

Designing for Manufacturability

Building Quality By Design

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The Age of Continuous Innovation

- ▲ Transition from the “Information Age” to the age of “Continuous Innovation”.
- ▲ Shift away from “Incremental Innovation Cycles” supported by reactive, standalone and fragmented processes and systems.
- ▲ Embrace a proactive, cohesive and fully integrated approach.

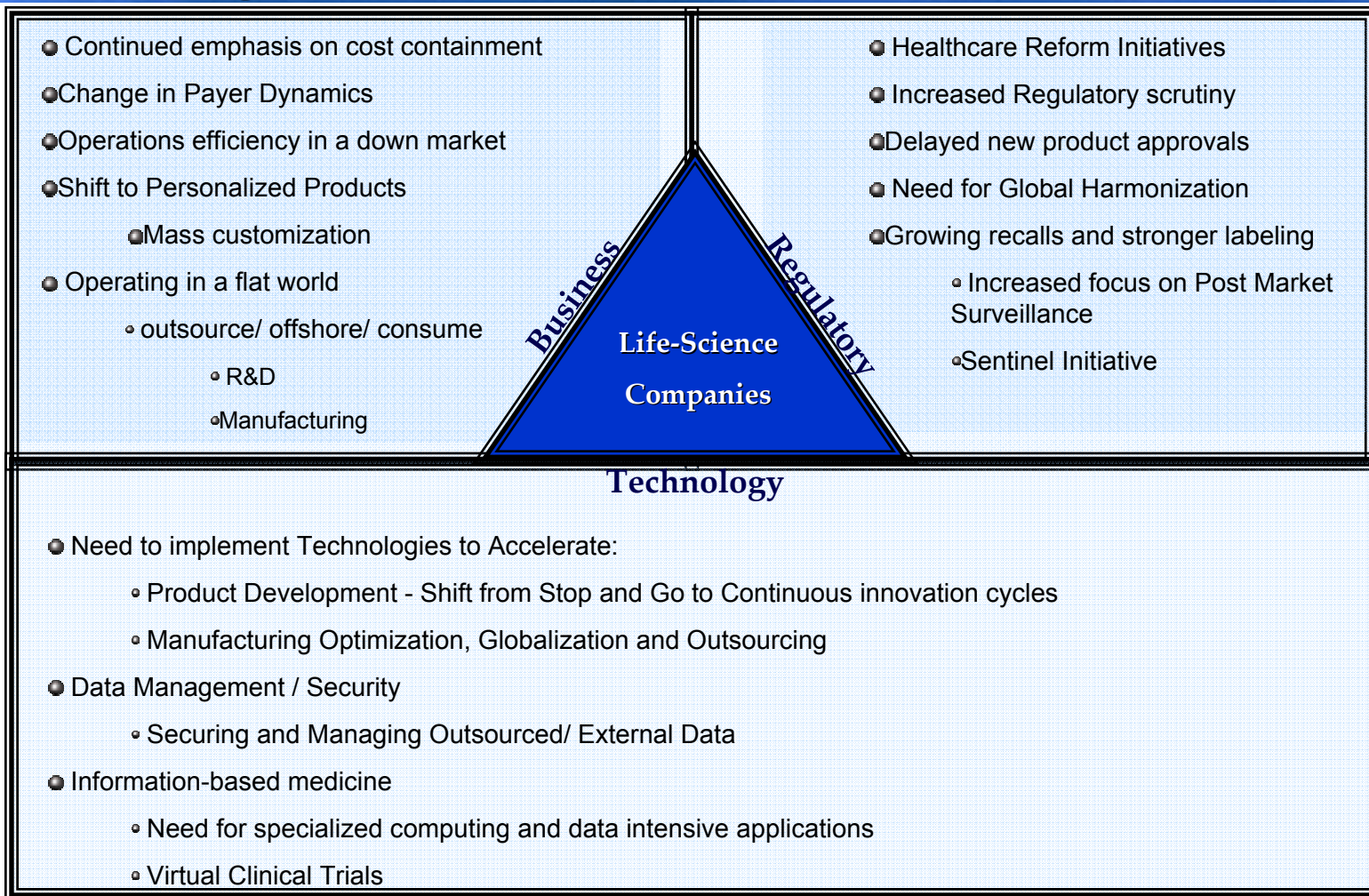
Even if you're on the right track...



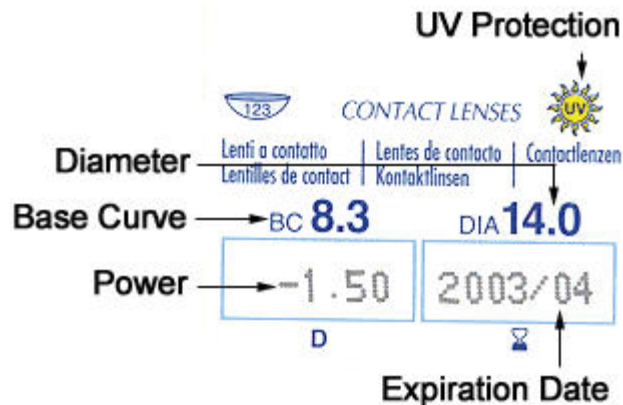
AXENDIA

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Industry Challenges in The Age of Continuous Innovation



Personalized Healthcare: Increasing Complexity



Computer-Assisted
Hip Replacement Surgery



BIOMET
Signature™
Personalized
Patient Care



The Current State of Quality

“Despite the slogan ‘building quality in’, most quality assessment today relies on end-product testing. This is a problem in and of itself.

