
Impact of Improving Pharmaceutical Product Development and Manufacturing

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Motivation for this work

- Considerable public attention as well as industry and government funding are directed to the discovery and clinical trials steps of the pharmaceutical pipeline.
- Total funding for basic research in the science of pharmaceutical development and manufacturing is minimal.
- We believe that savings in the area of product development and manufacturing can be considerable
- Reducing Cost of Drug Development and Cost of Goods Sold (COGS)

Motivation (Contd)

- There exists no current estimate of cost of product development or the potential savings in it
- Cost of new drug development ranges from \$800 million to \$1.7 billion
- Total Cost of Goods Sold for all pharmaceutical products worldwide ranges from \$112 billion to \$160 billion
- The basis behind estimating these numbers often not stated explicitly leading to their misinterpretation

Outline

- Review of Cost of drug development estimates
- Projected estimate for 2005-2006
- Estimate of Product development costs
- Impact of improving product development
- Estimates of COGS and potential savings

Cost of developing a new drug

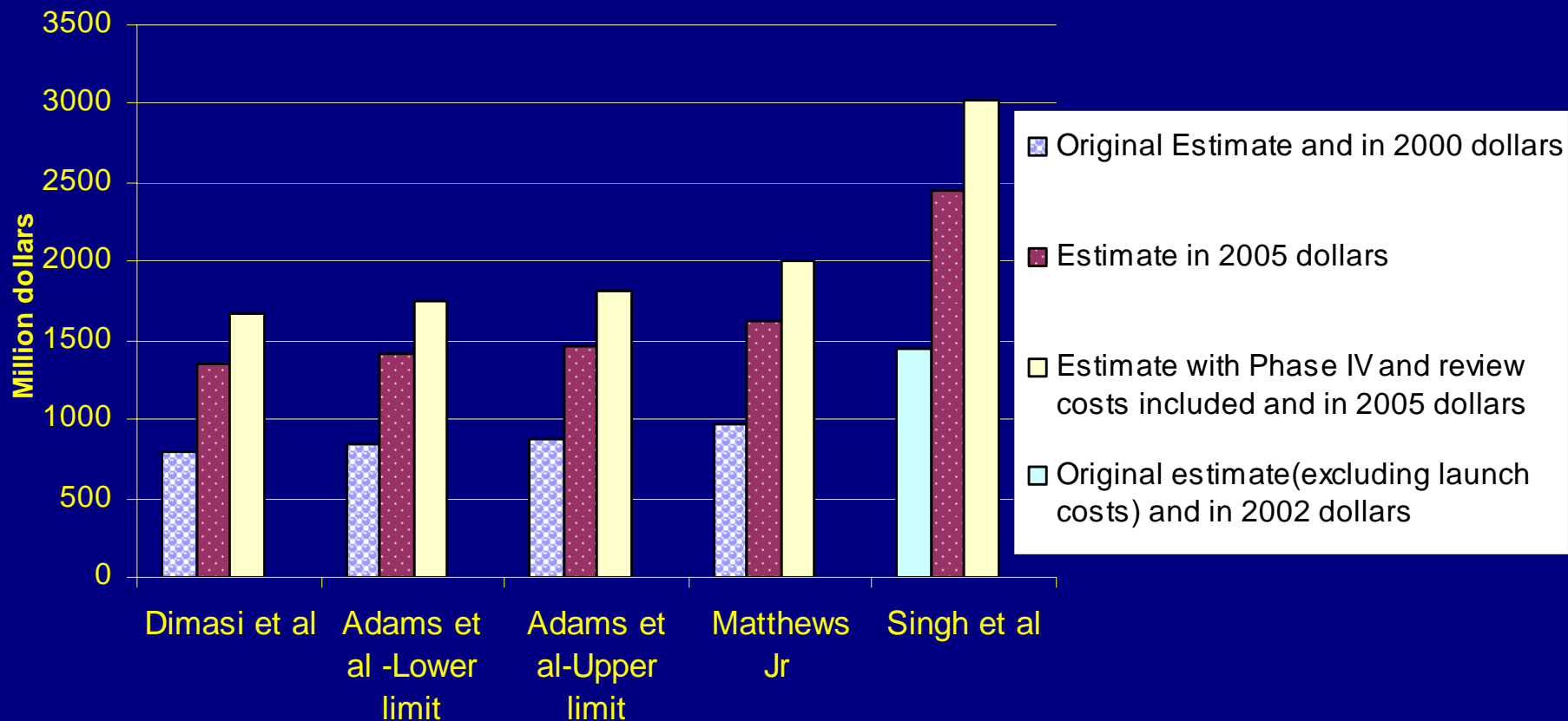
- “We estimated that total R&D cost per new drug is US \$802 million in 2000 dollars”
-Tuft’s Center for the Study of Drug Development, 2003
- “it costs approximately \$964 million per drug approved in 2000”
-Matthews Jr, 2002
- “Declining R&D productivity..... have driven up the average cost per successful launch to \$1.7 billion in 2002 dollars”
-Bain&Co., 2003
- “This paper finds that the expected capitalized cost per approved drug is between \$839 and \$864 million in 2000 dollars”
-Brantner et al, 2004

