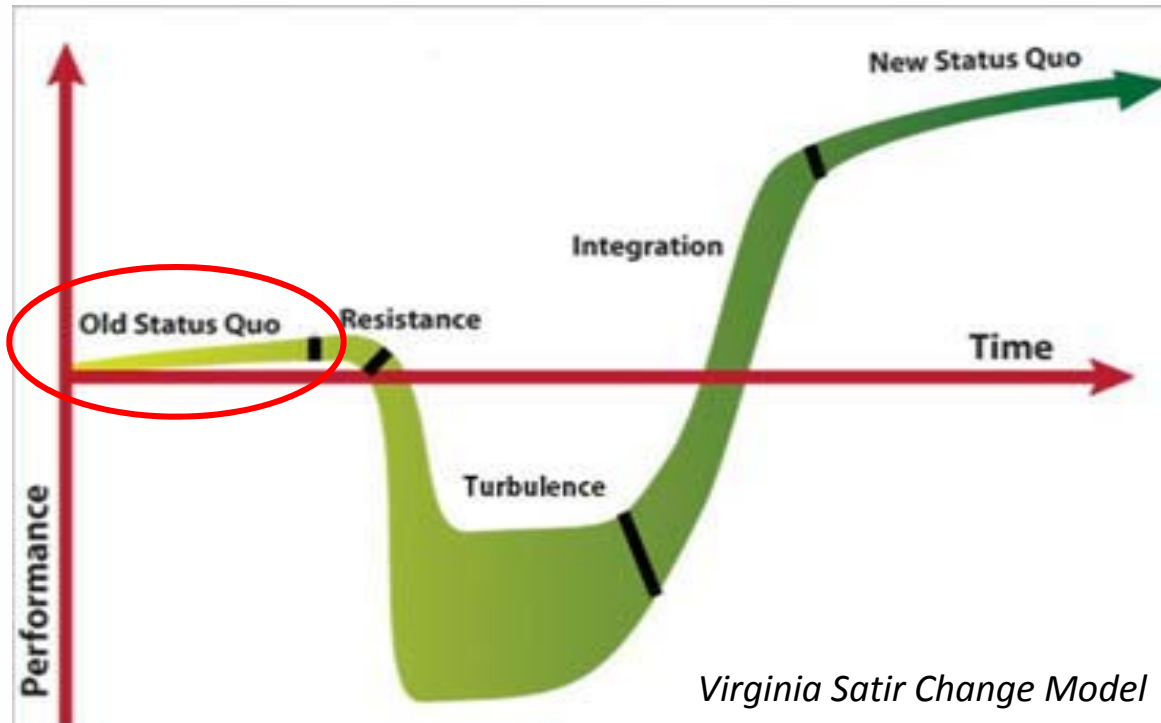
- Often viewed by company personnel and regulators as “police”
- Monitoring daily activities and operations
- Review / approve SOP’s, protocols, validation, etc.
- Managing Quality Systems
- Performing internal / external audits
- Final reviewer of deviations & corrective action plans
- Drug product release



Organizational Change Curve



Organizational Change Curve



Expanding QA Roles & Improving Quality Culture



Require QA partnership in:

- Development of new product or process
- Design, construction and qualification phases of new facilities
- Re-design and qualification of renovated facilities
- Other large projects (e.g. installation & validation of new IT systems - SAP)
- Ensuring Quality Culture principles at contract facilities align with internal principles





What is a Quality Culture?

“Leadership, vision and values make up the foundation for a culture of quality...An organization’s culture - the way it does things, the way it “lives” - has a direct impact on how well its processes and people operate.”

