Delivering Affordable Innovation

in the Pharmaceutical Market

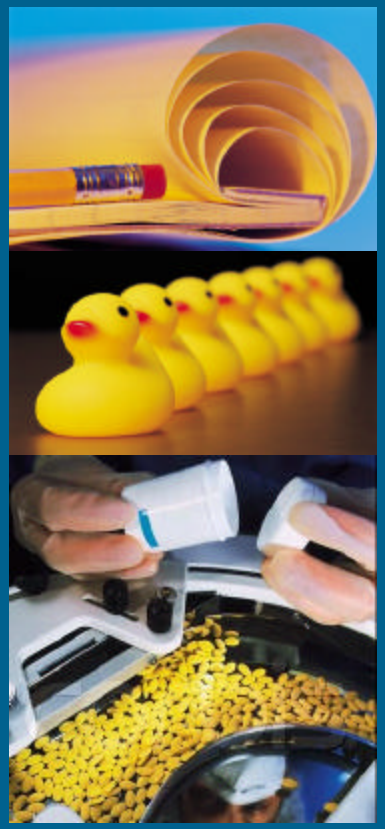
Presented by Andrew A. Signore, P.E. IPS

Sponsored By: AIChE, Delaware Valley Section

January 19, 2005

Union League, Philadelphia

Agenda



1. What is Affordable Innovation
2. Why is it important/ What is the challenge
3. Current Pharma Industry Status
4. What's New in Pharma Manufacturing
5. Summary/Discussion

Definitions

"Afford(able)"

- To have enough or the means for…
- Bear the cost without the serious inconvenience
- To manage to do something without risking serious consequences

"Innovation"

- Some thing newly introduced, new method…custom device
- Change in the way of doing things

Refer: Webster's New World Dictionary, 3rd Edition

AI- Affordable Innovation

One definition:

The challenge to deliver life-enhancing medicines to a needy, graying world at lower cost and with certainty of fitness for use (quality).

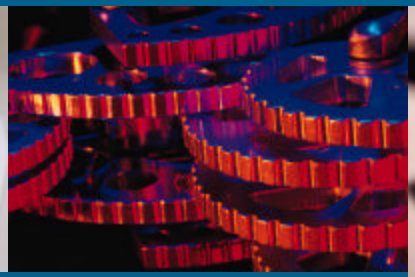
In other words…

deliver more high quality products at lower prices.

***Needed**: Better Manufacturing and Compliance processes*

The AI Challenge: Manufacturing Issues

- Long FDA approval cycles
- Costly compliance mechanisms
- Small batch, unit processes (inefficiency)
- Hazardous handling conditions
- High costs of product failure (recalls)


The AI Challenge: Manufacturing Issues

" The industry needs to wring every buck it can to offset the loss of some big sellers as more patents expire."

"Executives fear Washington will get tough in the wake of the Vioxx debacle."

Business Week 1/10/05

Current Pharma Industry Profile: Brief Recap

- World Drug Sales ≈ $500 billion
- US Market ≈ 50% of world market and growing
- Top 20 Pharma companies ≈ 50% of world sales
- Biotech sales ≈ $50 billion

(10% of total world pharma market)

Drug Marketing Exceeds R&D Costs

Top 10 US Drug Companies

	% Sales (2002)
R&D	14%
Mktg/Admin	31%
Proftis	17%

Over the last six years (1997-2003)

483 drugs introduced….67 new chemical compounds

Marcia Angell
New England Journal of Medicine
08/04

Pharma Industry Profile: Brief Recap

- Drug Pricing: very high political profile
- Puerto Rico: 16 of top 20 US pharma products made there
- Cost Increases: above inflation rates
- Coming off-patent: 35-40% current branded products in next 4-5 years
- New product introduction costs: $800 million each

Pharma Industry Profile: Brief Recap

- "Four More…Bush's election was good news for Pharma"
- "Policy Makers are under pressure to make new therapies affordable and accessible."