Cost estimates from literature

- The variability in these estimates is due to
 - Difference in estimation methodology
 - Origin of drugs used in study
 - Time period considered for study
 - Clinical success rates estimated/used
 - Therapeutic category of drugs studied
- All these estimates are discussed in detail in our report [1]

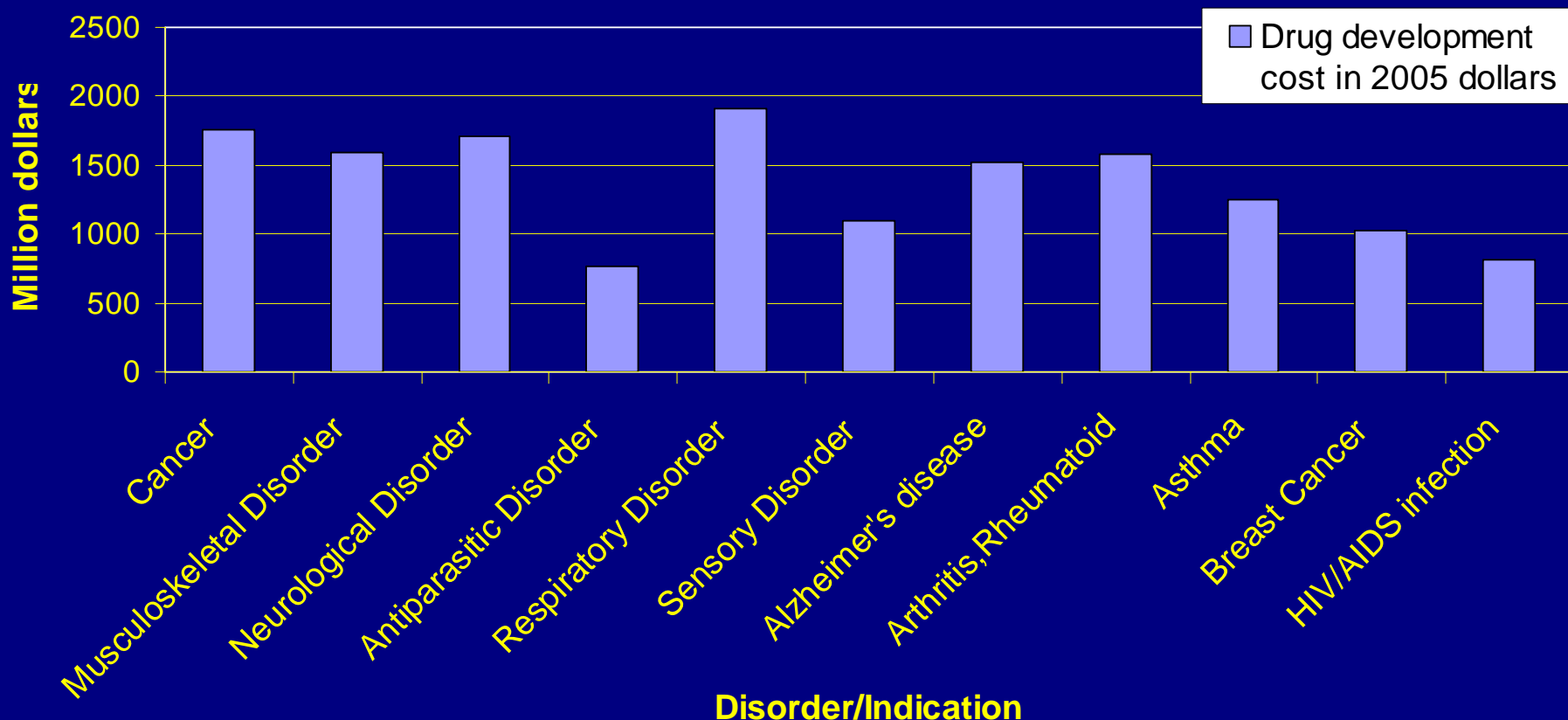
[1] Suresh, P & Basu, P. , *Pharmaceutical Technology & Education Center Report, Purdue University, August, 2005.*

