

ENGINEERING PHARMACEUTICAL INNOVATION



“New innovative business models in an environment of continuous dynamic change”

*Theo Iliopoulos June 12, 2007*



# ***What is the Business Environment***

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- All generic companies are operating in increasingly crowded and competitive environments
- Focus is switching from UK and US to growth markets such France, Spain, Brazil and Italy
- The number of new generic drug opportunities is reducing in line with the decline of NDAs
- Branded industry is far more aggressive to protect revenues (IP, product life cycle management)
- Introduction of biotech products will present regulatory, development and scale up hurdles to generic manufacturers in the future

## *Business Drivers*

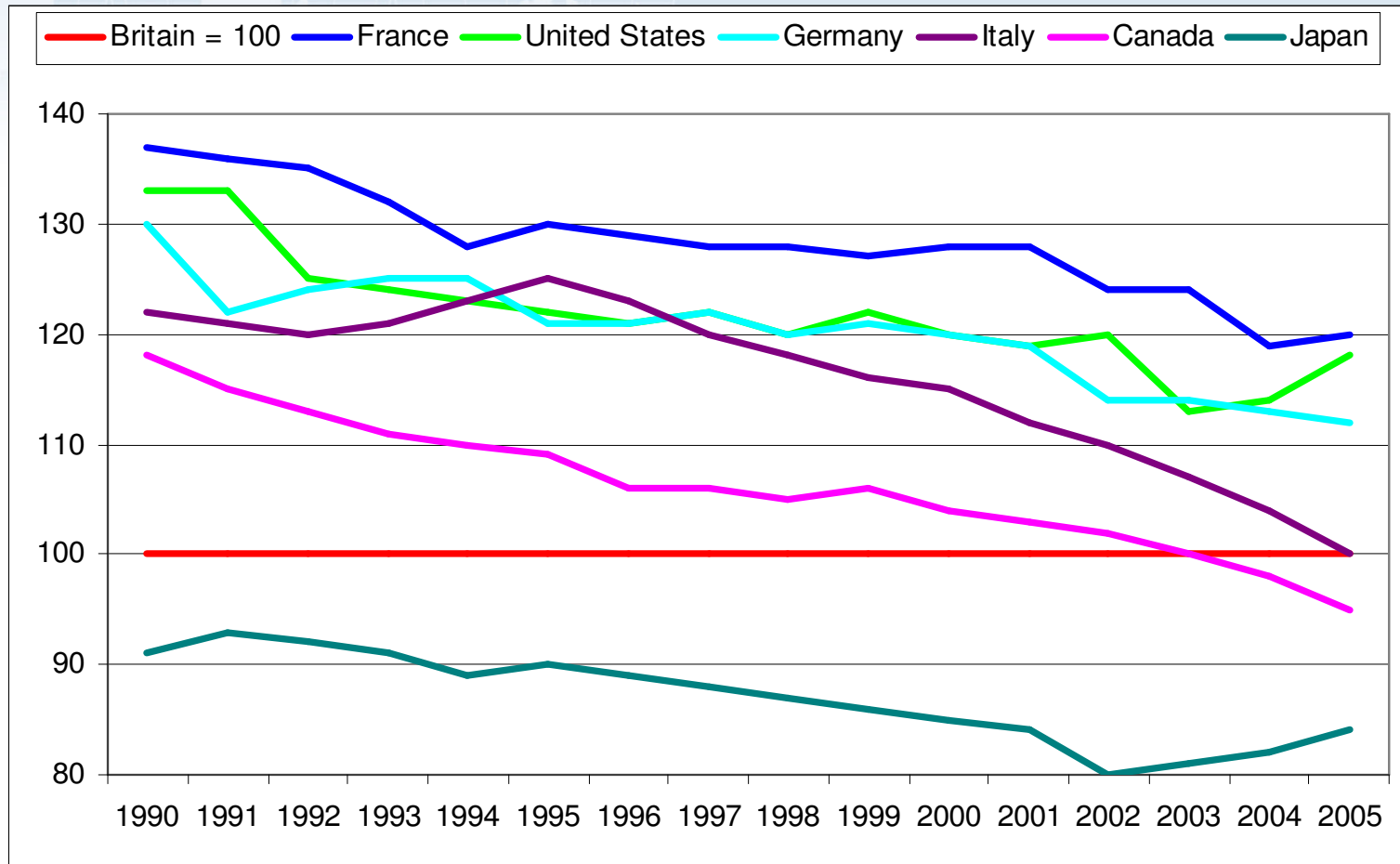
- M & A (Pressures to go global explain the wave of consolidation which has swept through the industry)
- Cost Pressures
- Intellectual Property rights
- Regulatory and Compliance Requirements  
e.g. SOX
- Health Care spending and pricing drive margins
- Price erosion with many entrants (6 competitors can get the price down to 25%)
- „Less Paper“
  - Electronic submission
  - Electronic batch recording
  - Online customer interaction