  Jill Wechsler-Pharma Executive Magazine

  January 2005
- Government (state and local) will soon be purchasing 50% of all medicines

Pharma Industry Profile: Brief Recap

- Negative 2004 publicity:
  - Vioxx recall
  - flu vaccine shortages
- Graying of America: people over 55 have 5 x's more consumption
- Generic drug competition: ≈ 50% of drug unit volume
- Billion $ drugs: over 50
- Medicines represent:
  - 10% of total health care spending
  - 40% of consumer's personal spending on health care

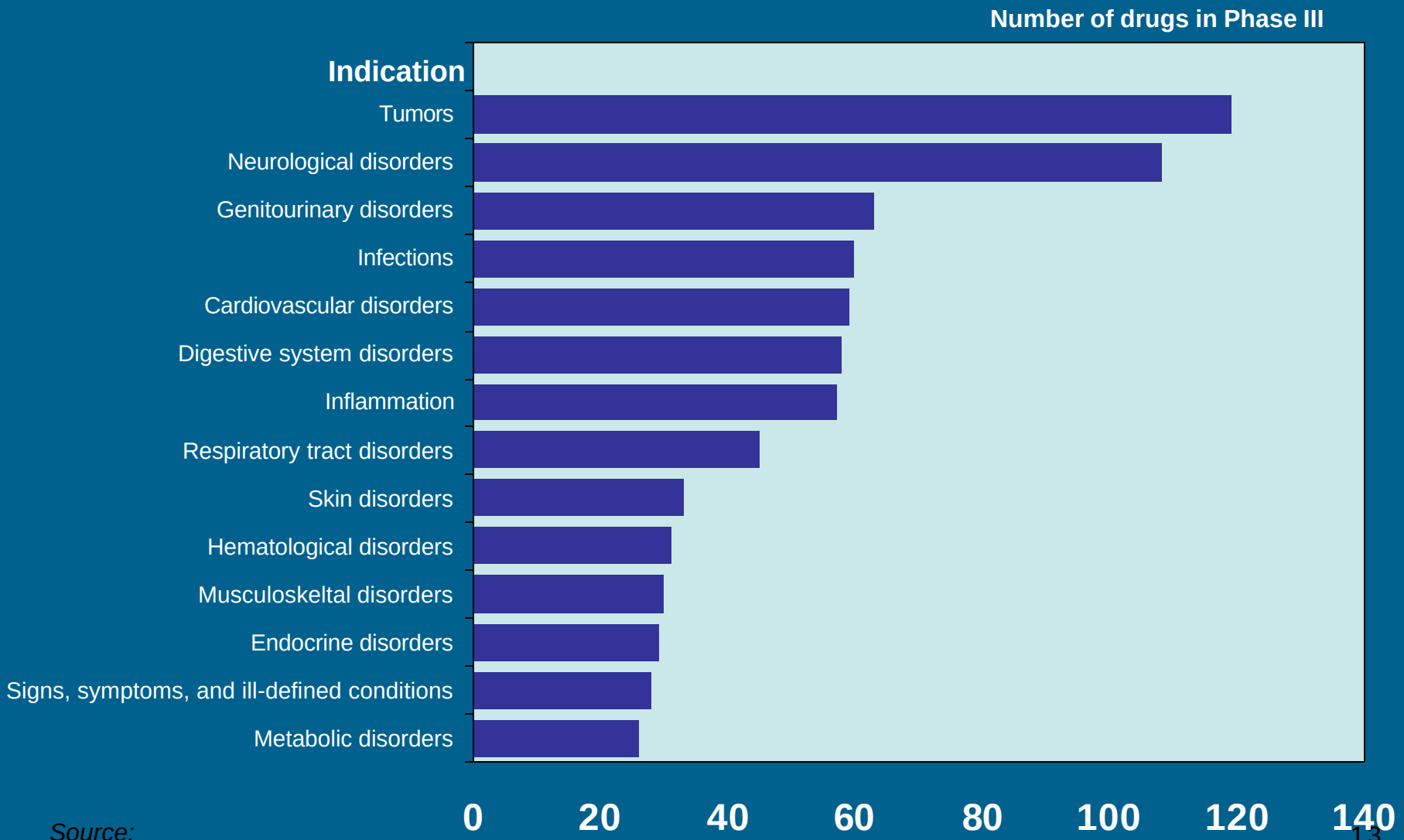
Pharma Industry Profile: Brief Recap

- Typical cost of goods: 15% to 25%
- India's pharma industry growing at 9
- GMP Mfg Failures… Serious financial consequence
- FDA Fines… Schering Plough (2002): $500 Million