Clues About Culture, Amanda Hankel, Quality Progress, August 2014

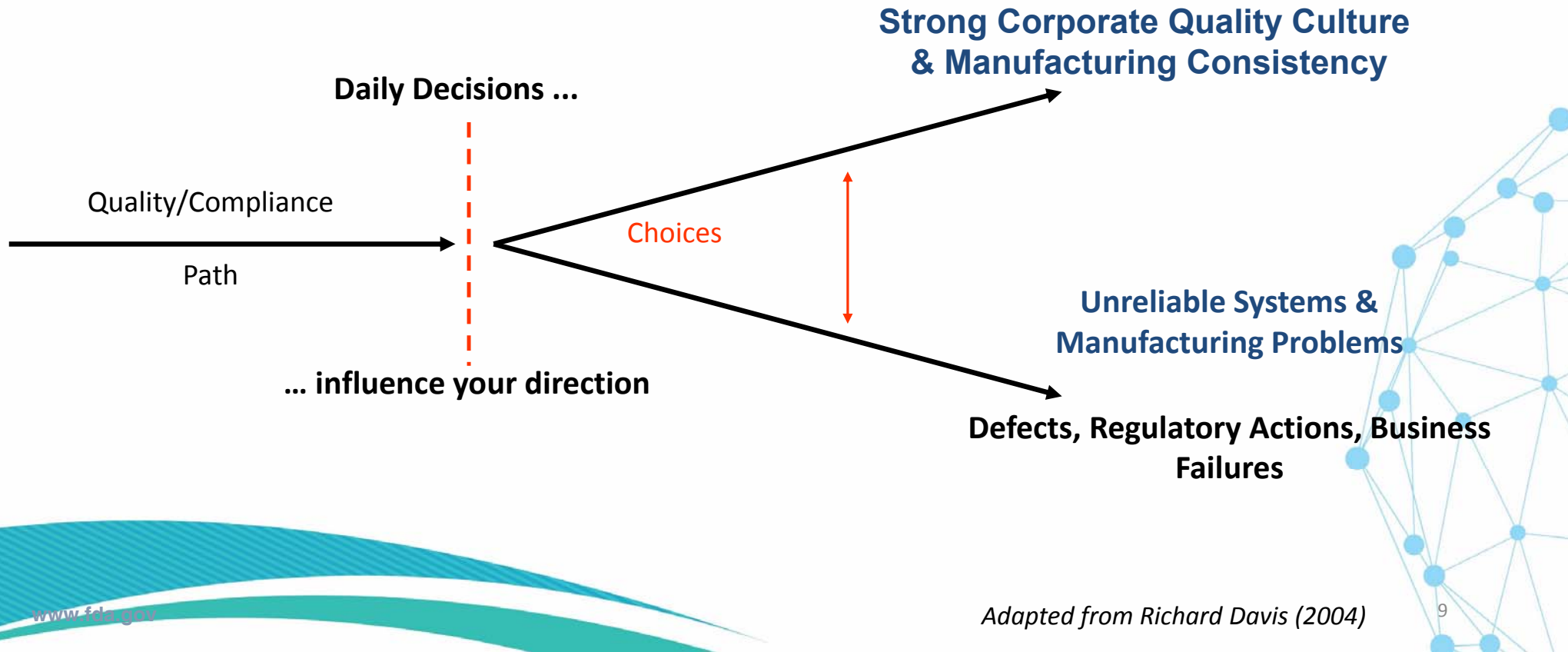


Quality Culture is Driven by Leadership

- Definition of “CGMP” amended to explicitly include management oversight of manufacturing to ensure quality
- *“For purposes of paragraph (a)(2)(B), the term ‘current good manufacturing practice’ includes the implementation of **oversight** and controls **over the manufacture of drugs to ensure quality**, including **managing the risk** of and establishing the safety of raw materials, materials used in the manufacturing of drugs, and finished drug products.”* – SEC. 711. Enhancing The Safety And Quality Of The Drug Supply. Section 501 (21 U.S.C. 351)
- “Leadership is essential to establish and maintain a company-wide commitment to quality...” – ICH Q10

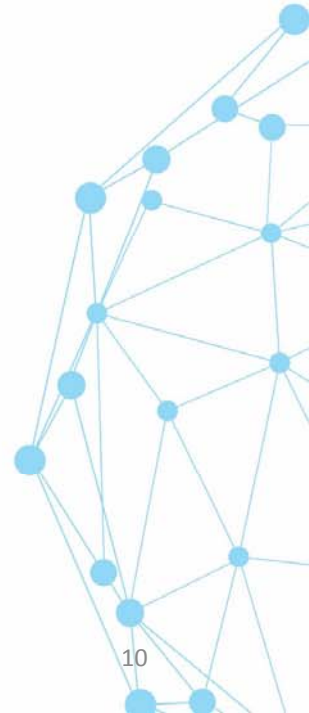


Employees at All Levels can Demonstrate Leadership





The Cost of (Poor) Quality





The Cost of (Poor) Quality

- Direct Costs
 - Related to Product Failure, Scrap, etc.
- “Continual Crises” Costs
 - Unexpected costs associated with GMP non-compliance
 - Reactive versus preventive approaches
- Remediation Costs
 - Related to problem identification, correction and reporting
- Employee Costs
 - Lower productivity, distrust, morale issues, turnover/loss of talent, etc.