## *The Globalization of the Pharma Industry*

- Highly dynamic economic growth and distribution of wealth not experienced before
- Government policies and Economic incentives
- Investment in emerging regions driven by incentives
- Seasoned managers returning home
- Internet connecting us all
- Proliferation of high value/low cost services
- Risk sharing partnerships
- The productivity crisis in Western countries

*Things are changing rapidly but  
still to change*

# Output per hour worked in the big 7



Source: ONS

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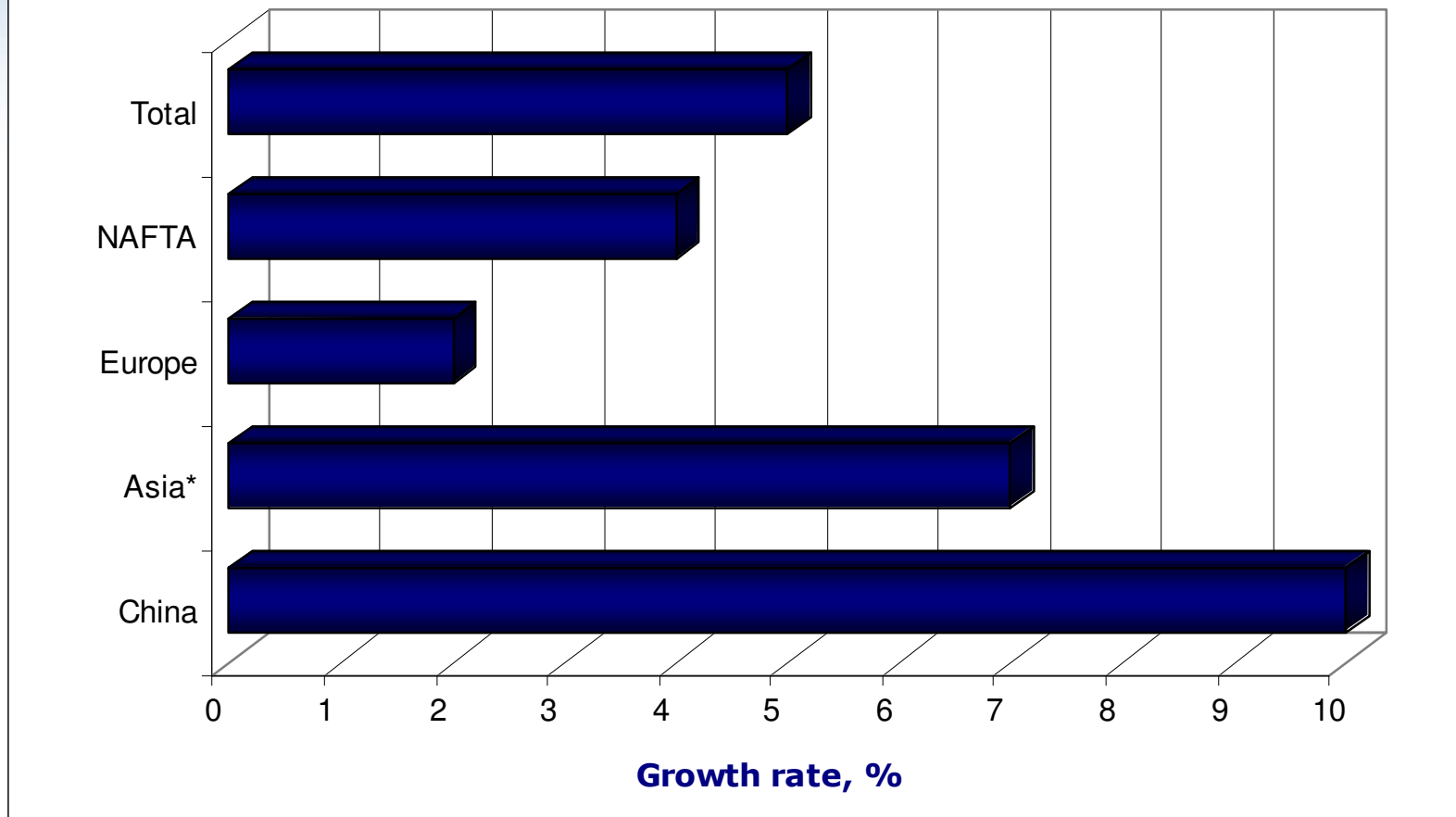