  Abbot (1999): $100 Million



Top 15 Indicators for drugs in Phase III

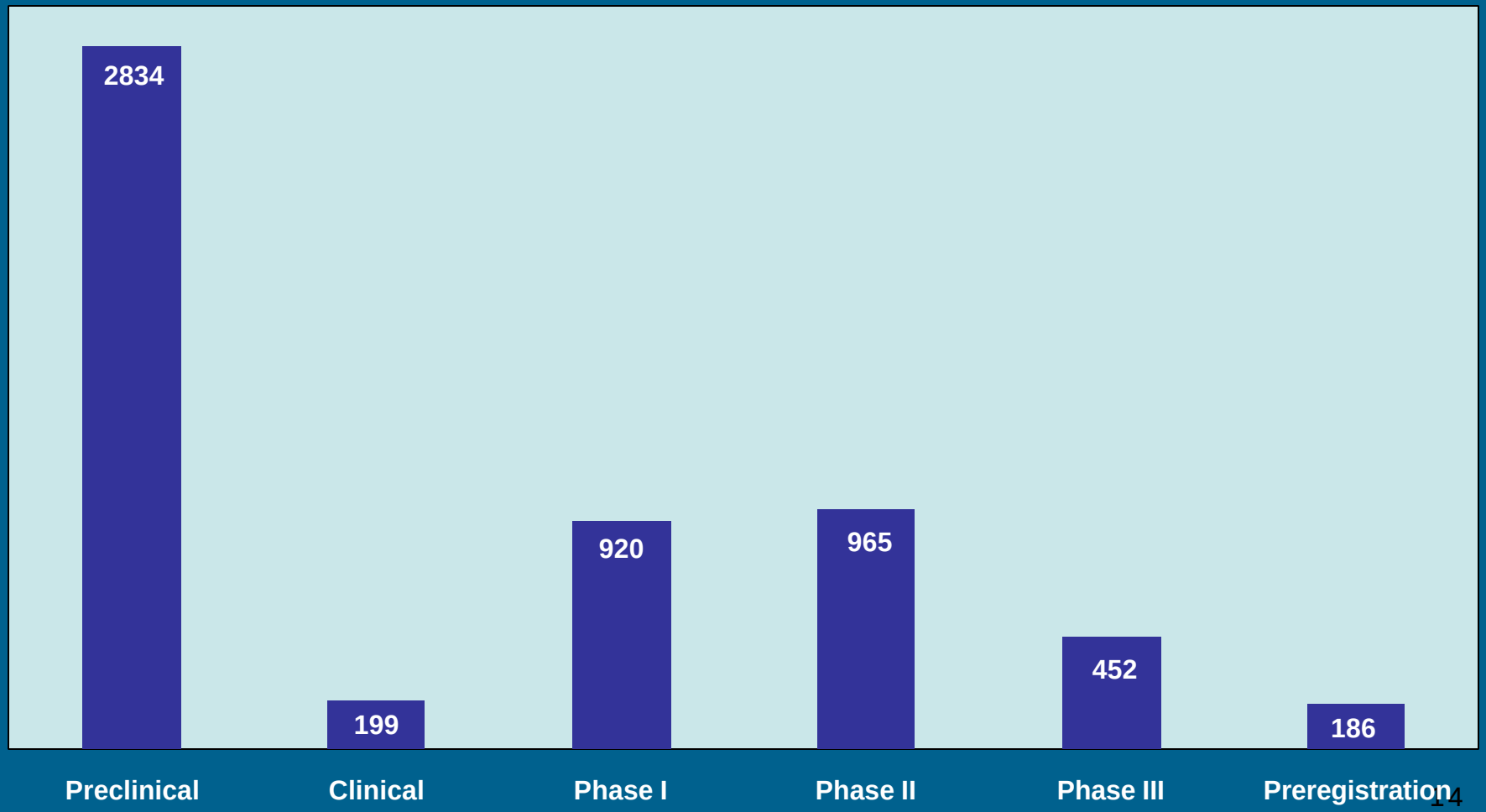


Source:
Pharmaceutical Executive-January 05

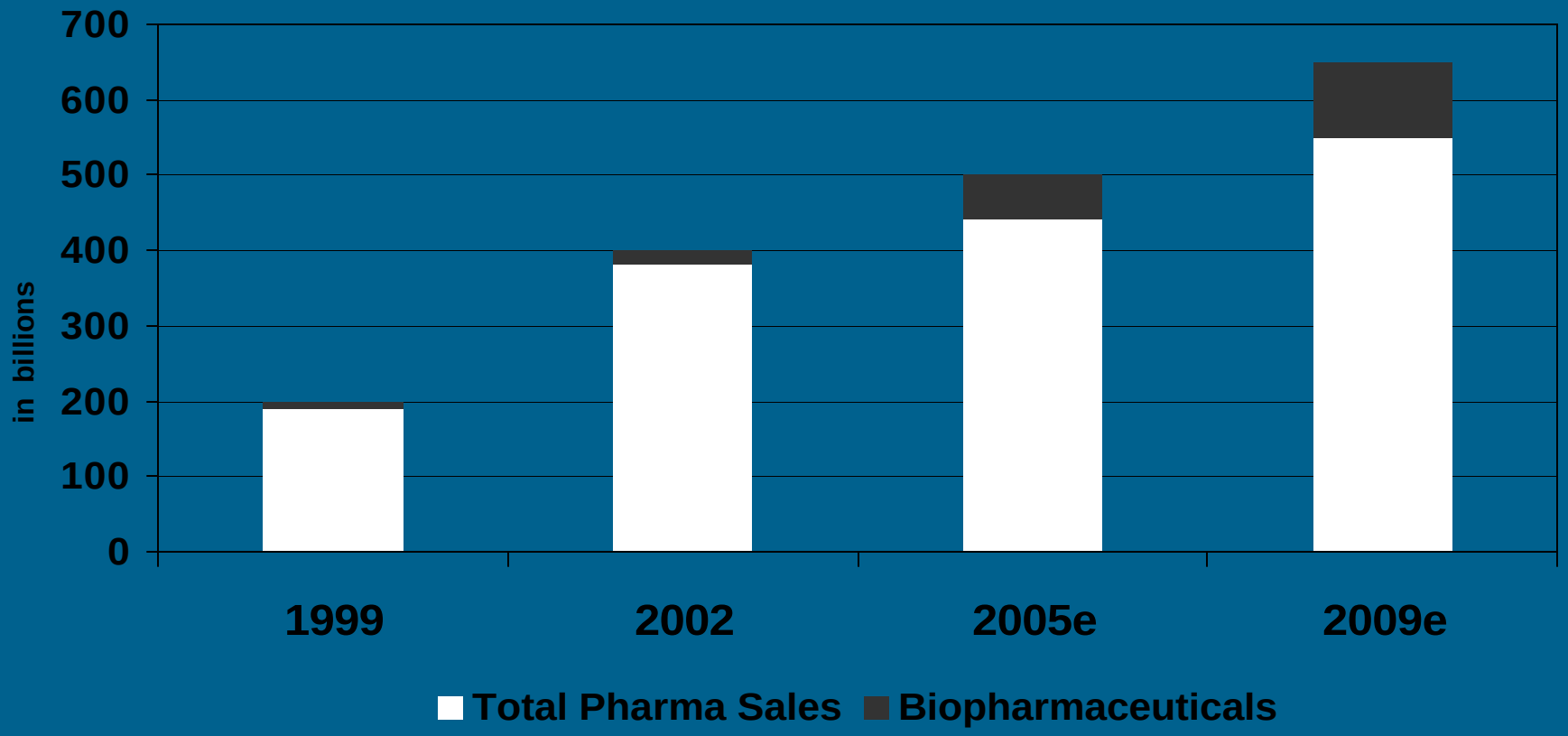
Drugs Under Development By Phase

More Funnel Than Tunnel

Source: Pharmaceutical Executive-January 05



Biopharmaceuticals' Share Of Global Prescription Sales



Sources: IMS Health Inc. (imshealth.com) and BioGenerix AG (biogenerix.com) 12/04

Pharma & Wall Street

2004 Stock Prices

Biotech	+7%
Big Pharma	–18%
Pharma Group Totals	–10%

Selected Results

		'04 Results
Merck	$32	-32%
Pfizer	$27	-24%
BMS	$24	-18%
Wyeth	$40	-6%
J&J*	$63	+23%

Note: (*): J&J only major pharma to gain in 2004

Recent Drug Withdrawals

Drug	Purpose	Year	Reason
Vioxx	Pain	2004	Cardiovascular risk
Baycol	Cholesterol	2001	Muscle condition
Propulsid	Heartburn	2000	Heart-rhythm disorders
Rexulin	Diabetes	2000	Liver damage
Duract	Pain	1998	Liver damage
Poicor	Blood Pressure	1998	Bad drug interactions
Seldane	Allergies	1998	Bad drug interactions
Pondimin	Weight loss	1997	Heart-valve damage
Redux	Weight loss	1997	Heart-valve damage

Sources: Government Accountability Office: Food & Drug Administration

Wall Street Journal 12/31/04

Did You Know?
"State of Manufacturing"