Comparison of estimates



Cost by therapeutic category

Drug development costs by therapeutic categories



Estimated cost of developing a new drug

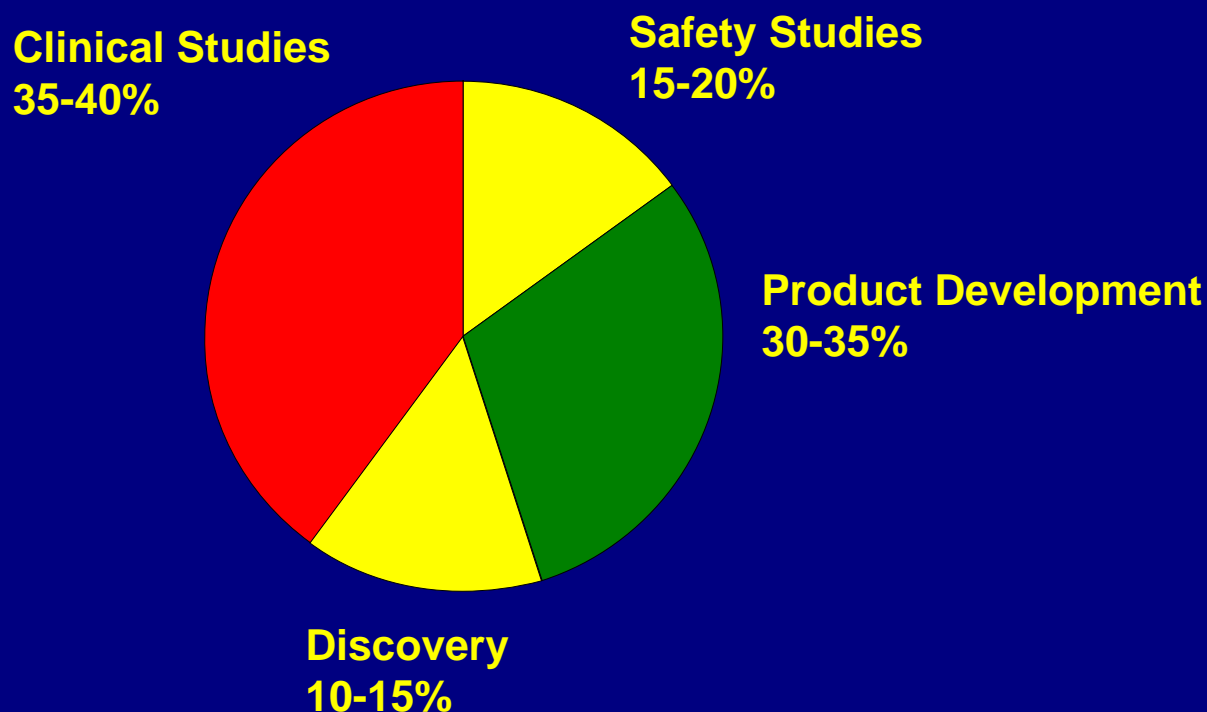
- We estimated the cost of drug development in 2005 using
 - Methodology of Dimasi et al (2003)
 - 14% clinical success rate
 - 11% discount rate
 - Review and Phase IV costs as 22.7% of total cost
- The estimated cost of new drug development in **2005 dollars** was as high as:

\$1.75 billion to \$2.5 billion

- Cost of Product development is a major contributor

Cost of Product Development

- Cost of Product development includes costs of Preclinical Phase (CMC and testing) as well as costs of clinical supplies manufacturing
- Cost of product development is estimated to be in the range of 30 to 35% of the overall cost of developing a new drug:



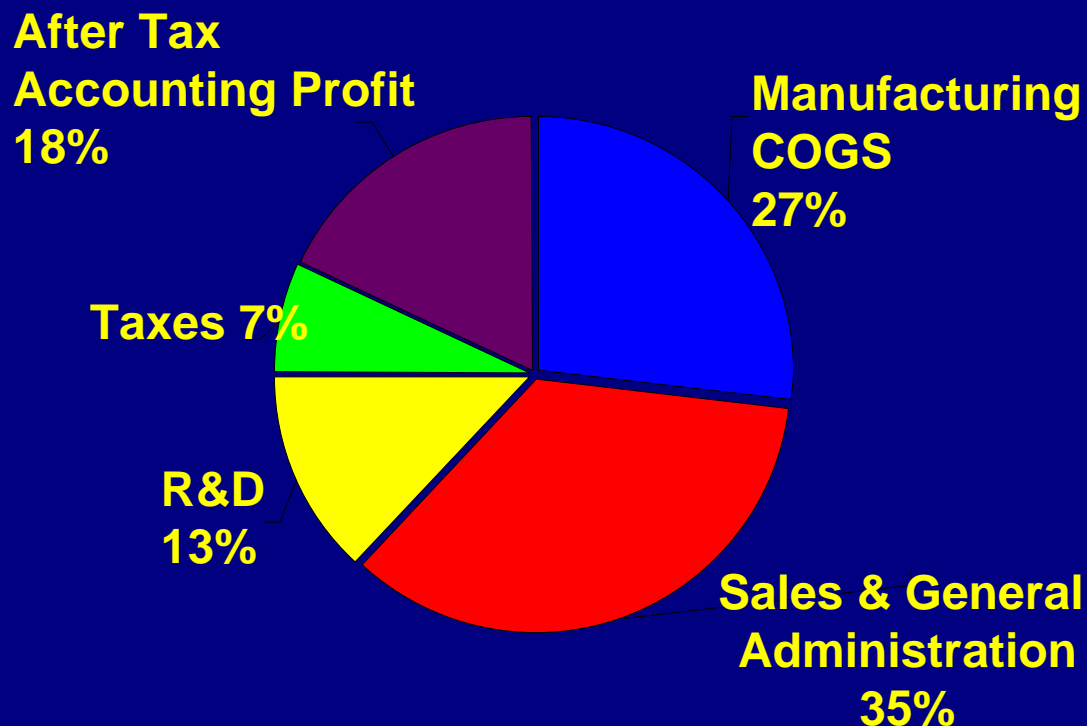
Impact of improved product development

- Reducing product development costs by 30% * could potentially reduce the cost of bringing a new drug to market by a factor of at least **10-15%**.
- PhRMA's member companies invested \$49.3 Billion in R&D in 2004. Thus, improving process development has the potential to save **\$5 to \$7 Billion per year** in overall R&D costs in 2004 dollars.
- Reduction of time-to-market due to improved quality of process development.
- Quality of the product development process (largely empirical currently) dictates the quality of the manufacturing process that follows

* More details at NIPTE's technology roadmap session at AIChE

Pharmaceutical Manufacturing

Disposition of the sales revenue earned by eight largest research-based pharmaceutical manufacturers in 1998



*U.E. Reinhardt, Health Affairs, Page 136,
September/October 2001*

Pharmaceutical Manufacturing

- Though pharmaceutical products manufactured are of 2.5 sigma variability, products reaching the market are almost 5 sigma!! How?
- In pharmaceutical industry quality control systems are at least 5 sigma ensuring the product reaching the market is also close to 5 sigma
 - ➔ High Cost of Compliance or quality control
- To reduce cost of manufacturing, we need to improve the manufacturing processes.
 - Improving quality sigma from 5 to 5.5 sigma will improve overall failure rate only marginally, whereas improving process sigma from 2.5 to 4.5 (with the same effort) decreases failure rate from **16% to 0.15%**

Review of Cost of Goods Sold estimates

- COGS were estimated to be \$145 billion using $\text{COGS} = 27\% \text{ Sales}^*$ for brand name pharmaceuticals
- Studies at Purdue University, estimated COGS in 2005 was ~ \$160 billion for world-wide pharmaceutical manufacturing.
- Dr. Nickerson estimated Industry total of COGS to be \$112 billion in 2002 dollars at least for U.S. pharmaceuticals.
- Based on other such estimates we conclude that Global COGS ranges from **\$120 to \$160 billion per year.**

* The estimate of global pharmaceutical sales in 2005 is \$602 billion (IMS Health (RX) Report 2006)

Potential for COGS Savings is High

- Estimates of possible savings resulting from improved manufacturing are as follows
 - Assuming that total COGS in 2005 was \$100 billion, a 20%-30% reduction in COGS would save the pharmaceutical industry globally around \$24 billion to \$36 billion per year
 - McCabe(2004) estimates possible worldwide savings of \$90 billion each year by efficiency improvement is achievable.
 - Therefore Global potential COGS savings ranges from \$24 billion to \$90 billion per year

