



Life Science industry in Transition

LogistikTAG 2008

29. April 2008

Ernst & Young

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“Our clients expect [...] a real global approach”

Herbert Müller, Chairman of Ernst & Young AG

EY Germany

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21 headquarters,

1,08 EUR billion turnover,

One of the “Big Four”,

Number one in TAX Advice,

Excellent Reputation.

Our focus on services

Assurance Services

Advisory Services

Tax Services

Transaction Services



Industry Trends

Current Market Forces

- ongoing **consolidation** of market players
- Governmental interests and Generic Competition **hit prices** and **margins**
- Shift from **Customer** to **Consumer Focus**, from **individual Practitioner** to **HealthCare Value Networks**
- **Global Brand Management** and **Regional Co-optition** in Sales and Marketing
- **Sales & Marketing and Manufacturing regulatory oversight** significant new area of risk and cost
- **R&D Pipeline Productivity** not keeping pace with growth requirements and patent expirations, **Paradigm Change in Research**
- **New Technologies** and **Players** driving alternate research, development, and delivery modes Cost of **Clinical Trials** growing

Big Business „Pharmaceuticals“

Global Pharmaceutical Sales, 1999 – 2006

| Global Sales US\$BN | 1999 | 2000 | 2001 | 2002 | 2003 | 2004 | 2005 | 2006 |
|--|-------|-------|-------|-------|-------|-------|-------|-------|
| Total World Market (current US\$) | \$334 | \$362 | \$387 | \$427 | \$498 | \$559 | \$601 | \$643 |
| Growth Over Previous Year (% Constant US\$ Growth) | 14.5% | 11.7% | 11.8% | 10.6% | 10.4% | 8.0% | 6.8% | 7.0% |

Global Pharmaceutical Sales by Region, 2006

| World Audited Market | 2006 Sales (US\$BN) | % Global Sales | % Growth Year-over-Year (Constant US\$) |
|----------------------------|---------------------|----------------|---|
| North America | \$289.9 | 47.7% | 8.0% |
| Europe | 181.8 | 29.9 | 4.8 |
| Japan | 56.7 | 9.3 | -0.7 |
| Asia, Africa and Australia | 52.0 | 8.6 | 9.8 |
| Latin America | 27.5 | 4.5 | 12.9 |
| Total IMS Audited* | \$607.9 | 100% | 6.5% |

Source: IMS MIDAS®, MAT Dec 2006

All information current as of March 20, 2007.

Source: IMS MIDAS®, MAT Dec 2006

Leading Products by Global Pharmaceutical Sales, 2006

| | Leading Brands | 2006 Sales (US\$BN) | % Global Sales | % Growth Year-over-Year (Constant US\$) |
|-----|--|---------------------|----------------|---|
| 1. | Lipitor (atorvastatin) | \$13.6 | 2.2% | 4.2% |
| 2. | Nexium (esomeprazole) | 6.7 | 1.1 | 16.9 |
| 3. | Seretide/Advair (fluticasone+salmeterol) | 6.3 | 1.0 | 10.3 |
| 4. | Plavix (clopidogrel) | 5.8 | 1.0 | -3.4 |
| 5. | Norvasc (amlodipine) | 5.0 | 0.8 | -0.5 |
| 6. | Aranesp (darbepoetin alfa) | 5.0 | 0.8 | 35.6 |
| 7. | Zyprexa (olanzapine) | 4.7 | 0.8 | -0.4 |
| 8. | Risperdal (risperidone) | 4.6 | 0.8 | 12.3 |
| 9. | Enbrel (etanercept) | 4.5 | 0.7 | 18.4 |
| 10. | Effexor (venlafaxine) | 4.0 | 0.7 | 2.7 |
| | Total Leading Brands* | \$60.0 | 9.9% | 8.0% |