USA

- lost 2.7 million manufacturing jobs since 2000
- Mfg segment of GDP

  15% 1998

  13% 2003

- Jobs lost to Mexico are now moving to far east

Lessons Learned? Mfg Failures

- 1937 Massengills Elixir USA : 105 deaths due to ethylene glycol in liquid formulation
  Toxicity testing was bit required
- 1969 South Africa : 7 deaths(children) ethylene glycol in sedatives
- 1986 Bombay : 14 deaths: ethylene glycol (191)in glycerin
- 1990 Bangladesh : 236 children deaths: ethylene glycol
- 1990 Nigeria : 40 children deaths ethylene glycol
  Instead propylene glycol

Pharma Industry Manufacturing Responses

1. **Outsourcing**
   - Manufacturing
     - Bulk
     - Packaging
     - Clinical Development
   - Services
     - Engineering
     - Construction
     - Validation

2. **Procurement (Supply Chain)**
   - Bulk (leveraged) purchasing
   - Serve agreements/preferred suppliers
   - E-based auctions
   - Incentives

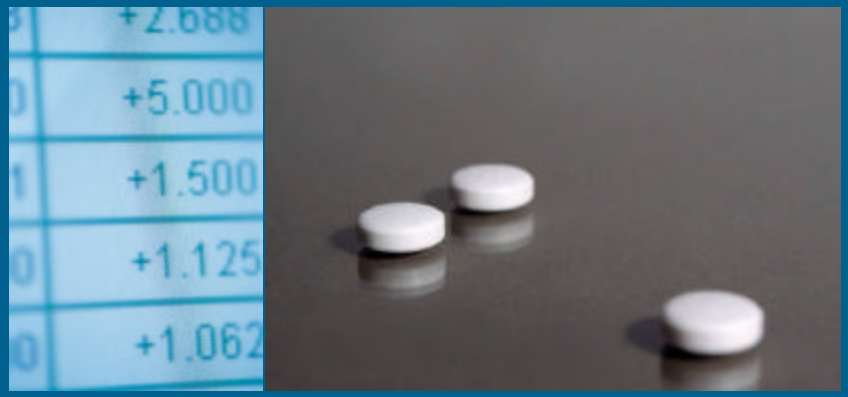
Pharma Industry Manufacturing Responses

3. **Project Delivery**
   - Design/Build: Single source
   - Pre-Engineered Equipment/Systems
4. **Manufacturing**
   - Focused centers of technology
   - Economies of scales
   - Tax-haven sites
     - Singapore
     - Puerto Rico
     - Ireland

What's New

Concept of Pharma Quality

Janet Woodcock, MD
Acting Deputy Commissioner for Operations
Food and Drug Administration
American Pharma Review
December 2004



Addressed challenge of defining pharmaceutical quality:

- Meeting/Exceeding customer needs
- "Fitness for use" meets label claims and is available/
- Been manufactured in accordance with GMP's
- Risk and science based approaches

What's New

FDA: Pharmaceutical cGMP's for the 21st century: a risk-based approach

September 2004 Final Report

"to modernize FDA's regulation of pharmaceutical quality…"

- Encourage early adoption of new tech advancement
- Facilitate industry application of modern quality management techniques
- Encourage implementation of risk-based approaches
- Ensure regulatory review, compliance and inspection policies are based on state of the art pharma science

What's New

Guidance for the Industry

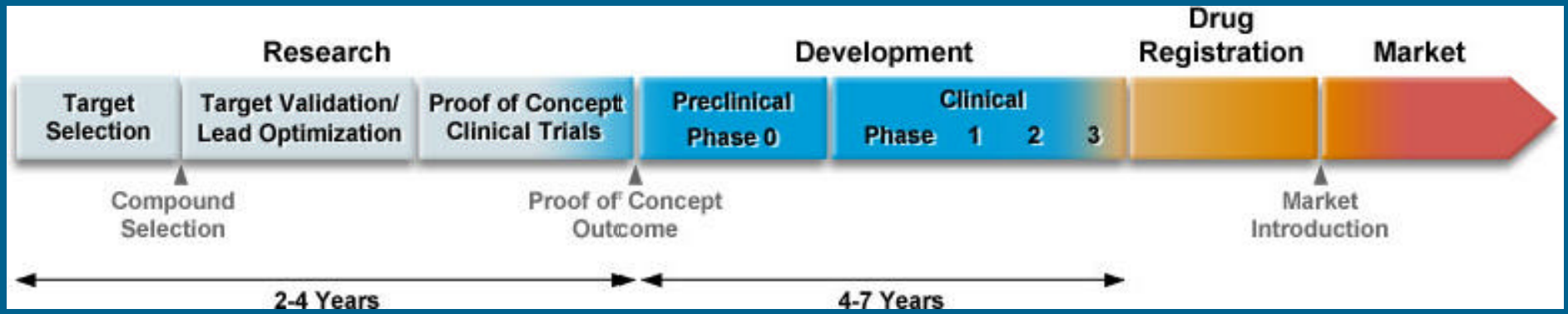
Sterile Drug Products Produced by Aseptic Processing-Current Good Manufacturing Practice