[Dr. Jeffrey Macher, Assoc Professor at Georgetown University]



The Cost of (Poor) Quality

- Regulatory Action Costs
 - Related to legal fees, 3rd party consultants, etc.
 - Related to recalls, discontinuation, suspended operations, etc.
- Market Share Costs
 - Related to volumes, supply availability, supply reliability, etc.
- Reputation Costs
 - Credibility, adverse publicity, loss of business, etc.

[Dr. Jeffrey Macher, Assoc Professor at Georgetown University]



The Cost of (Poor) Quality



Source: Principles of Quality Costs, 3rd Edition, Campanella, Pg. 8



The Chiron Corporation Case

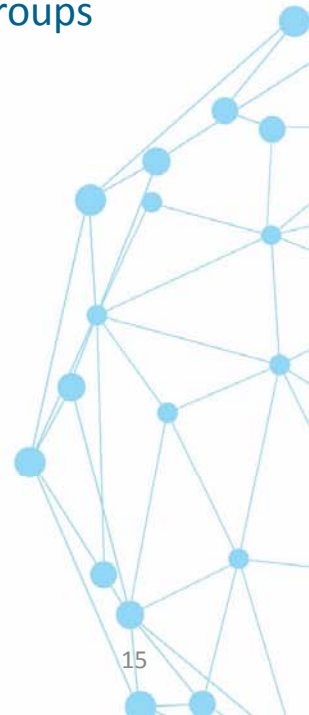
- Manufacturer of Fluvirin influenza virus vaccine expected to supplied nearly half of the U.S. supply of flu shots for the 2004-2005 season
- Numerous bulk and final product sterility failures
- Numerous bioburden failures (>50%) for intermediates
- Numerous environmental excursions with the same organism, also identified in product-related testing
- The company looked at each failure/excursion as a **discrete incident rather than** looking across all the data (quality metrics) and **recognizing trends** and relationships between the data (e.g. how environmental excursions related to bioburden failures).
- “FDA and MHRA’s review of Chiron’s investigation...led FDA to the conclusion that the **sterility, and therefore safety**, of the vaccine Chiron produced for the 2004-2005 influenza season **could not be assured.**”

– Dr. Jesse Goodman, Congressional Testimony, May 4, 2005



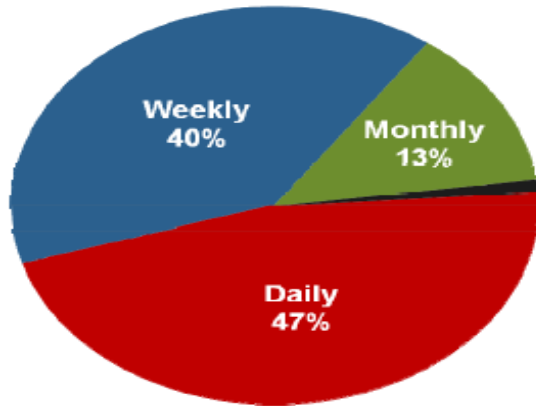
Impact on Public Health

- ~ 50 million doses of flu vaccine for the US 2004-2005 unavailable, **leading to a severe shortage**
- Who needs a flu shot?
- Impacted all persons aged 6 months and older (rare exceptions). Priority given to at-risk groups including:
 - Children aged 6-59 months
 - People aged 50 years and older
 - Pregnant women
 - Health care providers
 - Caregivers
 - Immunosuppressed patients





Further Impact of Drug Shortages

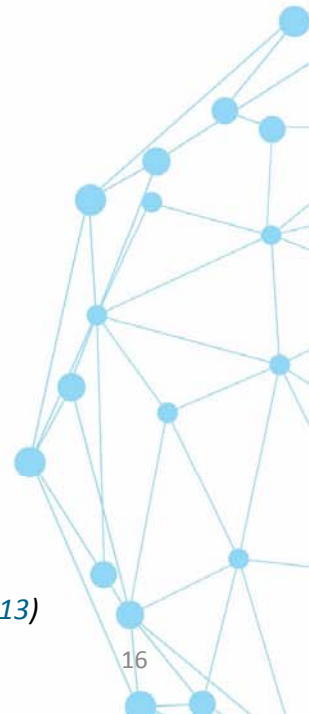


→ Percent of Hospitals experiencing a drug shortage by frequency. Only 1% reported not experiencing any shortages.