In addition, many of the test methods currently being used have severe limitations in the modern, mass production environment.”

Dr. Janet Woodcock,

FDA’s Deputy Commissioner and Chief Medical Officer

Source: USFDA



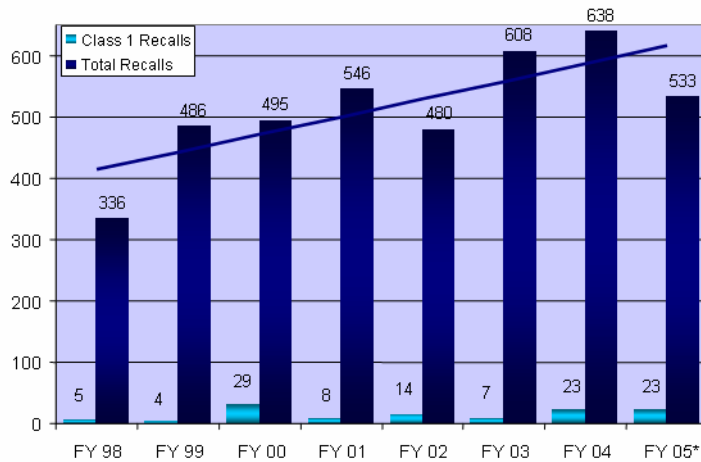
The State of Quality

- △ An industry study points out that one leading manufacturer of medical implants estimates that of the 2.1 million people who received their products over a ten year period, only 0.03% had to have an implant removed (explanted) because of a defect.
 - △ 0.03% represents 630 patients requiring explantations
 - △ or 300 defects per million implants sold