Final Issue-September 2004

Summary

- Updates Terminal Sterilization and Aseptic Processing Issues
- Stresses harmonization to European Union Guidance (refer to ISO 14644-1 Controlled Environment)
- Addressees validation, lab controls and stability testing
- Discusses Aseptic Processing Isolators, Blow Fill Seal Technology

Drug Development Cycle



What's New in Pharma Manufacturing Technologies

1. **RFID-Radio Frequency ID**

- Computer chips on labels to track drugs from manufacturing to consumer
- reduce counterfeiting
- protect integrity of pharma supply chain

Note: *WalMart is driving RFID*

What's New

PAT: Process Analytical Technology

FDA Final Guidance September '04

PAT Interpreted:

Systems for analysis and control of manufacturing processes based on controlled measurement of critical quality parameters and performance attributes of raw and in-process materials.

J.M.Geoffroy PhD
Abbott Labs
American Pharma Review 11/04

Caution: *"effect of all this" additional data…could easily be confusion.*

PAT: Another Definition

(Near) real time , (semi) continuous data about process monitoring, control and/or automation or can be converted into process knowledge. Continuously very flying that our processes are heading in right direction

Joe Timmerman, PhD

Pfizer

PDA/FDA Joint Conference 10/04

PAT

Practical Example:

In OSD Manufacturing Facility, Product Analysis times have been reduced to 15 minutes allowing continuous manufacturing" as data allows release of materials while being purchased/blistered.

**Quarantined have been reduced/eliminated.*

Dr. Timmermans

Pfizer 1004

Undisclosed facility

Note: Continuous manufacturing is not continuous processing. Batch unit processes are still employed… (Signore)

PAT Applications: Oral Solid Dosing

Raw Material Dispensing

- Vision Particle Analyzer (lab based)
- NIR Conformance testing (lab based)

Dispensing

- NIR Material I.D.

Dry Compaction/Wet Granulation/FBD Milling

- Power consumption granulation end point
- Acoustic granulation end point
- On-line vision particle size analysis
- NIR Loss on Drying
- On-line UV cleaning

Compression/Capsule Filling

- NIR Core Potency
- NIR Chemical Imaging (lab-based)

Coating

- NIR Coating Thickness

Blister Packaging/Bottle Filling

- Imaging of Blisters

Dr. Timmerman, PhD
Pfizer

How Can Engineering/ Project Management Help Deliver AI

Through Better Manufacturing

1. Reduce Cycle Times (10-20%)

- Faster Projects
- Pre-engineered/ modular systems
- Standard Design/ Guides
- Combine start-up/commissioning/validation process

How Can Engineering/ Project Management Help Deliver AI

Through Better Manufacturing

2. Reduce Costs /Increase Efficiency (10-20%)

- Disposable
- Process automation
- Better Processes/ knowledge
- Target cost

How Can Engineering/ Project Management Help Deliver AI

Through Better Manufacturing

3. Improve Quality (Reduce Risks)

- Display
- Process Analytical Technology
- Benchmarking (learning from others)
- Key alliances with vendors/equipment installers/ A/E/C's
- Staff Training/development/certification

Helpful Manufacturing Guidance

ISPE Baseline Guides

Engineering Design Guides for new and renovated pharma manufacturing facilities

- Active Pharmaceutical Ingredients
- Orals Solid Dosage
- Sterile Products
- Water and Steam Systems
- Qualification and Commissioning
- Biopharmaceuticals

Bioreactor:

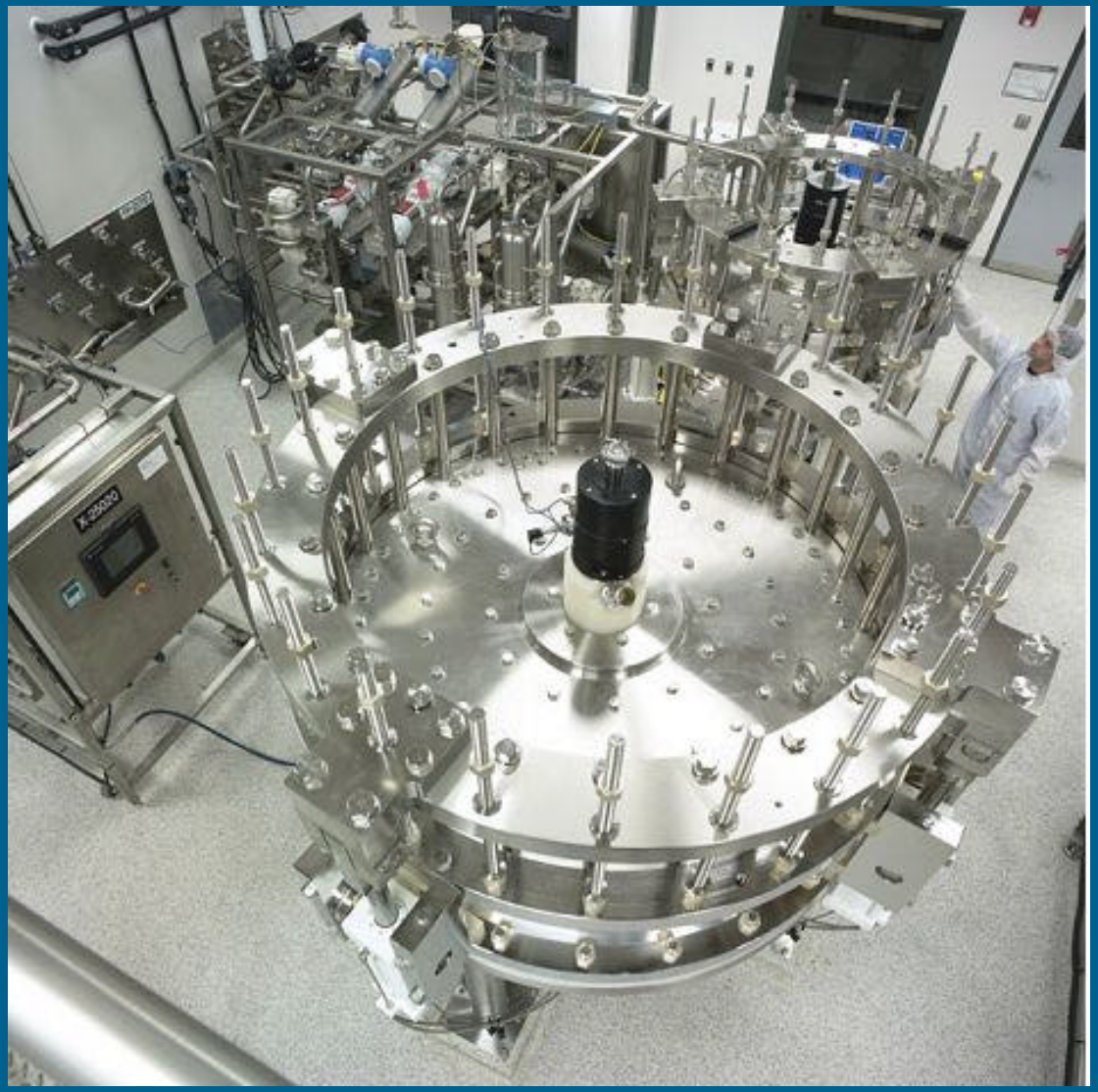
Pre-Engineered System

Cell Culture:

Pre-Engineered System

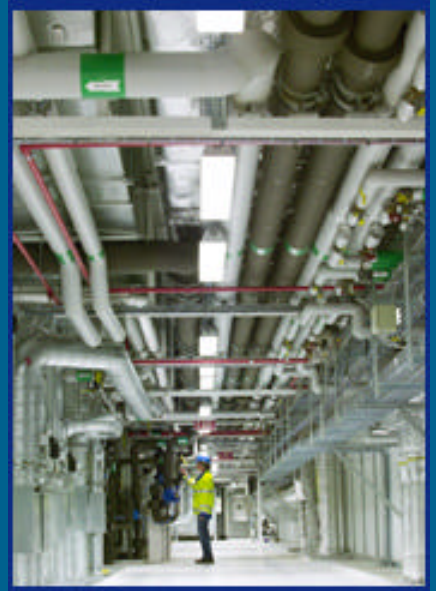
Harvest & Recovery Area: Skid Mounted Systems