- AHA survey of 820 non-federal acute care hospitals June 2011

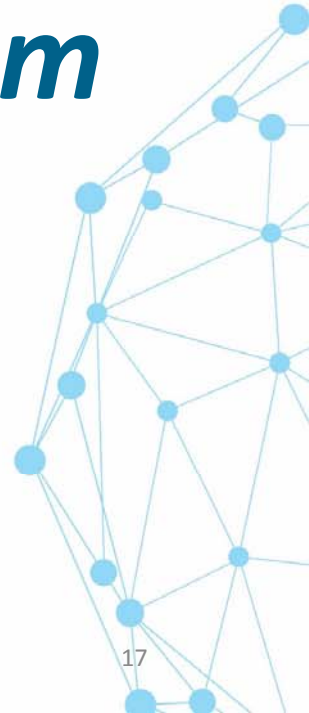
- Added strain on the healthcare system
- Added burden on physicians and pharmacists
- Diverted resources from patient care
- Increase of adverse events and medication errors
- Delayed therapies, inadequate care, cancelled care. . . .

- Journal of Managed Care Pharmacy, Vol 19 No 9 , pp 783-789 (2013)





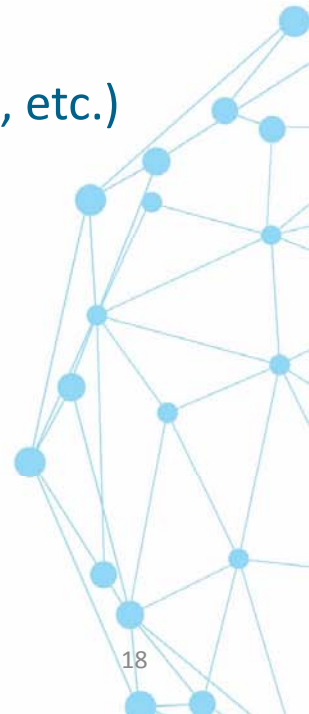
Implementing an Effective Pharmaceutical Quality System (PQS)



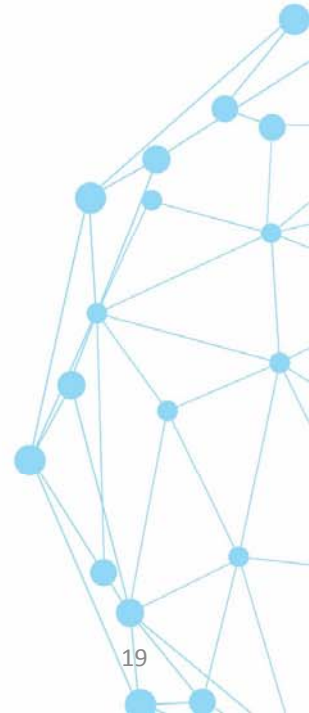
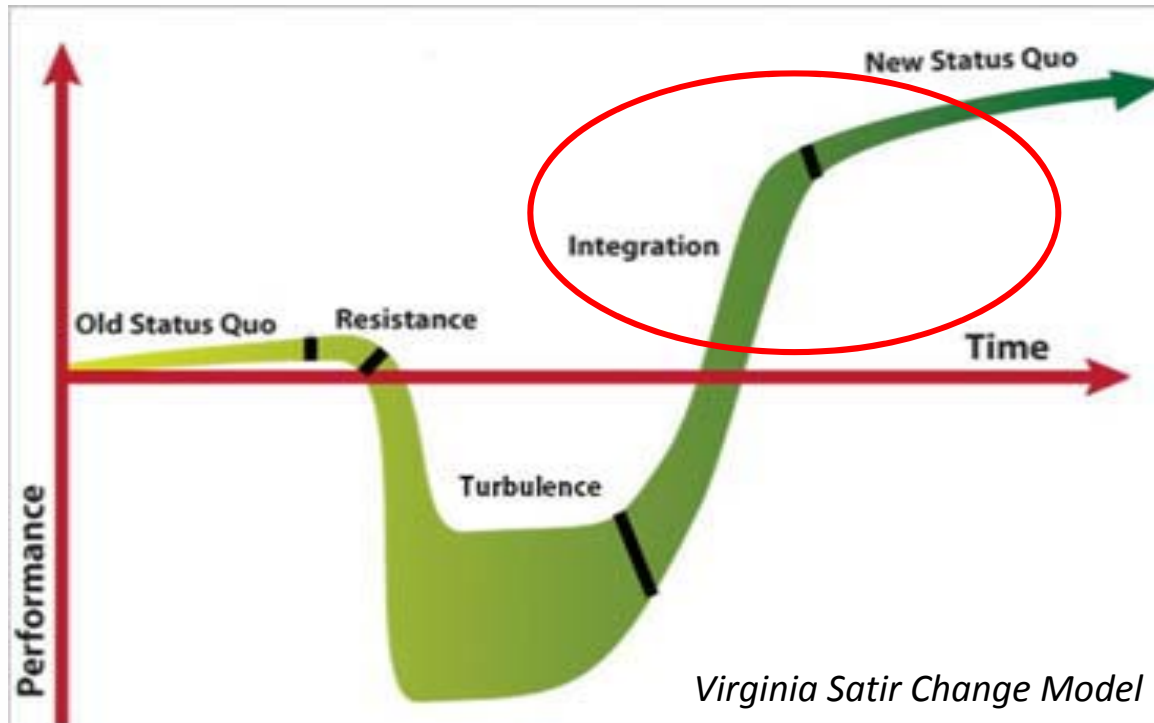