SIGMA LEVEL	PARTS PER MILLION (PPM)
3	66811
4	6210
5	233
6	3.4

The State of Quality

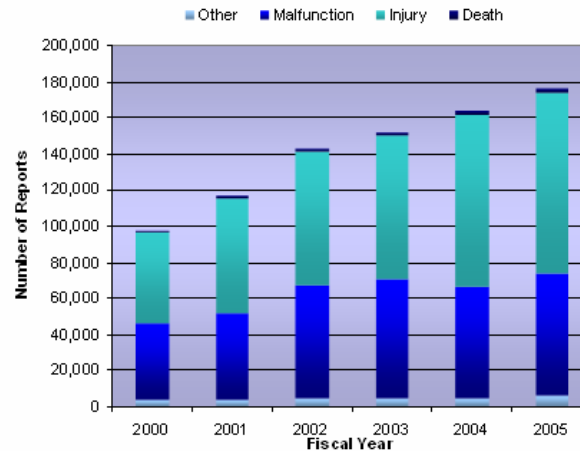
Medical Device Recalls are Increasing



* FY 2005 Data as of 9/13/05

Medical Device Reports are Increasing

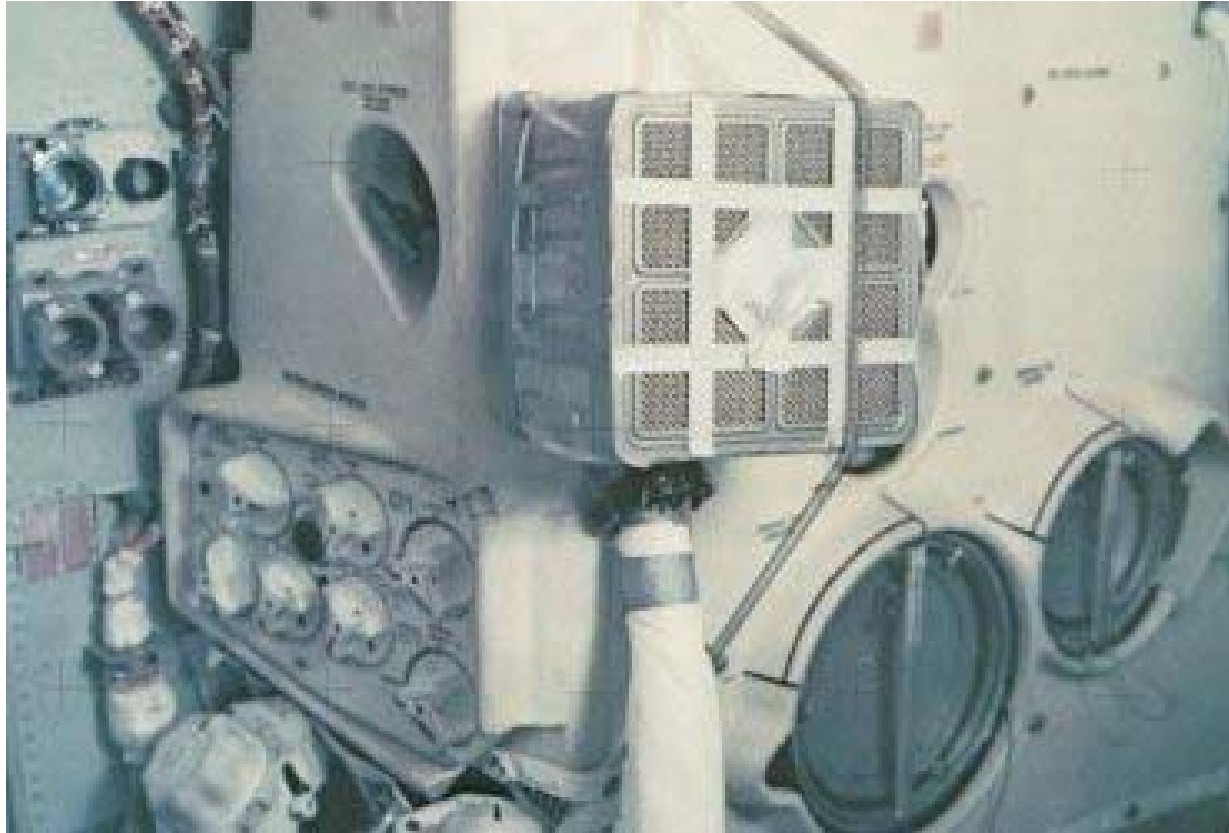
REPORTS RECEIVED - FY 2000 - 2005



In FY 05 CDRH received about 176,000 reports
> 1,125,000 total



Rockville, We've Had a Problem



Emergency scrubbers built by Swigert and Haise. Consisted of a taped-over double canister holding one end of a suit nozzle. The canister was built of arched cardboard, which was covered by a plastic bag

Got CAPA?

- ▲ How many have a CAPA system?

- ▲ Why do you have a CAPA system?
 - ▲ FDA requires each manufacturer shall establish and maintain procedures for implementing *corrective and preventive action*.

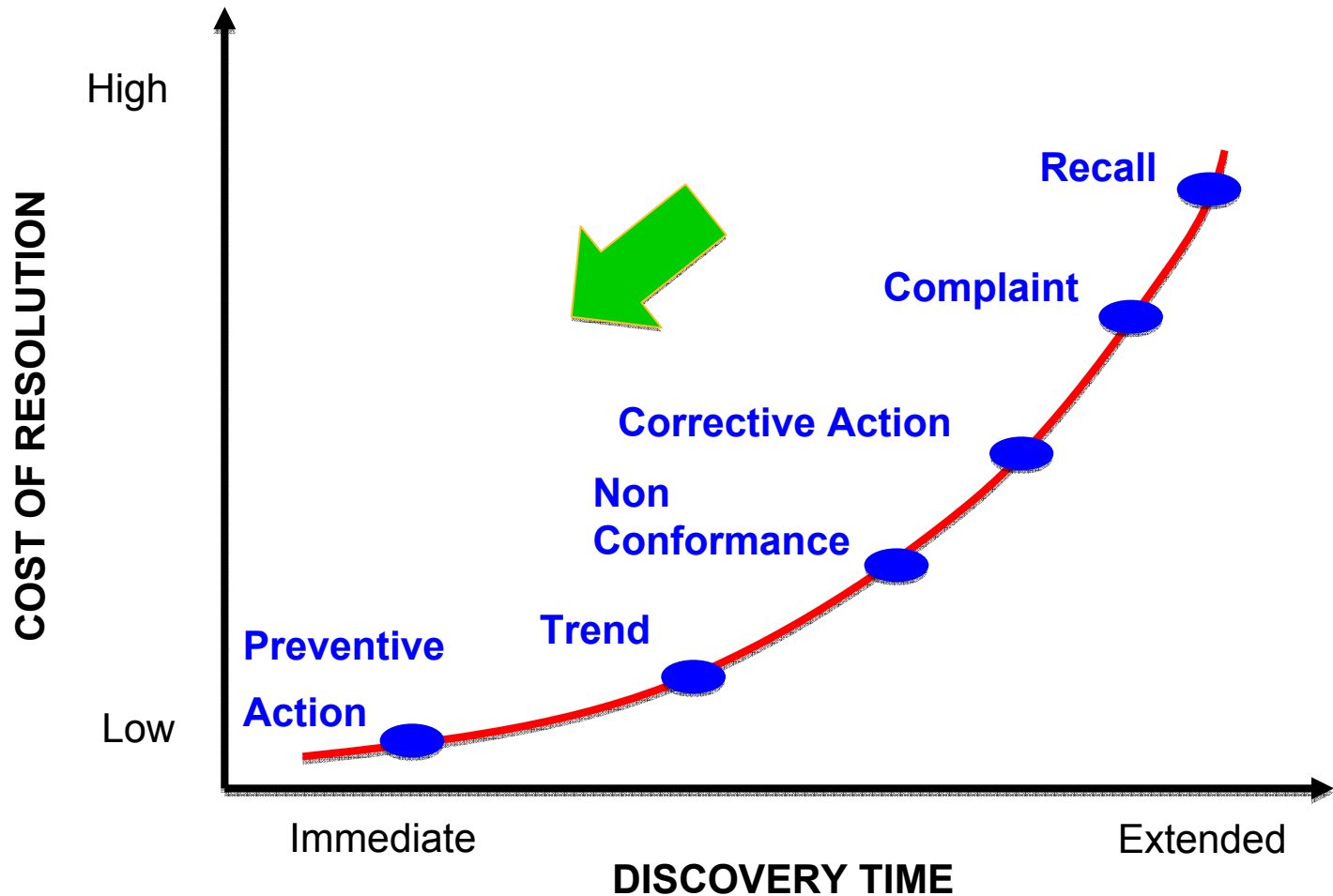
- ▲ What is the key measurement for CAPA?
 - ▲ Time to Closure
 - ▲ Result: CACA
 - ▲ CA-CA-CA

Stop Tracking CAPAs



Start Preventing Them

Shifting to CAPA to PACA



If we asked people in the industry,

- △ How do you know that a component or a manufacturing process or a device or a certain parameter of a device is acceptable?
 - △ We do a certain amount of testing and we test the components.
 - △ Most of the test methodology is standardized.
 - △ For example, shock and vibration testing, mechanical stability, electrical characteristics of parts, etc. - those test methodologies are pretty well established.
- △ How many devices or components do you test with that methodology?
 - △ We test 10 devices or 15 components and see if they work.
- △ What is driving that quantity?
 - △ That's engineering practice.
 - △ That's what we've done all along.
 - △ That's something that the whole industry has been doing for 40-plus years.
 - △ It's basically based on engineering know-how and experience over the years.