Source: IMS MIDAS®, MAT Dec 2006

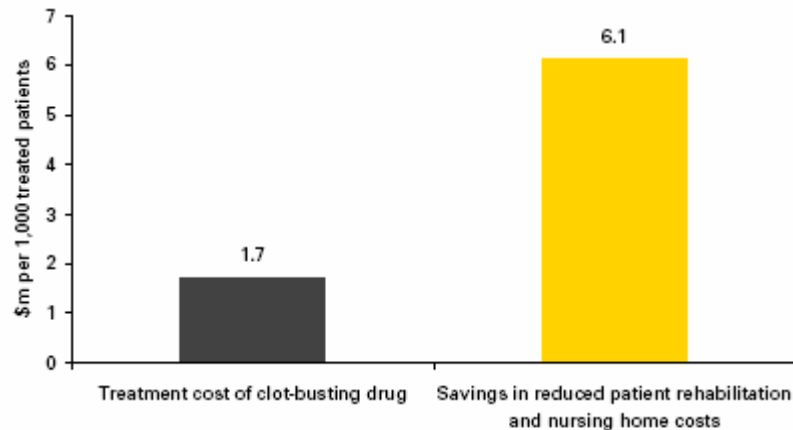
All information current as of March 20, 2007.

*Sales cover direct and indirect pharmaceutical channel purchases in U.S. dollars from pharmaceutical wholesalers and manufacturers. The figures above include prescription and certain over-the-counter data and represent manufacturer prices. Totals may not add due to rounding.

Health Economics

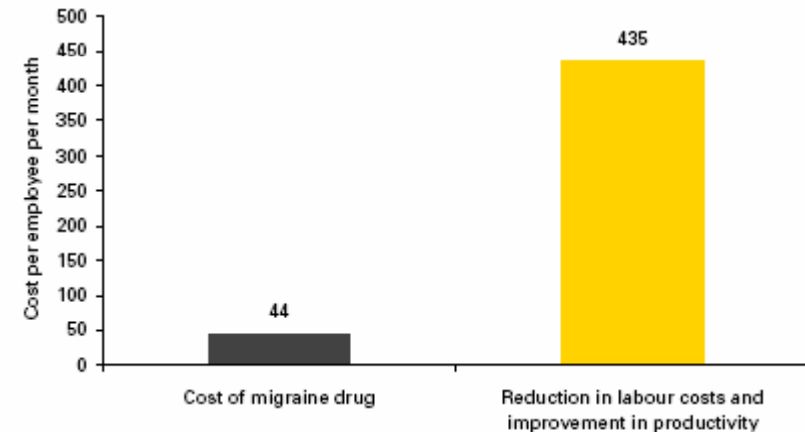
benefits versus costs

Cost vs. savings for anti-thrombotic (\$m)



Source: Fagan FC et al (1998)

Cost vs. savings for migraine drug (\$)



Source: Legg RF et al (1997)

- ▶ Compared to hospitalization, surgery and lost productivity, Pharmaceuticals are a very cost-effective for governments and insurance companies
- ▶ the use of pharmaceuticals saves society huge costs

Source: Deutsche Bank, Global Pharmaceuticals, 2005, S. 11

Health Economics Expectations

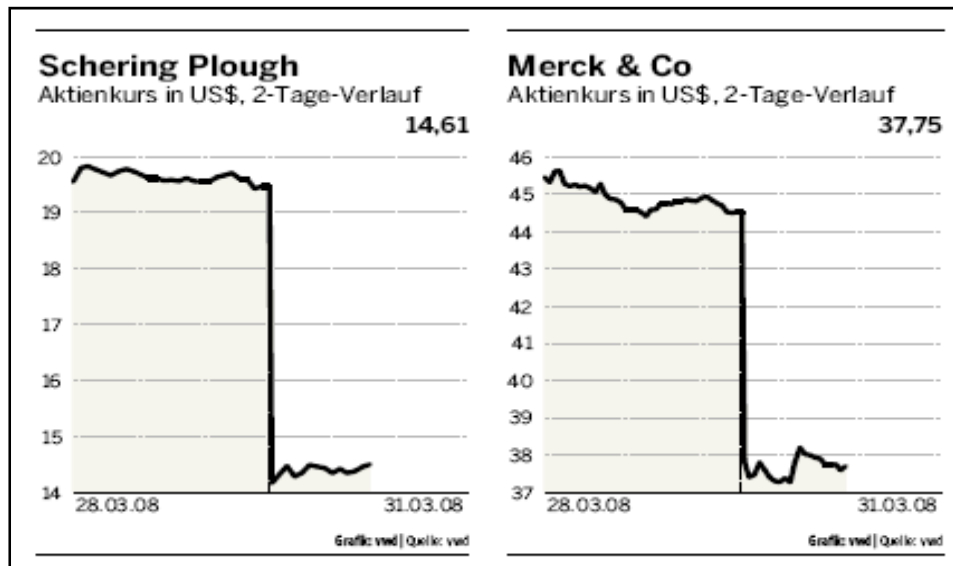
optimized drug: added value versus reality. Safety, Efficiency given

Harlan Krumholz

The Speech That Maimed Schering And Merck

Shares of Schering-Plough have dropped 26% this week, and Merck's stock is down 15%. The reason is a recommendation from a four-doctor expert panel at the American College of Cardiology that said physicians should sharply reduce the use of Zetia and Vytorin, ...