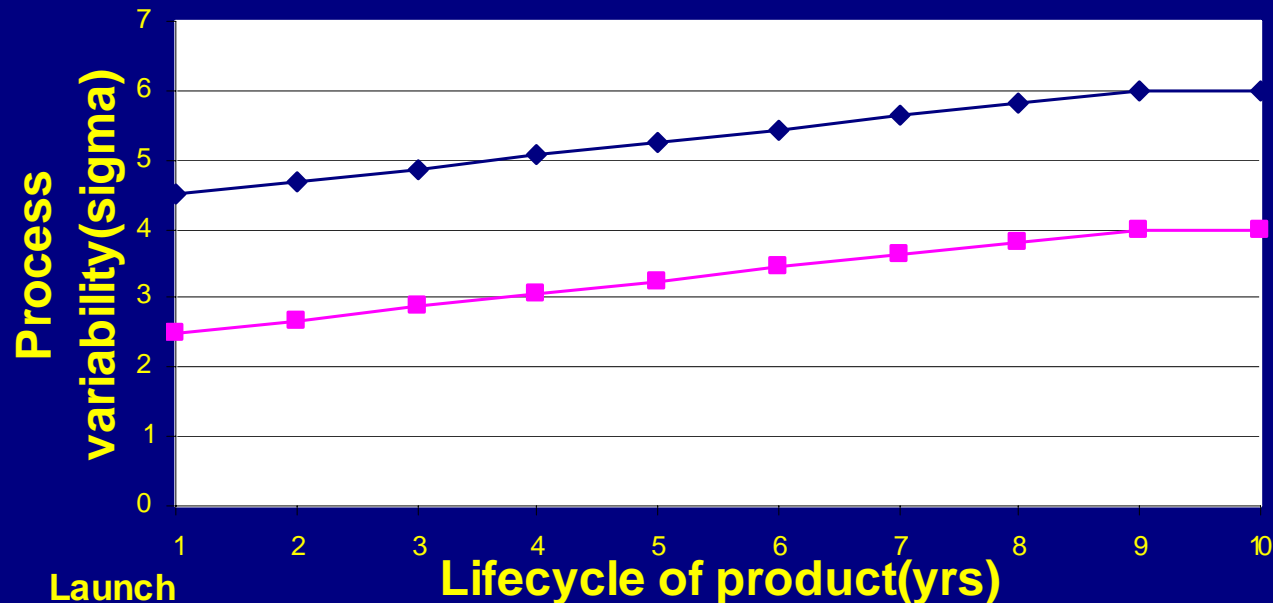
Savings Potential in manufacturing

- Better technologies to develop and manufacture pharmaceutical products can impact manufacturing in the following ways:
 - *More robust processes transferred to manufacturing*
 - *Lower defect rates*
 - *Reduced cycle times*
 - *Science-based regulations*
 - *Reduced risk in launching of new product*
 - *Higher plant capacity utilization*
 - *Higher yields*

Savings Potential in manufacturing (Contd)

- Further savings in COGS are possible in two ways
 - COGS savings due to improved efficiency which keeps improving throughout the lifetime of the drug

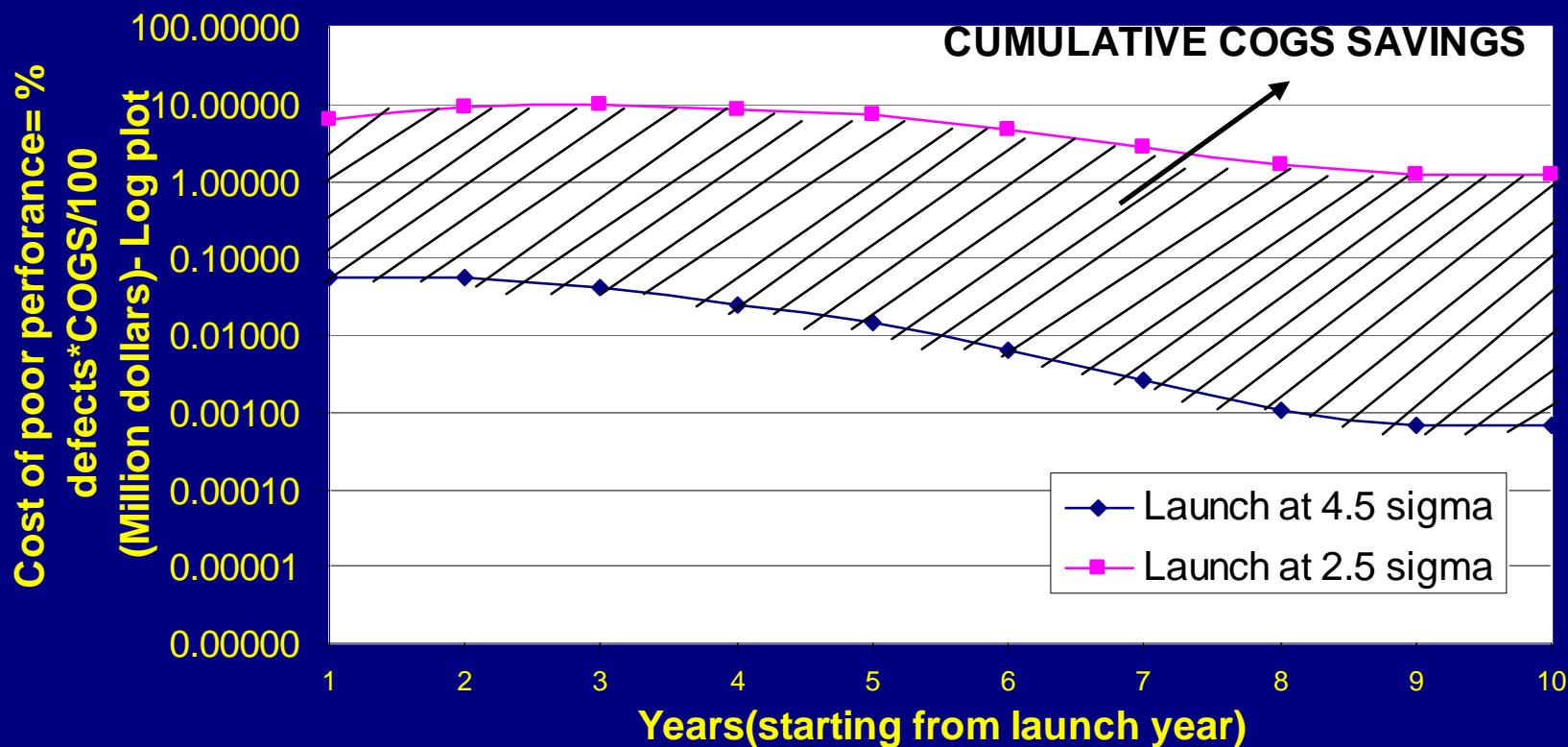
Impact of process robustness at launch-2 scenarios considered