## *The lightning speed of growth of China and India Reality or Myth*

With a difference in start of a decade both countries are emerging as global economic powers but both countries have serious problems:

- Both countries are facing environmental protection issues
- India has poor roads and insufficient water and electrical supplies. The government estimates that \$320bn to ease many infrastructure bottlenecks
- China's unbalanced economy has massive bad bank loans, and a government driven allocation of investment funding
- Energy consumption in China per unit of production is 40% higher than the world's average with only 30% recycling of its natural resources which is 20 percentage points lower than developed nations

## GROWTH RATE FOR FINE CHEMICALS PER REGION



Source: YU (2005)

Note: \*not including China

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*However*

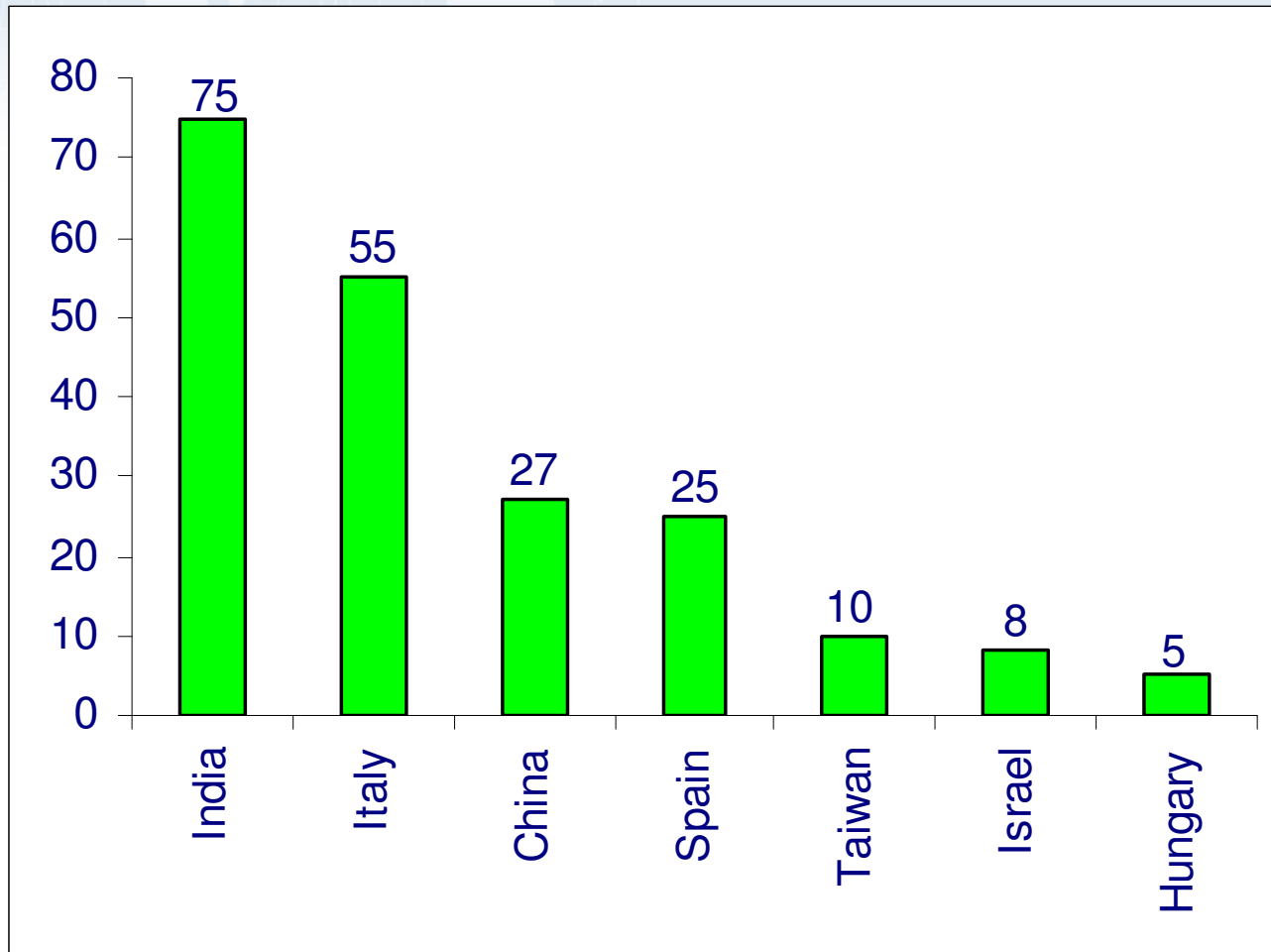
It will be a mistake to underestimate them or consider them as only cheap labor countries