The Business Case

- **GMP is Good Business Practice**
 - PQS further aligns GMP with basic business goals of process predictability (e.g., Right First Time) & product dependability
- **Deming's Chain reaction**
 - Reduce Variability → Improve Quality → Decrease Costs (rejected goods, etc.) → Better Products and Productivity... → More Competitive
- **Measuring Performance is Fundamental to Any Business**
 - **Actual Performance vs. Standard:** Identify process and product quality performance gaps, and promptly correct **root causes**
- **Prevention**
 - **Preventing manufacturing problems is good business**



Organizational Change Curve





ICH Q10 Pharmaceutical Quality System

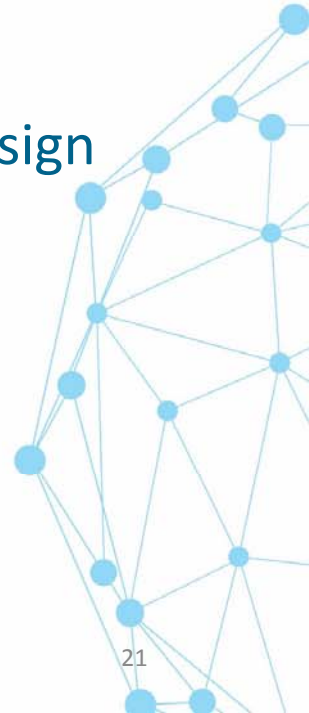
- **Foundation:** Regional GMP (drug product) requirements, the ICH guidance “Q7 Good Manufacturing Practice Guidance for Active Pharmaceutical Ingredients,” and ISO quality management system guidelines form the foundation for ICH Q10.
- **Harmonization:** ICH Q10 provides a harmonized model for a PQS.
- **Lifecycle:** Defines how a modern quality system assures science- and risk-based drug manufacturing and quality decisions throughout the lifecycle.





ICH Q10 Pharmaceutical Quality System

- Establish and maintain a State of Control
- Facilitate continual improvement
- Facilitate effective knowledge transfer and management
- Facilitate implementation & effective utilization of Quality by Design (Q8 Pharmaceutical Development)
- Risk Management (Q9 Pharmaceutical Risk Management)





Summary - Quality Culture

- An environment in which each and every person understands and embraces their responsibility for ensuring quality and protecting patient safety
- Quality culture drives decision-making and behaviors at all levels of the organization every day
- Without a strong quality culture, quality outcomes and delivery of quality medicines to patients cannot be assured
- *“Quality means doing it right when no one is looking.”* – Henry Ford





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