Fred Colen, President
Boston Scientific Cardiac Rhythm Management division

Source "[The Gray Sheet](#)" - July 28, 2008



Fred Colen's Answer

- △ That is the piece that we've changed.

- △ I compare this to a clinical trial where we say:
 - △ I have a hypothesis and I want to prove something.
 - △ If I want to prove or disprove the hypothesis with a certain confidence level, how many patients do I need to include in the clinical study?
 - △ It's a statistically-based approach and that is what we've now implemented in our organization.

- △ When we want to test a component or a device or a manufacturing process, we ask,
 - △ What is the statistically driven sample size that we need to use to say this with a certain level of confidence?'

 - △ And that determines the numbers.

Fred Colen, President
Boston Scientific Cardiac Rhythm Management division

Source "The Gray Sheet" - July 28, 2008



Tilting at Silos



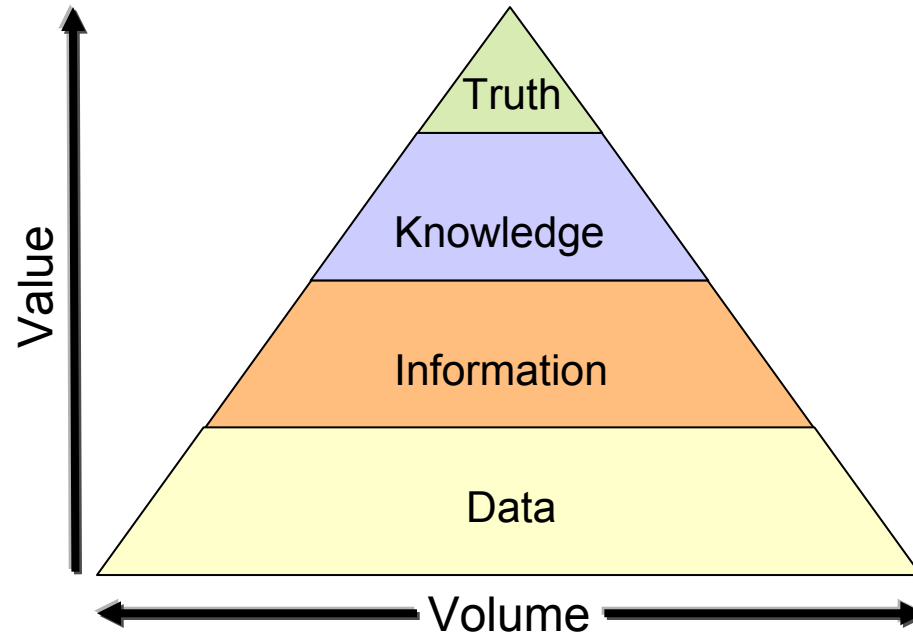
The Catapult effect



Looking For Truth In All The Wrong Places



The Pyramid Truth™



- ▲ Transform Wisdom to Truth or Facts
- ▲ Transform Knowledge to Wisdom
- ▲ Transform Information to Knowledge
- ▲ Transform Data to Information

The Desired State

- ▲ Product quality and performance achieved and assured by design of effective and efficient manufacturing processes
- ▲ Product specifications based on mechanistic understanding of how formulation and process factors impact product performance
- ▲ An ability to effect Continuous Improvement and Continuous "real time" assurance of quality