Both China and India are nowadays centers of innovation for new products and services

One third of multinationals with bases in Asia intend to expand through acquisitions or by building green field sites in the next year

Asia maybe the world's largest pharma market in the coming years

## *FDA approved plants outside of the US*





# ***Business Models***



## *The Business Models have totally changed but continue changing*

- Acquisitions in addition to geographical or national territory market share provide to acquirers technological capabilities and vertical backwards integration in R&D and manufacturing and the race among the generic pharma to expand in market share will continue squeezing out the small players
- The key of the success and survival is pursuing cost reduction programs and technological advantages and in depth knowledge of product profitability life cycle management

*The pace of corporate consolidation  
grows ever faster*

| Target         | Buyer               |
|----------------|---------------------|
| Andrx          | Watson              |
| Mayne Pharma   | Hospira             |
| Betapharm      | Dr Reddy's          |
| Pliva          | Barr Pharmaceutical |
| Matrix         | Mylan Labs          |
| Terapia        | Ranbaxy             |
| Hemofarm       | Stada Arzneimittel  |
| Sindan         | Actavis             |
| Negma          | Wockhardt           |
| Merck Generics | Mylan Labs          |
| Taro           | Sun                 |

*Who's next*



## *The Business Model paradox*

The API manufacturers are now becoming finished dosage form (FDF) manufacturers and from suppliers become competitors

and

The FDF manufacturers are now becoming API manufacturers and from customers become competitors!

