ARC Advisory Group

vision experience answers

THOUGHT LEADERS FOR MANUFACTURING & SUPPLY CHAIN

PAT:
Impacting Manufacturing Operations & Automation Platforms

From Procedural to Risk-based Compliance, Inspection, and Enforcement

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What is PAT?

- **There are many definitions**
  - FDA Web Site: http://www.fda.gov/cder/OPS/PAT.htm

    PAT is a system for designing, analyzing, and controlling manufacturing through timely measurements (i.e., during processing) of critical quality and performance attributes of raw and in-process materials and processes with the goal of ensuring final product quality
  - FDA Guidance for Industry: PAT – A Framework for Innovative Pharmaceutical Development, Manufacturing, and Quality Assurance
  - The last word on PAT extends its use from a manufacturing to a cradle-to-grave tool for gaining process knowledge

Dr. Ajaz Hussain
FDA Deputy Director
Office of Pharmaceutical Sciences

What is PAT?

The optimal application of analytical chemistry tools, feedback process, control strategies, information management tools and/or product/process optimization strategies to the manufacture of pharmaceuticals. The focus is on the science of "building quality in" and efficiency via continuous quality control, assurance, and/or validation.

Dr. Melvin Koch
Director
Center for Process Analytical Chemistry
University of Washington

Why is PAT important?

- **Part of the FDA's change from procedural to a new scientific risk-based approach to compliance, inspection, and enforcement**
- **Quality cannot be tested into products; it should be built-in or should be by design - true spirit of the cGMPs**
- **Manufacturing operations are being required to change from reactive to pro-active**
  - Impacts almost every manufacturing activity as well as those that "touch" manufacturing
  - Will cause significant organizational changes
  - Requires changes to most current automation platforms and architectures

Why is PAT important?

We would have adopted PAT with or without FDA because it's the right thing to do, an important component of our "Right First Time" program.

Norman Winskill, Ph.D.
V.P. Global Manufacturing Services
Pfizer

What's in it for me?

- **Complimentary to the new pharmaceutical business model for the 21st century**
- **Complimentary to the industry's urgent need to focus on manufacturing**
  - Manufacturing productivity, flexibility, and response improvements
  - Risk base approach to compliance, inspection, and enforcement that enables continuous improvement and innovation
  - Product quality, safety, security, and delivery
  - Technology transfer – time and cost

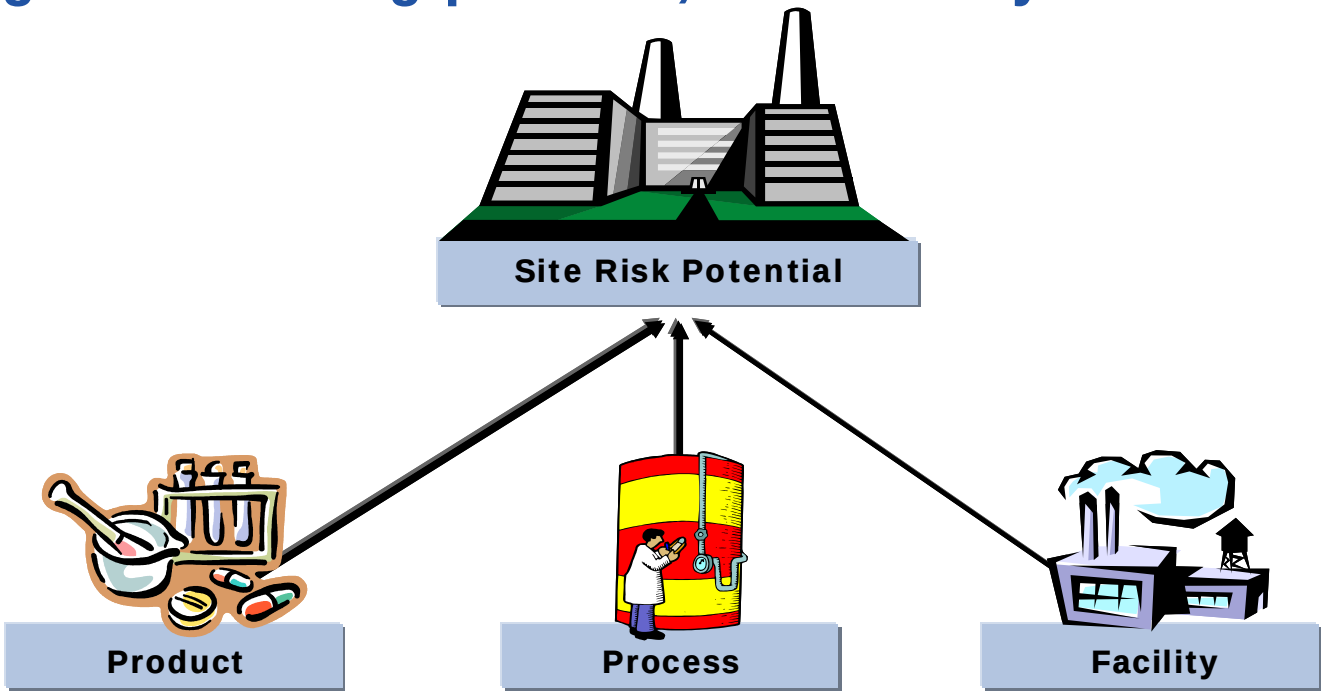
What's in it for me?