Source: USFDA



The Total Product Life-Cycle



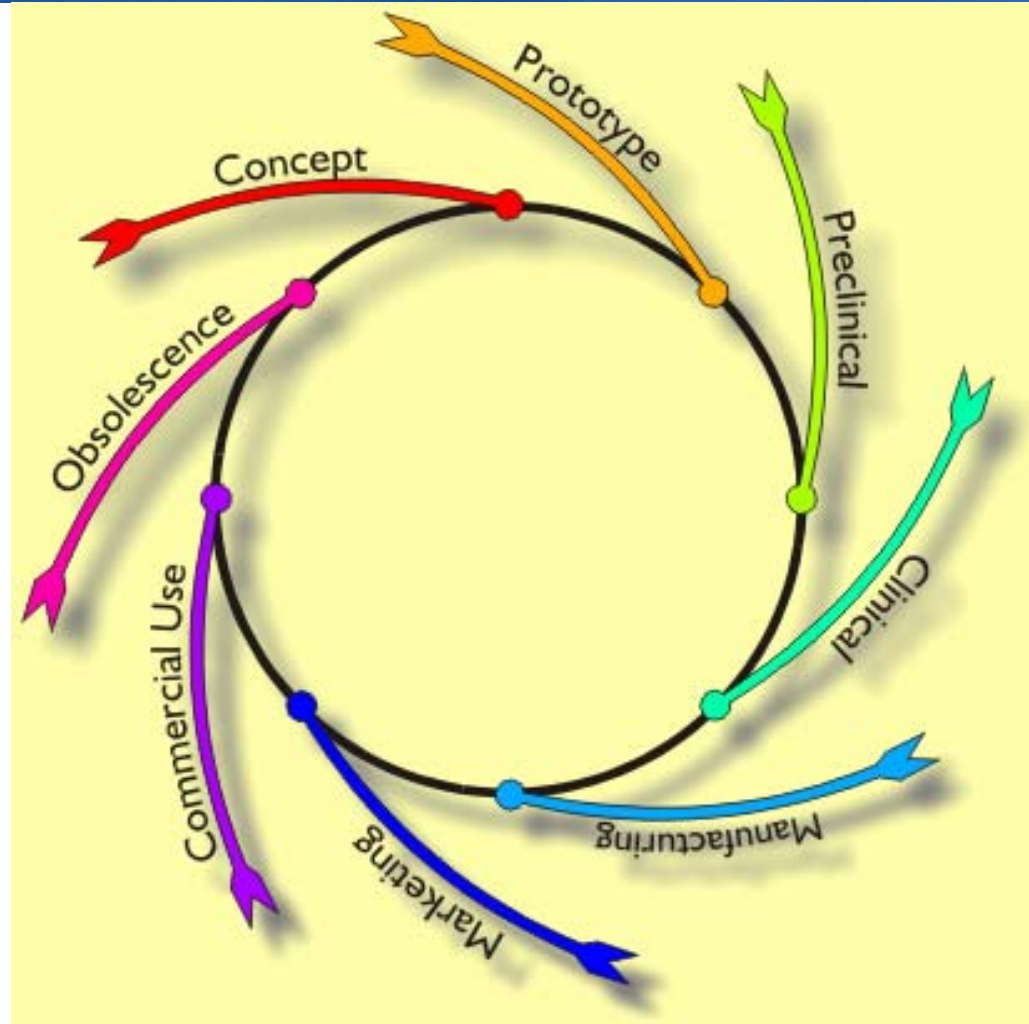
CDRH Vision:

Ensuring the health of the public
throughout the Total Product Life Cycle
(TPLC)