COGS Savings

- The estimated savings in COGS are **\$19 million (NPV)** over the lifecycle of the drug

Cumulative COGS savings of a drug with \$1 bn peak sales reached in five years when supply is not limiting



COGS savings (Contd)

- Revenue will increase due to reduction in time to peak sales (for the case where supply is limited by capacity to produce):
 - *A drug with peak annual sales of \$1 Billion generates extra \$600 million (NPV) over its lifetime if peak sales attained 2 years earlier.*
 - *Assuming 20-30 drugs launched every year, additional revenues of \$12 to \$18 billion assuming average peak sales of \$1 Billion and time to peak sales is 10 years.*

Conclusion

- Comparing the various estimates of cost of new drug development
- Projecting the cost of drug development today based on these estimates.
- Highlighting the qualitative and quantitative benefits of improved product development and manufacturing
- Comparing the various estimates of COGS and explores the magnitude of possible COGS savings
- This work hopes to act as motivation for promoting and funding fundamental research in these areas.

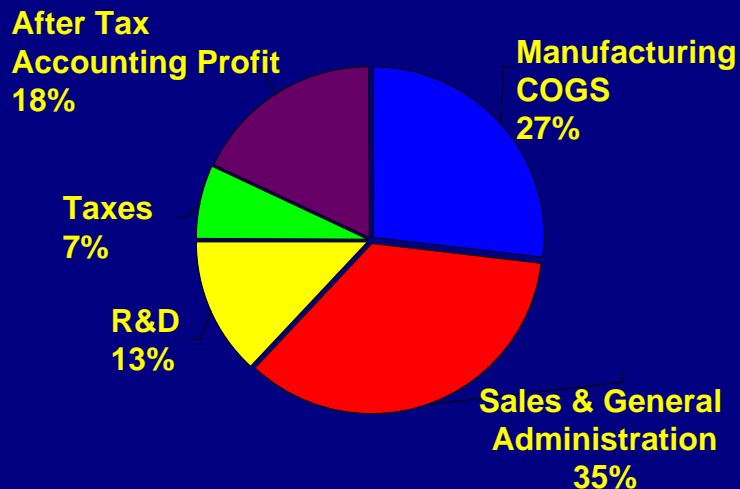
Questions??

Backup slides

Good Science will Help to Reduce Cost of Development and Manufacturing

Cost of Manufacturing of Pharmaceuticals

Disposition of the sales revenue earned by eight largest research-based pharmaceutical manufacturers in 1998