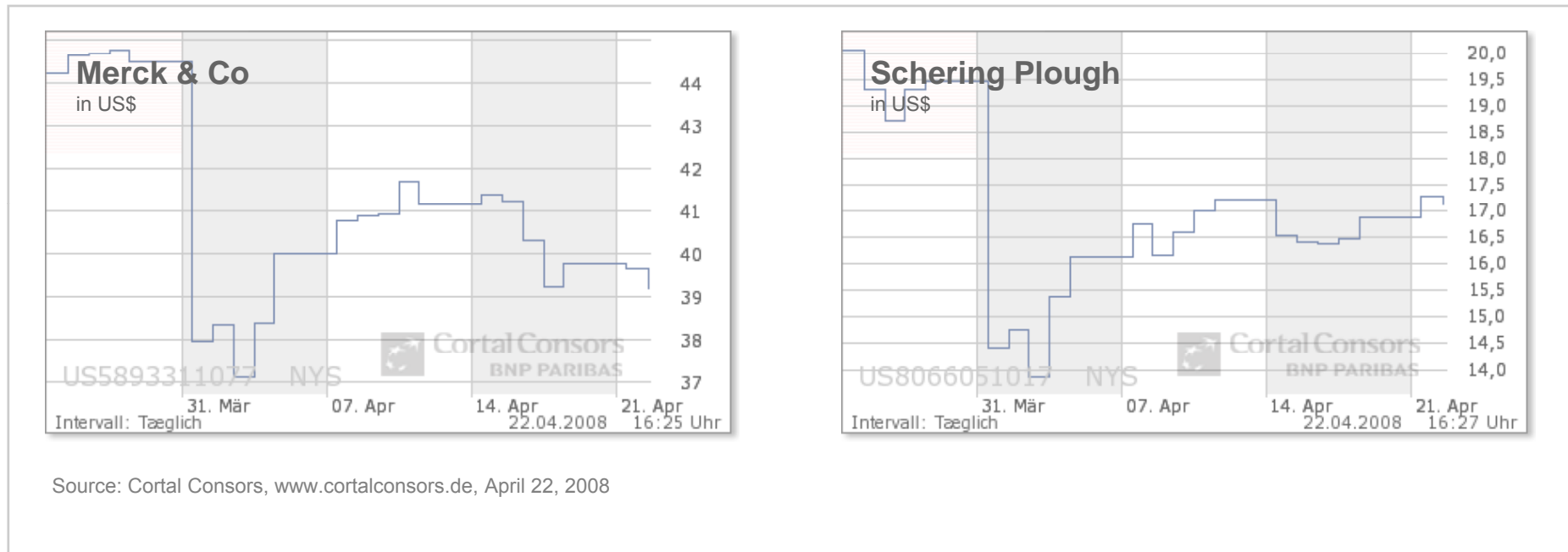
Source: reported by 04/03/2008 by Forbes.com



Source: Handelsblatt, 01.04.2008, nr. 63, p. 11; Handelsblatt, 04.-06.04.2008, nr. 66, p. 14

- ▶ Effectiveness from Vytorin is not as high as expected
- ▶ Merck shares the revenue with Schering-Plough
- ▶ Specialists recommend first the use of 5-fold cheaper statin e.g. Zocor
- ▶ Analysts estimate that Vytorin and Zetia stand for ~70% of earnings by Schering Plough
- ▶ Reaction: announcement of cost take out
Schering Plough 1,5 billion \$ → 8% of the sales
Merck & Co 5 billion \$ → 20% of the sales volume

nevertheless sales increase



- ▶ The Committee of the U.S. Senates and the New York prosecution investigate the processes of Vytorin.