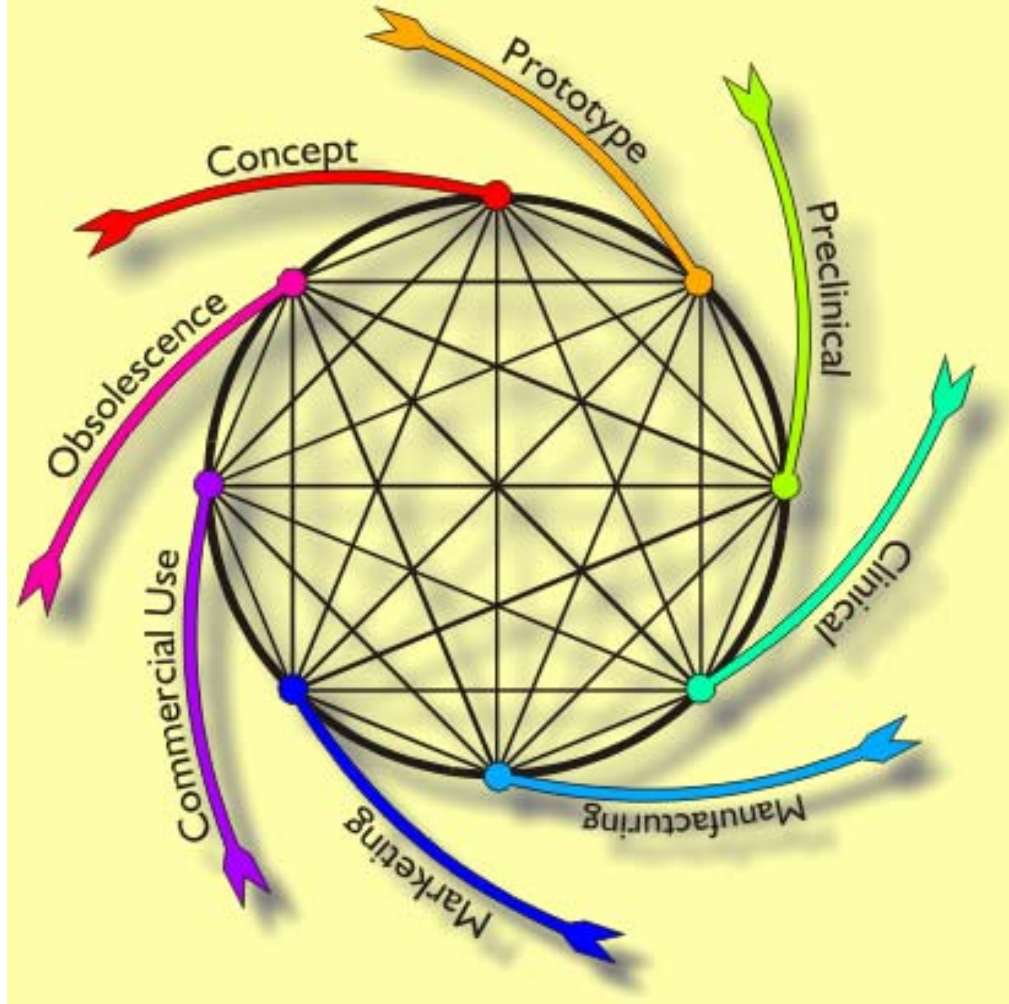
— *it's everybody's business*



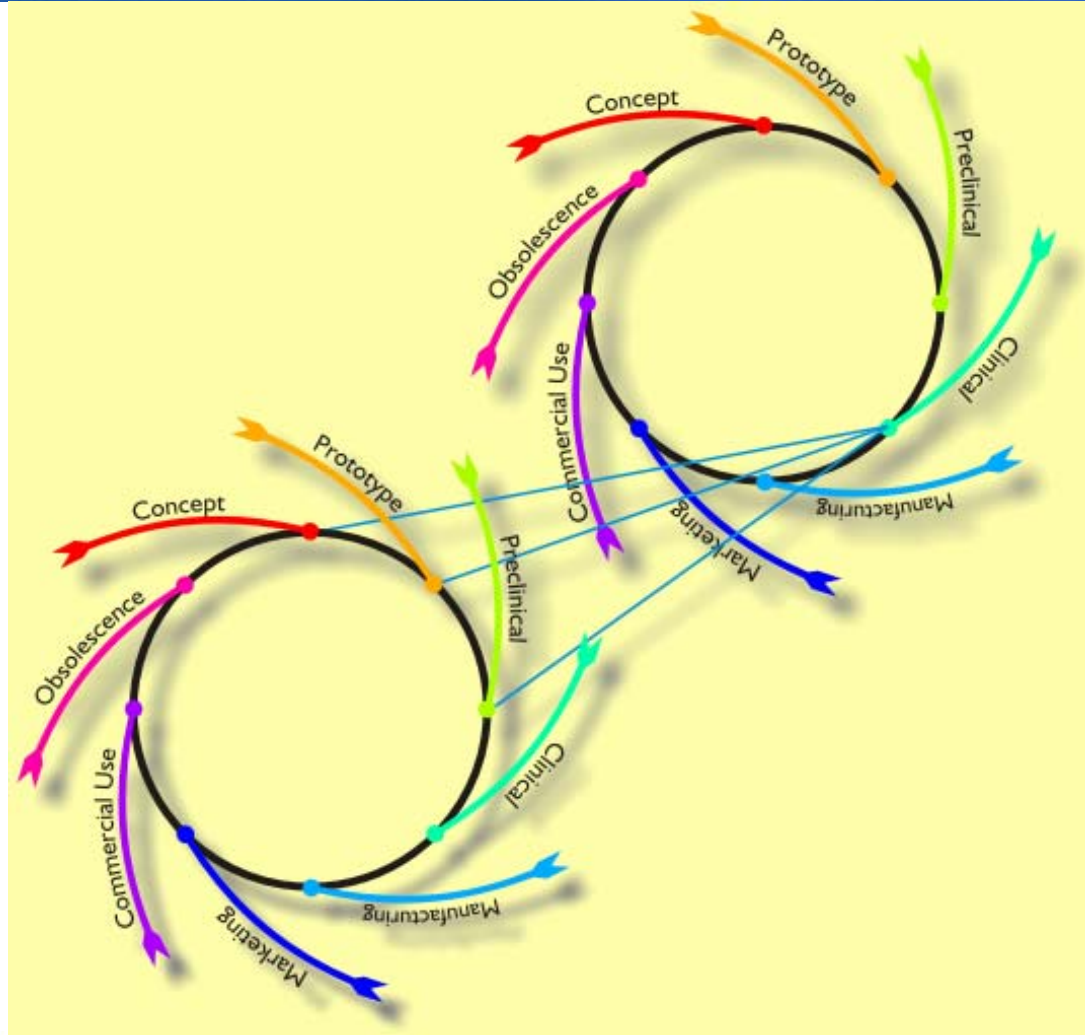
The Total Product Life Cycle (ideal)



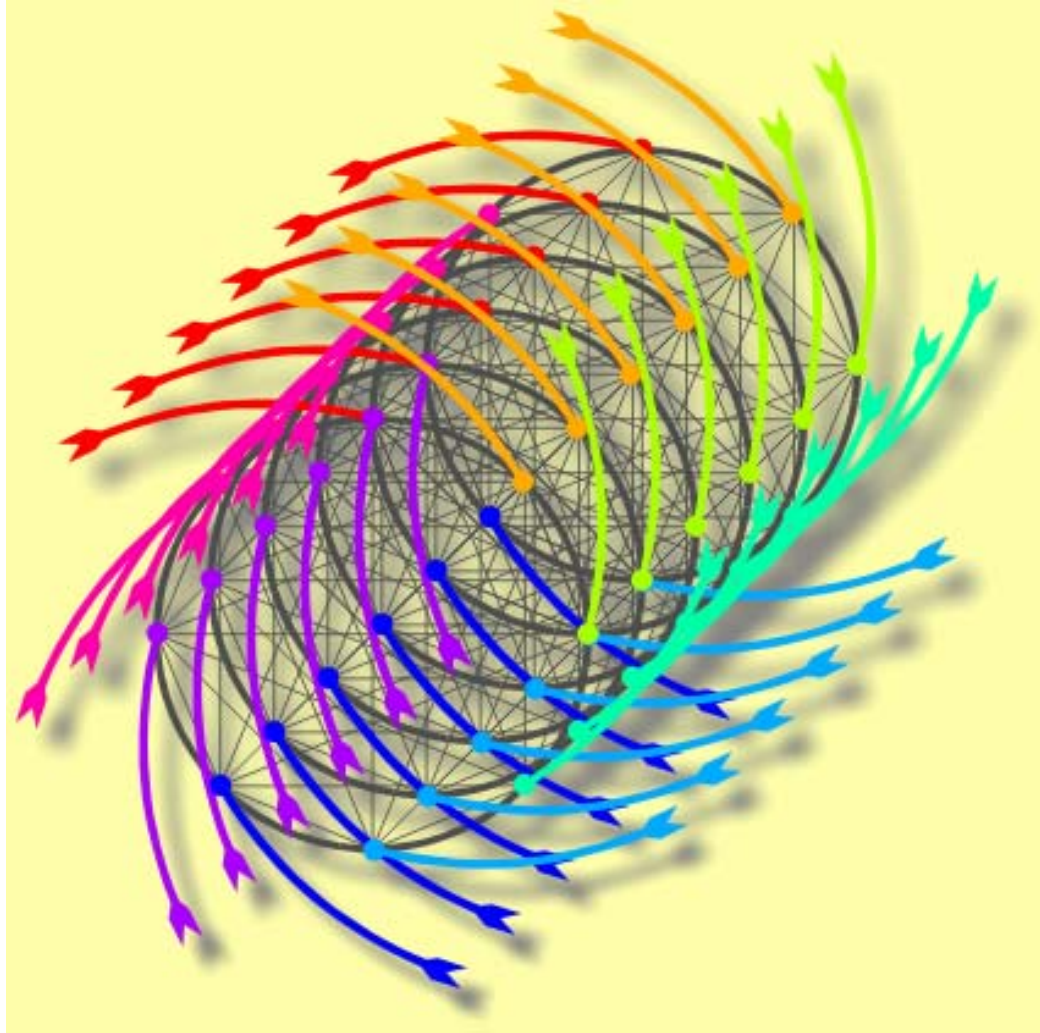
The Total Product Life Cycle (Real)