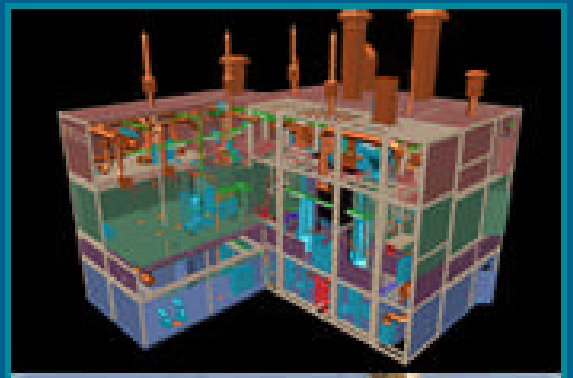
Chromatography Columns

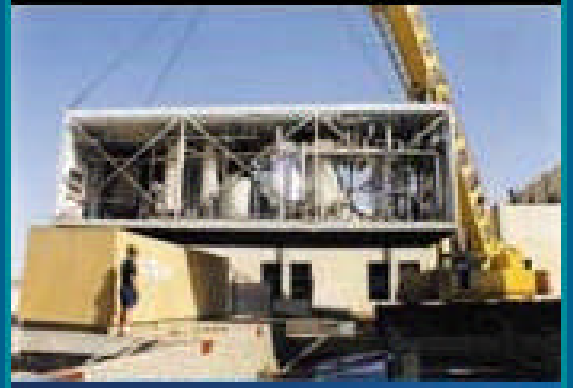


Nutche Filter

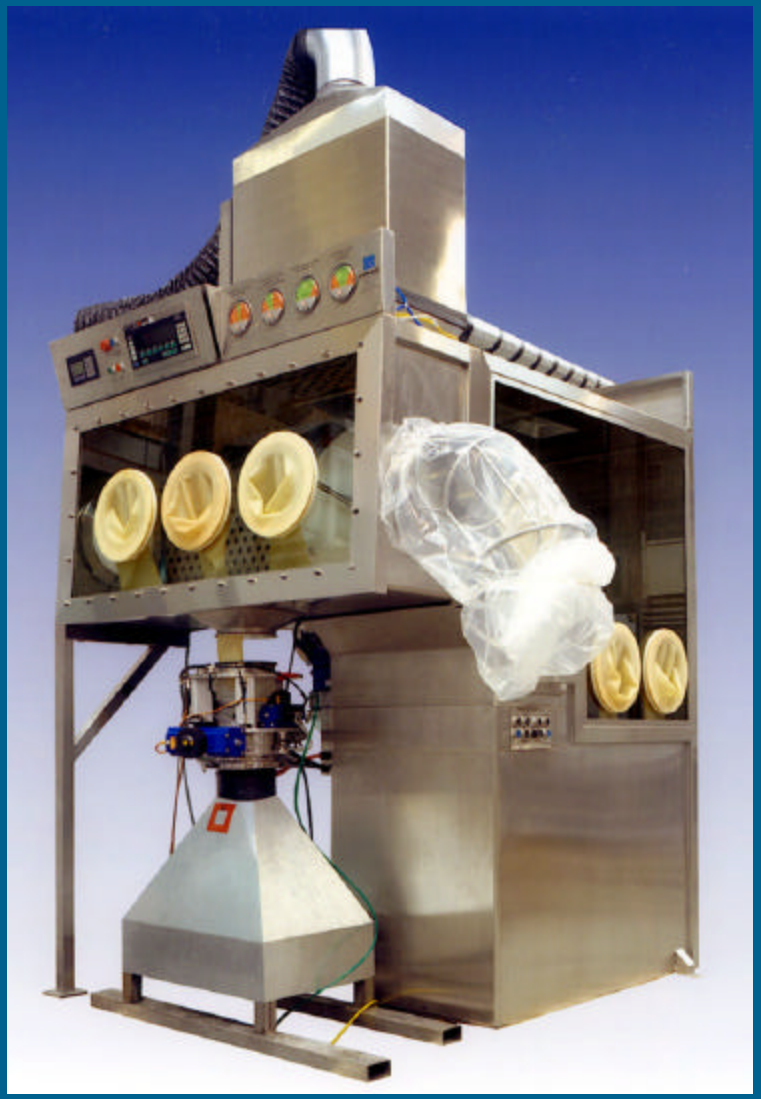
Pharmadule Modular Facilities







Charge Isolator



Product Recovery Skids

Summary

- Pharma Industry is in stress
- Will respond with AI initiatives
- Seizing Manufacturing opportunities will be helpful and strategic
- Engineers and PM’s have a role and will add value