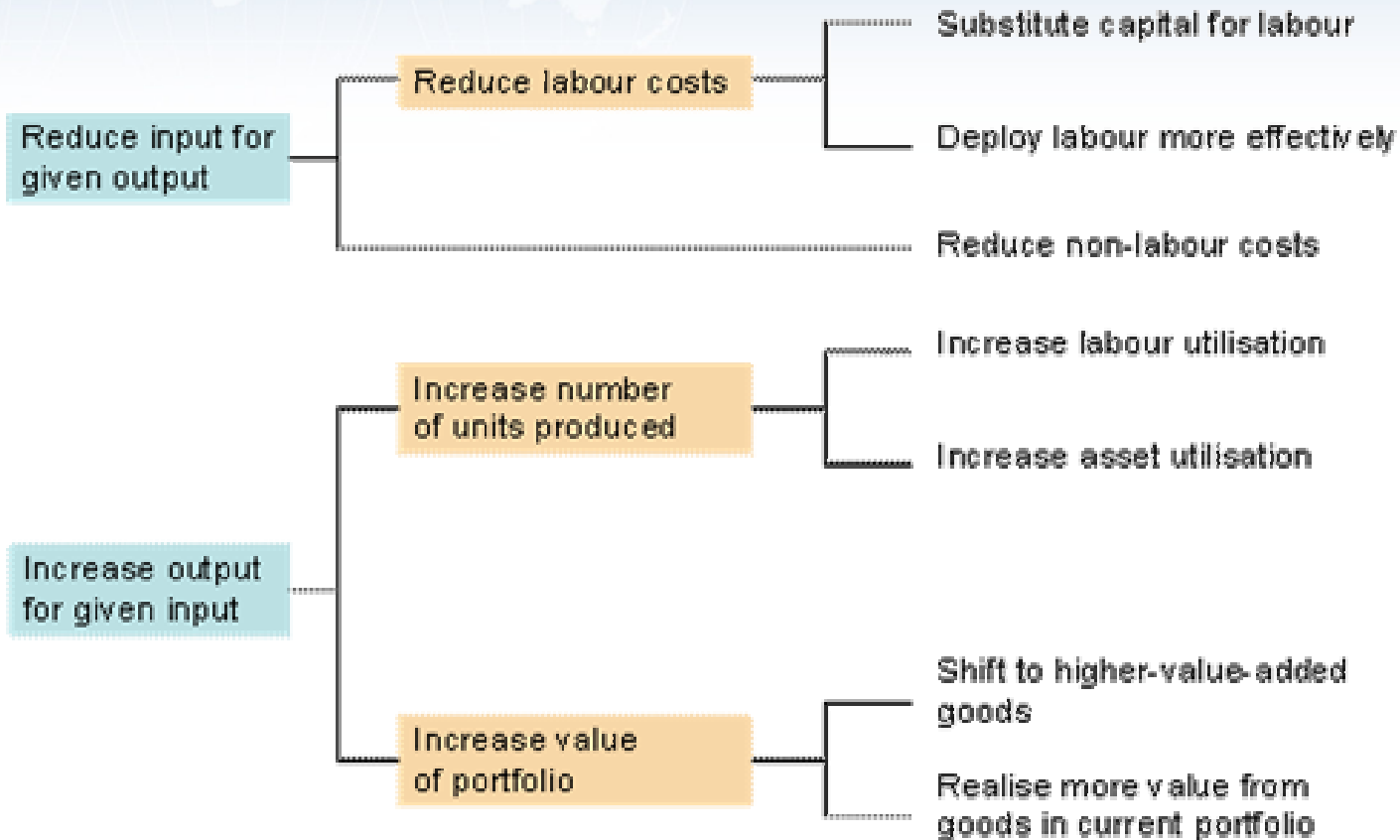
**Most of the FDA Inspected Indian fine chemicals vendors are active also in dosage form products**

| Company             | Drug Substance | Drug Product | Company              | Drug Substance | Drug Product |
|---------------------|----------------|--------------|----------------------|----------------|--------------|
| Alembic             | ✓              | ✓            | Malladi Drugs        | ✓              | -            |
| Aurobindo           | ✓              | (✓)          | Matrix Labs          | ✓              | -            |
| Avon Organics       | ✓              | -            | Morepen              | ✓              | ✓            |
| Cadila Laboratories | ✓              | ✓            | Natco Pharma         | ✓              | ✓            |
| Cipla               | ✓              | ✓            | Nicholas Piramal     | ✓              | ✓            |
| Dr. Reddy's         | ✓              | ✓            | Neuland Laboratories | ✓              | -            |
| Dishman Pharma      | ✓              | -            | Orchid Chemicals     | ✓              | ✓            |
| Divis Labs          | ✓              | -            | Ranbaxy              | ✓              | ✓            |
| FDC Ltd             | -              | ✓            | Shasun Chemicals     | ✓              | -            |
| Hetero Drugs        | ✓              | ✓            | Sri Krishna          | ✓              | -            |
| Hikal               | ✓              | -            | Sun Pharma           | ✓              | ✓            |
| IPCA Labs           | ✓              | ✓            | Suven                | ✓              | -            |
| Jal Limited         | ✓              | -            | Unichem              | ✓              | ✓            |
| Krebs Biochemicals  | ✓              | -            | Vera Labs            | ✓              | (✓)          |
| Lupin               | ✓              | ✓            | Wockhardt            | ✓              | ✓            |