TPLC Across Generations



TPLC and the Pipeline



Need Direct & Constant Feedback

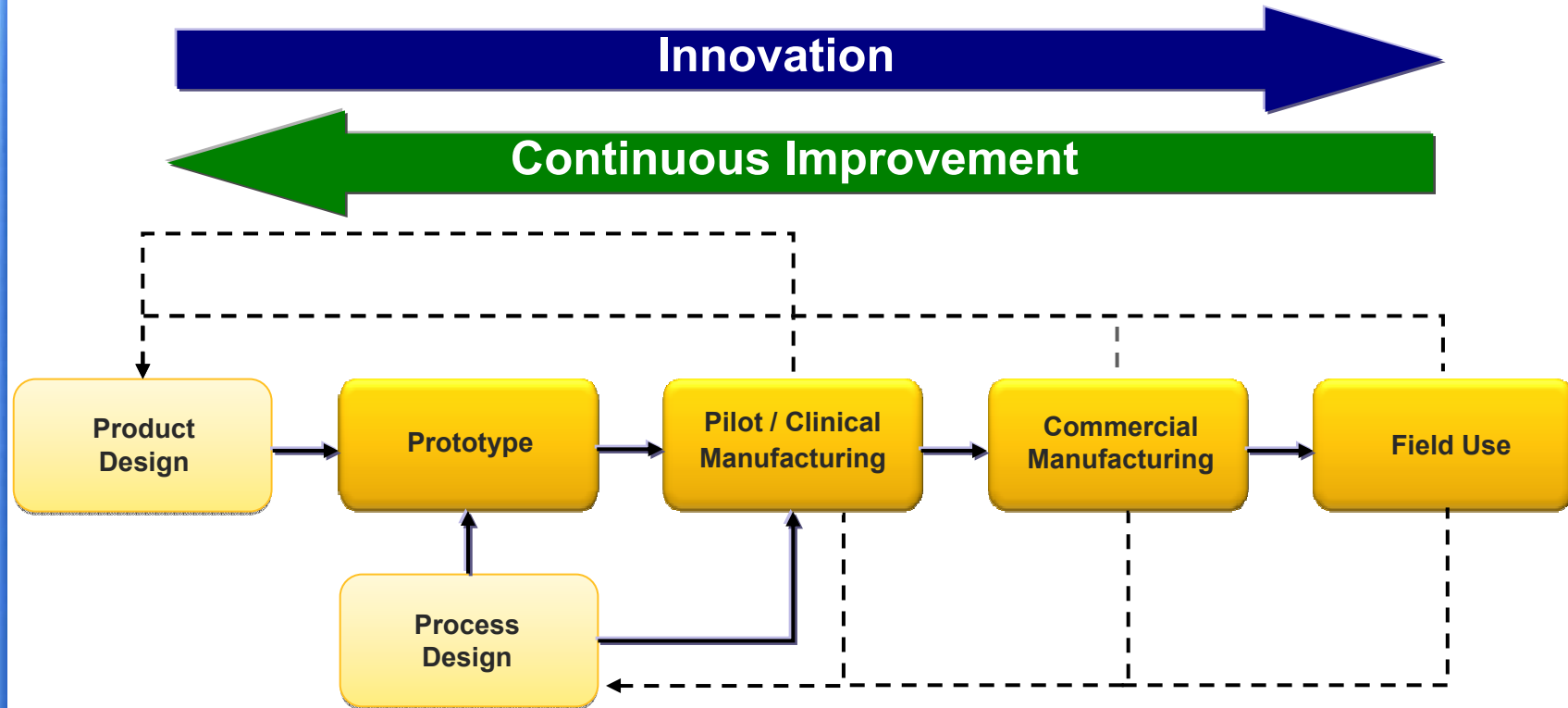
- ▲ To achieve Quality by Design, Medical Device manufacturers must establish a direct link and constant feedback loop between the DMR, DHR and DHF