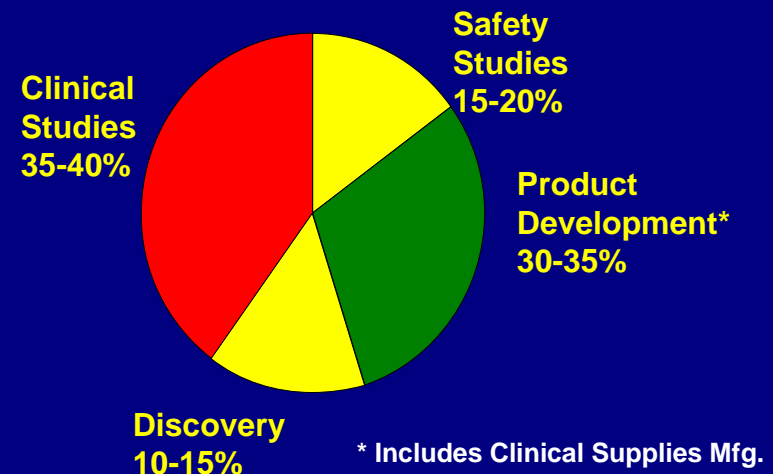


U.E. Reinhardt, Health Affairs, Page 136, September/October 2001

In 2006, total U.S. pharmaceutical expenditures estimated at \$300 billion in 2005 (IMS Health and PMPRB Annual Report, 2006) COGS (U.S) = ~ \$90 billion

Cost of Developing Pharmaceuticals

In 2005, the estimated cost of developing a new molecular entity into a registered drug is nearly \$ 2 billion. Total PhRMA company spent on R&D was \$51 billion.



Suresh, P & Basu, P. , Pharmaceutical Technology & Education Center Report, Purdue University, August, 2005.

Product Development Investment = \$15-18 billion in 2005

Cost Estimates from Literature

■ Dimasi et al (2003)

- Survey of 10 pharmaceutical firms, 68 NCE's which entered human trials between 1983-1994 from the CSDD database
- Self-originated NCE's only, licensed-in drugs not considered
- Clinical success rate of 21.5% used, timeline of 12 yrs was chosen, discount rate of 11% used
- Preclinical costs include discovery costs and their contribution to overall cost came down from 57% in 1991 compared to 30% in 2001

	UNCAPITALIZED	CAPITALIZED
CLINICAL COSTS PER INVESTIGATIONAL NCE	60.6	100.4
CLINICAL COSTS PER NCE APPROVED(with 21.5 % success rate)	281.86	467
PRECLINICAL COSTS(30% of total costs)	121	335
TOTAL COSTS	403	802

All figures in million 2000 dollars

Cost Estimates from Literature- Contd

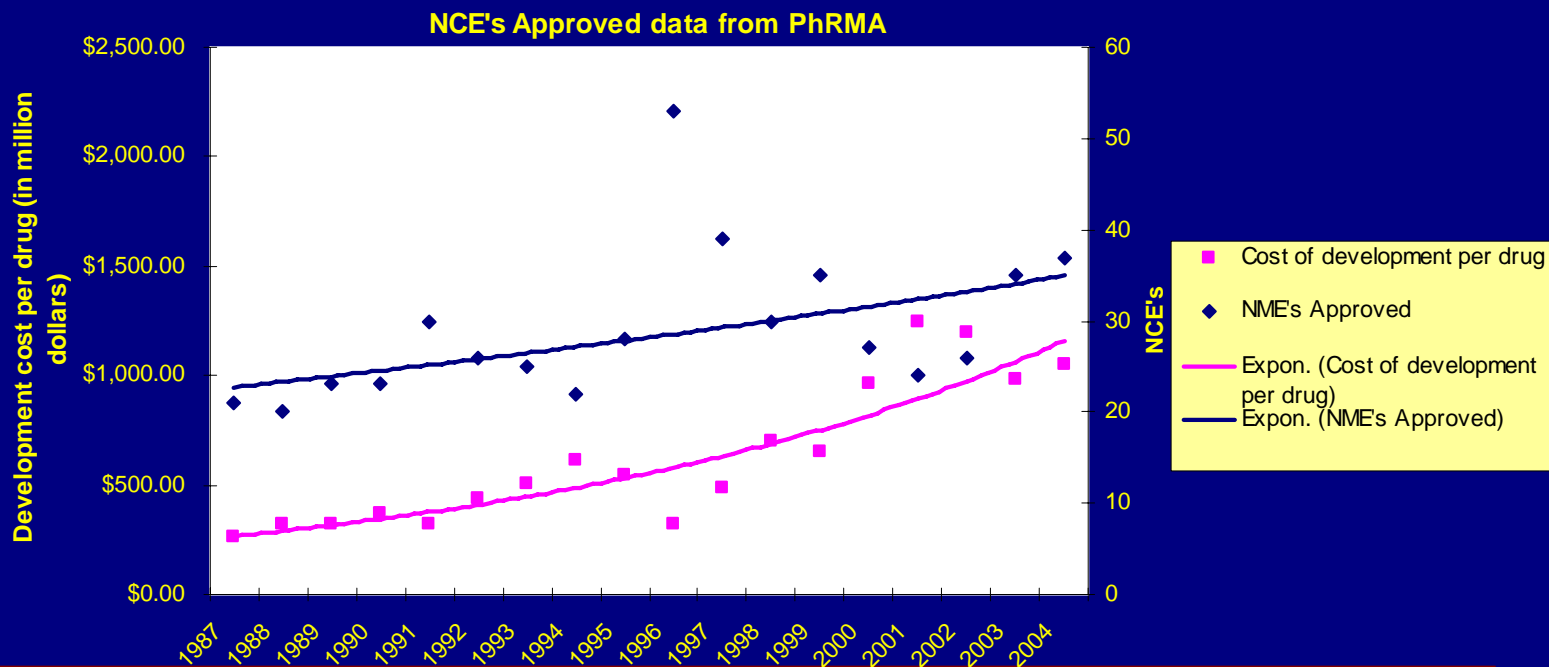
■ Brantner et al (2004)