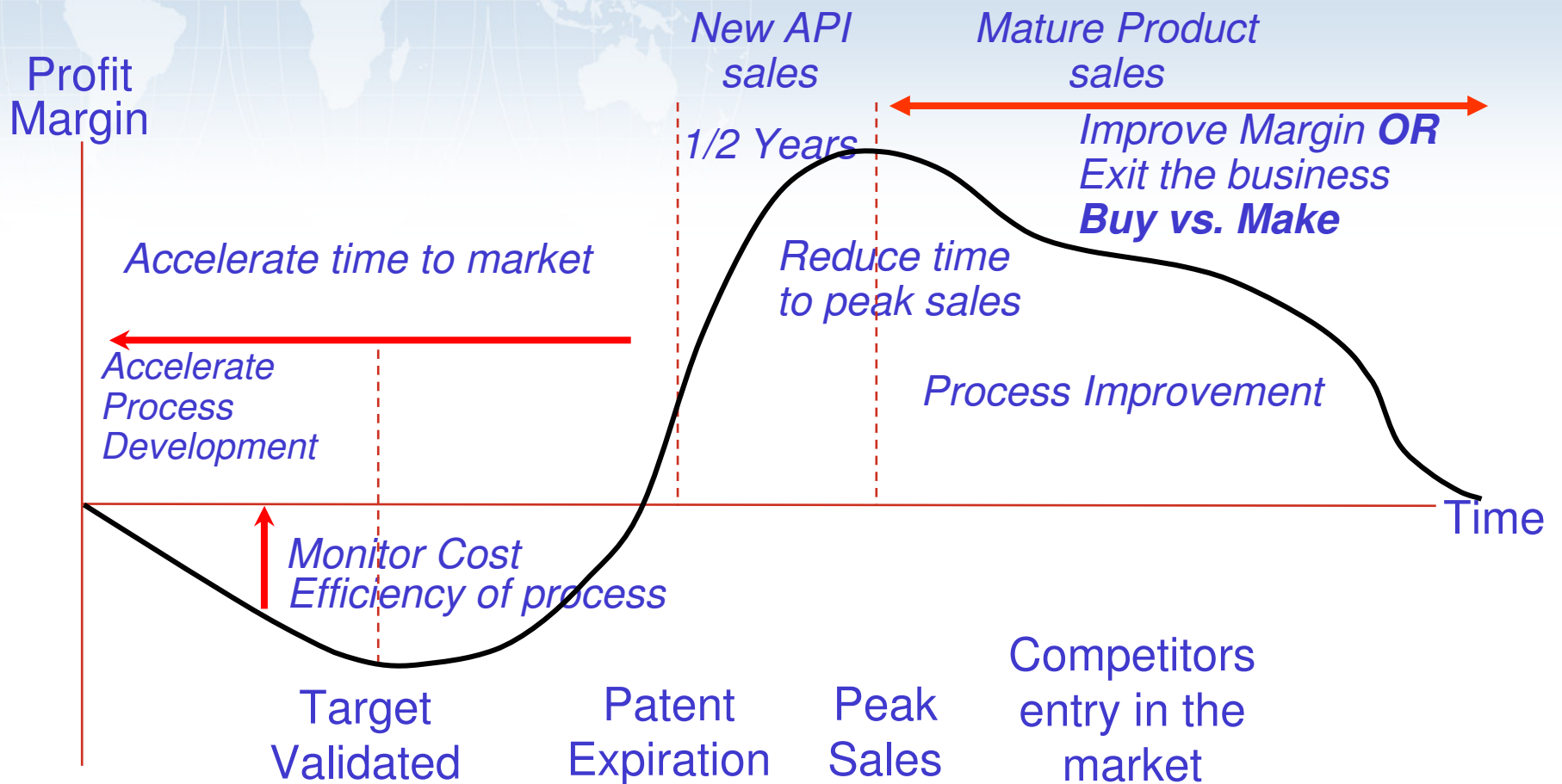
## *Factors affecting process performance*

- Experienced and talented staff
- Production problems (ex. downstream purification)
- Ability or inability to introduce new cutting edge technology
- Availability or lack of financing
- Cost reduction programs - reducing capital and driving out costs in manufacturing
- Product profitability life cycle method and capability

# Cost reduction programs (Operational Levers)



# Product Profitability Over the Entire Lifecycle





## *The most advantageous manufacturing network set up*

Establishment of stable manufacturing process  
but the latter requires high level of expertise

Launch sites with volume scaling up capability  
with next door vertically backwards  
integrated R&D with all expertise on hand  
ready to ramp up for commercial production

## *The myth and the reality of the vertical integration*

Do not vertically integrate unless absolutely necessary. This strategy is too expensive, risky and difficult to reverse if market structures change

There might be wiser for the companies to disintegrate vertically from product development and design to manufacturing and commercialization

This might be seen as a radical position but outsourcing innovation using strategic alliances and partners is gaining grounds and companies should consider the rich array of quasi-integration strategies.