Innovation Introduces Variability

- ▲ Risk and variability are manifested in:
 - ▲ New SOP's with product launch and ECO's
 - ▲ New processes being optimized
 - ▲ New test specifications for critical operations
 - ▲ New components within BOM

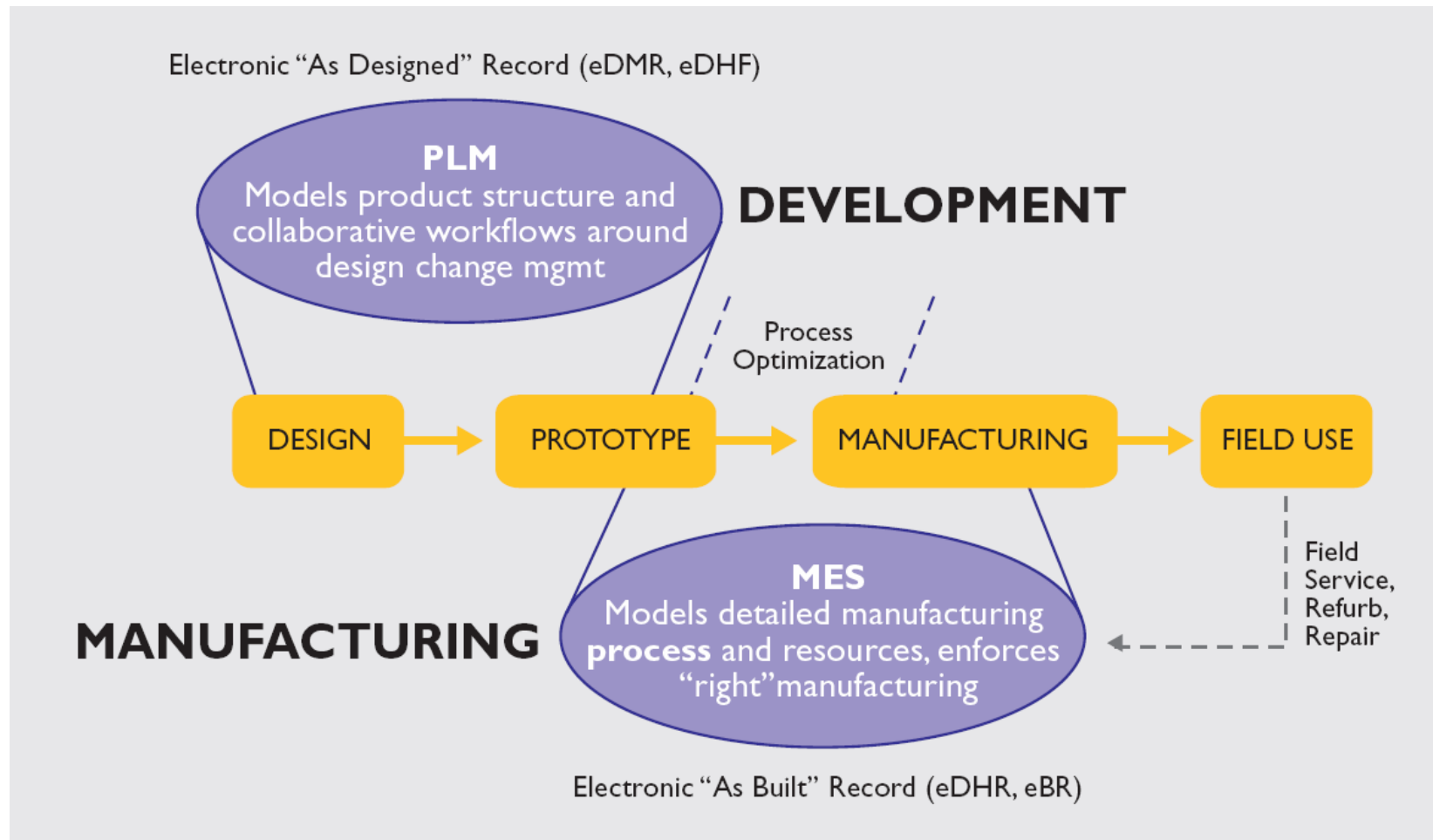
The Innovation Gap



Bridging the Innovation Gap

- ▲ Facilitate collaboration between design, engineering, quality and production
- ▲ Maximize yields by learning early (during pilot phase)
- ▲ Provide early visibility into manufacturing processes
- ▲ Require stricter enforcement of changes within manufacturing

Technology to the Rescue?



How Do We Get There?

- ▲ Drive to 0 CAs by increasing PAs
- ▲ Shift from silos to an integrated approach
- ▲ True Root Cause Analysis
 - ▲ based on real-time data (design, manufacturing, field)
- ▲ Deep understanding of critical to quality parameters
- ▲ Tightly controlled manufacturing process
- ▲ Shifting to building quality in, not testing it out
- ▲ Close the loop between
 - ▲ R&D
 - ▲ Design
 - ▲ Manufacturing (internal and cartners)
 - ▲ Quality
 - ▲ Field

Conclusion

- ▲ Business Impact vs. Regulatory Mandate
- ▲ Build on Foundational Standards
- ▲ Stop Tilting at Silos
- ▲ Shift from Reactive to Proactive and Predictive
- ▲ Total Product Lifecycle Management
- ▲ Concurrent Development
- ▲ Intelligent Root Cause Analysis
- ▲ Global Visibility Across *ALL* Stakeholders
- ▲ Situational Awareness
- ▲ Total Visibility & Control

Questions?

Thank You

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