- Uses Dimasi's methodology
- Drugs that went into clinical trials between 1989-2002 from Pharmaprojects Drug database
- Overall clinical success rate of 23.9% by multiplying observed success rates in each phase
- **\$839 million** estimate for a sample that does not include new formulations or previously approved drugs and **\$868 million** for a sample that does

Cost Estimates from Literature- Contd

■ Matthews Jr (2002)

- Looked at the annual aggregate research expenditure data reported by PhRMA and total number of drugs approved in that year
- Arrived at \$964 million in 2000 dollars, a crude estimate



Nov 15 2006

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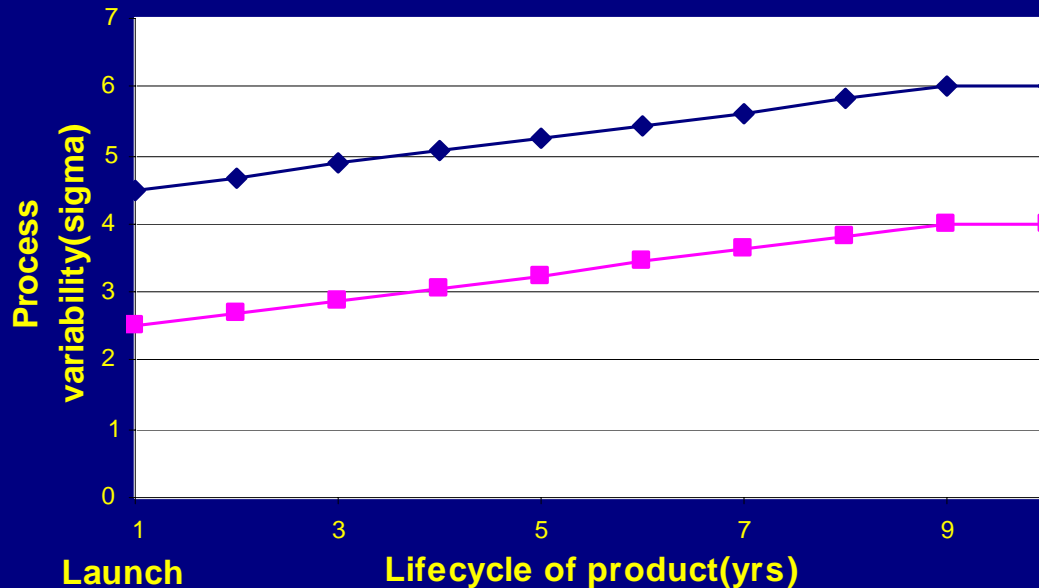
Cost Estimates from Literature (Continued)

■ Gilbert et al (2003)

- Data from 38 major pharmaceutical companies for all compounds developed in 1995-2000 and 2000-2002 in which the success rates were estimated to be 14% and 8% respectively
- Cost of new drug development was estimated as \$1.7 billion in 2002 dollars by running Monte Carlo simulations with the phase wise R&D money spent estimated using generally observed phase wise costs
- Additional Revenue due to reaching peak sales faster when supply is limiting
 - *A drug with peak annual sales of \$1 Billion generates extra \$600 million (NPV) over its lifetime if peak sales attained 2 years earlier.*
 - *Assuming 20-30 drugs launched every year, additional revenues of \$12 to \$18 billion assuming average peak sales of \$1 Billion and time to peak sales is 10 years.*

COGS Savings-Contd

Impact of process robustness at launch-2
scenarios considered



- When the drug supply is not limiting, the estimated savings in COGS are **\$19 million (NPV)** over the lifecycle of the drug
- When the drug supply is limiting, one has the same COGS savings but now with an additional rise in revenue valuing **\$577 million**