*Biosimilars/Follow on Biologicals*  
*the myth and the reality*


*50bn in the year 2005*  
*130bn by the year 2009*

*Biotech is almost insulated from the generic threat because:*

1. Biotech portfolios are often too young to contain expired products. Biotech pipelines have a formidable number of 140 mabs.
2. Even if products have expired, the predominantly biologic nature of biotech portfolios is a major barrier to generic entry
3. The approval of biosimilars/follow-on biologics is much more complicated than the approvals of generic equivalents of conventional pharmaceuticals due to the intrinsic complexity and the heterogeneity of proteins produced by different manufacturing processes
4. Companies wishing to enter the generic market will require new skills in manufacturing

*Biotech is almost insulated from the generic threat because:*

5. According to FDA, demonstrating similarity would be more complex than an originator showing comparability after a change in manufacturing process. Moreover, the agency may be limited in its ability to determine whether follow-on protein products could be substituted
6. Demonstrating the similarity of a follow-on protein product to a reference product will typically be more complex – and thus require more new data – than assessing the similarity of products before and after manufacturing changes made by the approved product



*However EMEA expects  
12 filings for biosimilars in 2007  
vs. the 4 applications of 2006  
and have issued guidance  
for clinical and no clinical studies  
for 15 biosimilars*

*However New provisions offering a pathway for approving biogenerics should be included in the bill raising user fees and dealing with paediatric exclusivity – called the FDA Revitalization Act – that will be debated soon in the US Senate.*



# ***Innovative Technologies***

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# The changing nature of innovation

## Features of Historical Innovation

## Features of Future Innovation

- |   |   |  |
|---|---|--|
| <ul style="list-style-type: none"><li>• Focus is on product &amp; service innovation</li></ul>            | ➔ | <ul style="list-style-type: none"><li>• Broad agenda includes business model innovation</li></ul>                                  |
| <ul style="list-style-type: none"><li>• Development and technology driven</li></ul>                       | ➔ | <ul style="list-style-type: none"><li>• Customer and technology driven</li></ul>   |
| <ul style="list-style-type: none"><li>• Research and Development (R&amp;D) plays a central role</li></ul> | ➔ | <ul style="list-style-type: none"><li>• Leadership and individuals play key roles while R&amp;D is one of many processes</li></ul> |
| <ul style="list-style-type: none"><li>• Closed and internal to the enterprise</li></ul>                   | ➔ | <ul style="list-style-type: none"><li>• Open and collaborative, across organizational boundaries</li></ul>                         |
| <ul style="list-style-type: none"><li>• Technology is a differentiator</li></ul>                          | ➔ | <ul style="list-style-type: none"><li>• Technology and business integration are differentiators</li></ul>                          |

Source: IBM Institute for Business Value

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# *Novel drug delivery methods and technologies*

## Success will depend on

- Excellent Science (Labs, skills etc.)
- Modern technologies and instrumentation
- R&D and Manufacturing capabilities
- Lean QC and Manufacturing
- Creative partnering
- Networks of creation where hundreds if not more of participants learn from one another and build on one another's work
- Hire, educate and train and retain talents
- Utilize R&D grants and
- Get tax breaks

# *Novel drug delivery methods and technologies*

## Potential Pitfalls

- Not understanding the challenges the pharma industry faces
- Wrong focus
- Wrong direction
- Wrong Information
- Missing links with knowledge networks
- Not embracing the change
- Missing the opportunity

*The differentiation between the winners and the losers is in:*

- world class R&D
  - the process modelling and
  - the optimization of the process by improving the upstream and downstream yield
- flexible and knowledge workforce,
- access to world and market knowledge, technological innovation and intelligence
- outsourcing non critical non strategic business to carefully selected partners

## Questions the industry is called to answer:

- Are available technologies and delivery systems really meeting market/patient needs
- What technology and innovative platforms might be used to reduce costs
- Are they actively track technology and industry developments so they don't miss the opportunity especially when the pace is accelerated
- What focus

*Barriers to entry provide potential for growth*



***Thank you***