..as we increase process understanding and show we're in control of our processes, we would expect that FDA will consider Pfizer operations to be low-risk, and under its risk-based GMP initiative give us less scrutiny and more leeway to implement continuous change ourselves, says Winskill.

Pharmaceutical Manufacturing Magazine

Where do I start?

- The FDA's new Risk Ranking Model identifies and ranks "possible" hazards or sources of harm rather than "probability" or the likelihood of occurrence of harm
- The Site Risk Potential (SRP) is then determined by rating contributing product, and facility hazards or risks



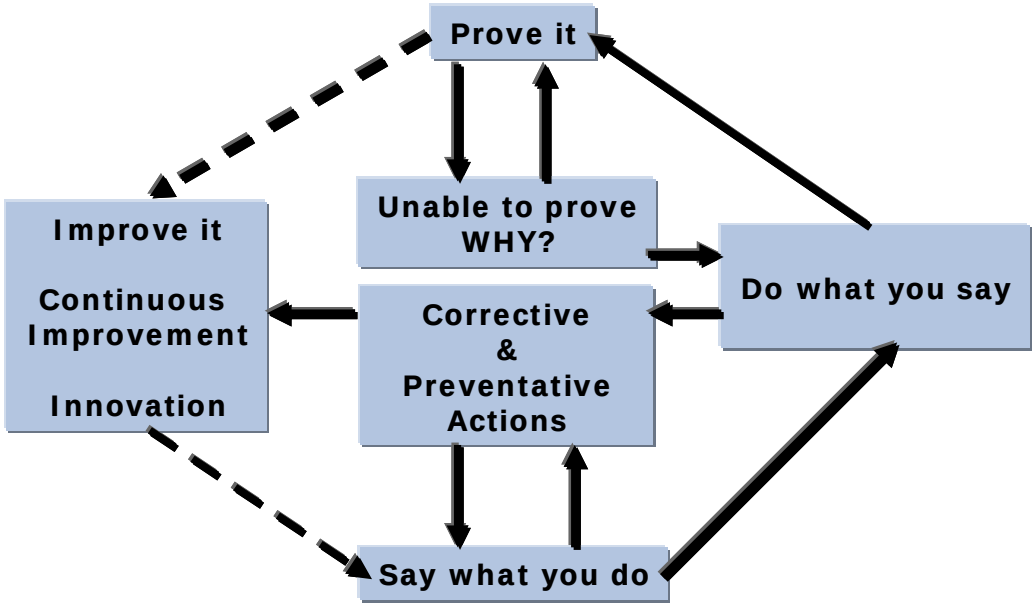
Where & when do I start?

Product	Process	Facility
Sterile	Process complexity	Type of facility
Prescription	State of control	Estimated production volume
New	Risk mitigation capabilities	Inspection history
High propensity for recall		History of violations
High severe hazard threat		

The FDA's Risk Ranking Model and its Component Criteria will Determine 50 Percent of Sites Inspections

How do I start?

- **A modern quality system**
  - Risk mitigating functionality
  - Enables continuous improvement and innovation
- Knowledge management functionality for improving knowledge of product/process chemistry

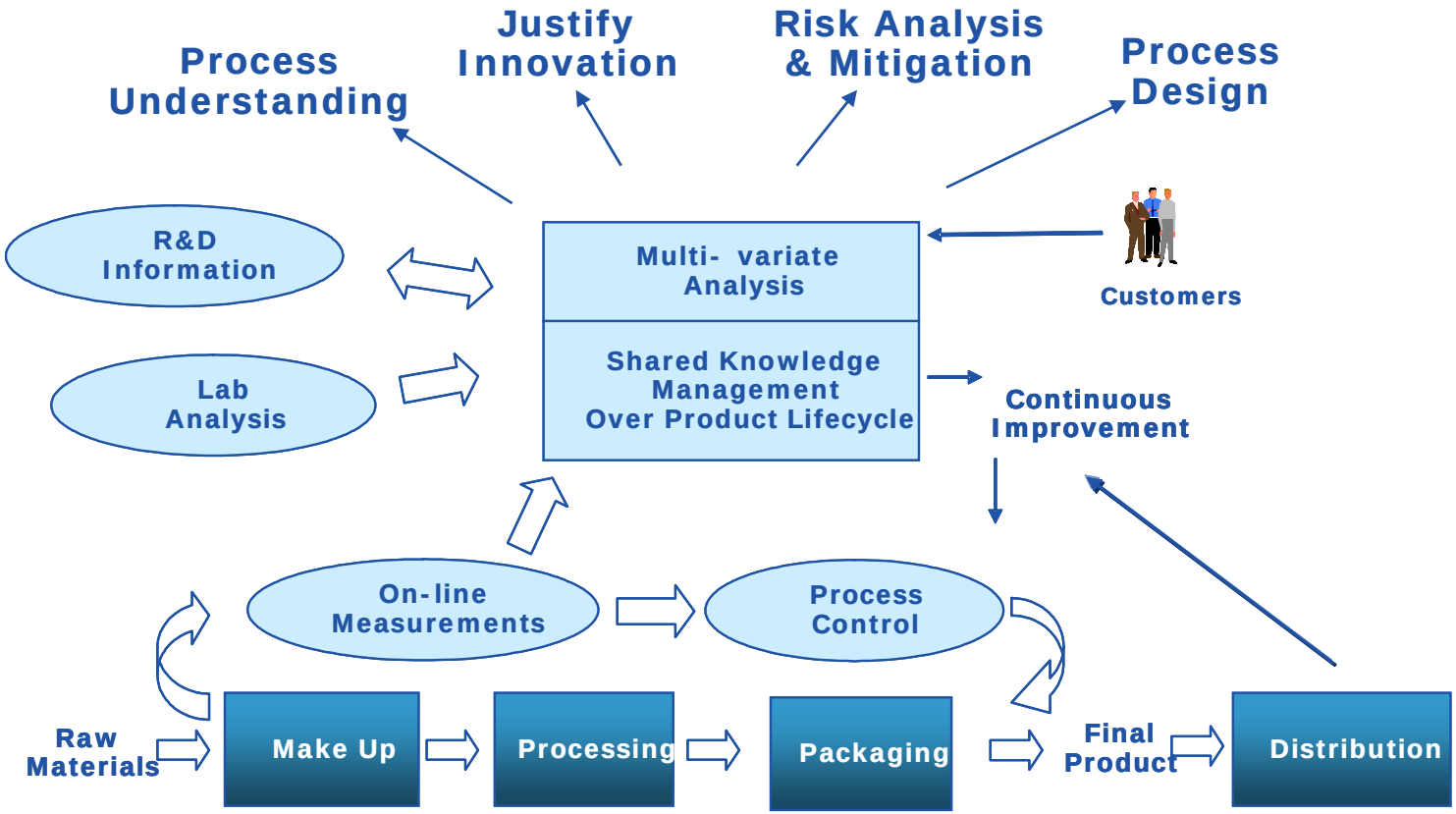


Source: Vibhakar Shah
FDA PAT Forum, December 2004

It will require highly automated electronic records systems and the infrastructure to support it …
….that enable the exchange of information among business and production systems and sub-systems as well as trading partners, enabling multivariate data analysis

PAT Enabled Platforms and Architecture

Must support collaborative arrangements for extensive information collection, management, analysis, and sharing for decision support



PAT Enabled Platforms and Architecture

- **Highly automated systems must be based on current and evolving standards that enable interoperability**
  - ISA 88, Make2Pack, BatchML, IEC 1131-3, ISA 95, B2MML (XML), OPC, PAT (evolving), Safety & Security, and others
- **Date certainty**
  - Authenticity
  - Integrity
  - Accuracy
- **High reliable data storage through software and hardware solutions**
- **Data warehouse and federated data design are a critical components**
- **Well defined work flow processes**
- **Extensive multivariate analysis and optimization tools**

"SAP xMII enables Adaptive Manufacturing to drive manufacturing excellence by synchronizing manufacturing operations with business systems to deliver "one version of the truth"".

ARC White Paper April 2006
"Pursuing Manufacturing Excellence through Real-time Performance Management and Continuous Improvement "

".....It took 40 years for businesses to figure out how to redesign their factories and processes so that electricity could deliver a productivity payoff. Managers cannot afford to wait decades to harness the greater productivity offered by today's IT advances.

Productivity's Technology Iceberg
by Erik Brynjolfsson,
Professor of Management
MIT Sloan School of Management

The technology platform is a critical component and accelerator in this transition