Source: Handelsblatt, April 22, 2008, p. 15

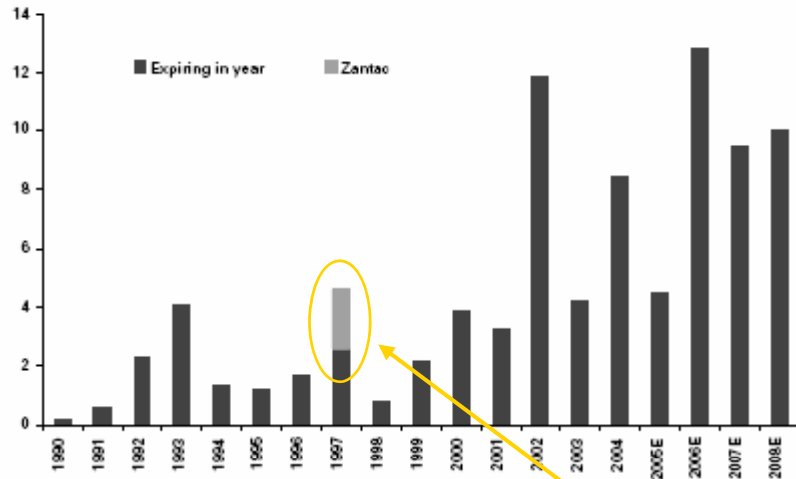
- ▶ Sales of cholesterol medicines Vytorin and Zetia increased 6% to \$1.2 billion in 1st quarter 2008 (Merck & Co.)

Source: International Herald Tribune, April 22, 2008, p. 15

Impact of Generics

Imperative for innovation for research based pharma

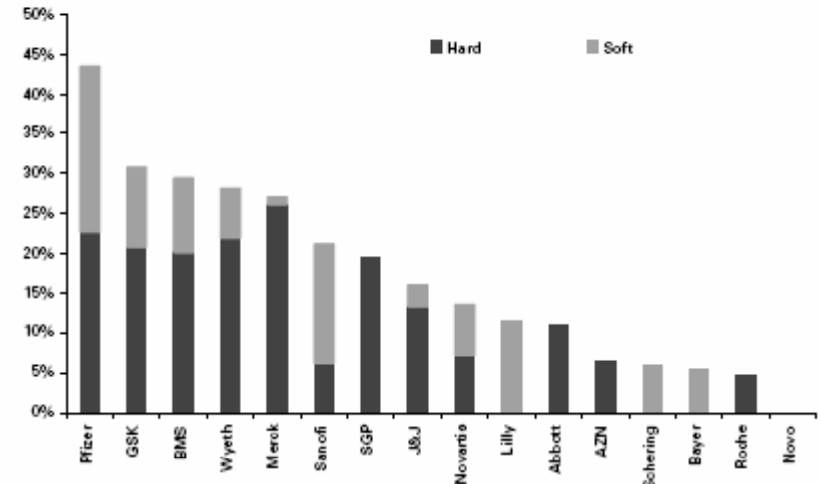
**Revenues lost to US patent expiry
1990-2008E (\$ bn)**



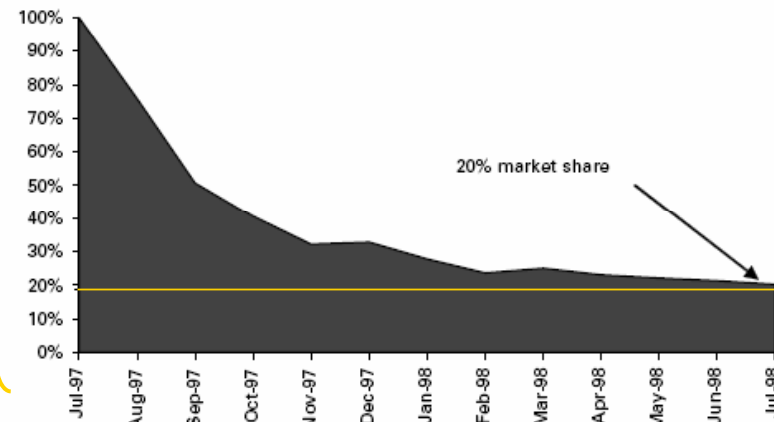
Source: Company data, Deutsche Bank estimates

- ▶ increasing part of revenues is threatened by patent expiry
- ▶ Zantec lost 80% of sales to generics after patent expiry

**US exposure by company 2004-2008E
(% 2004 sales)**



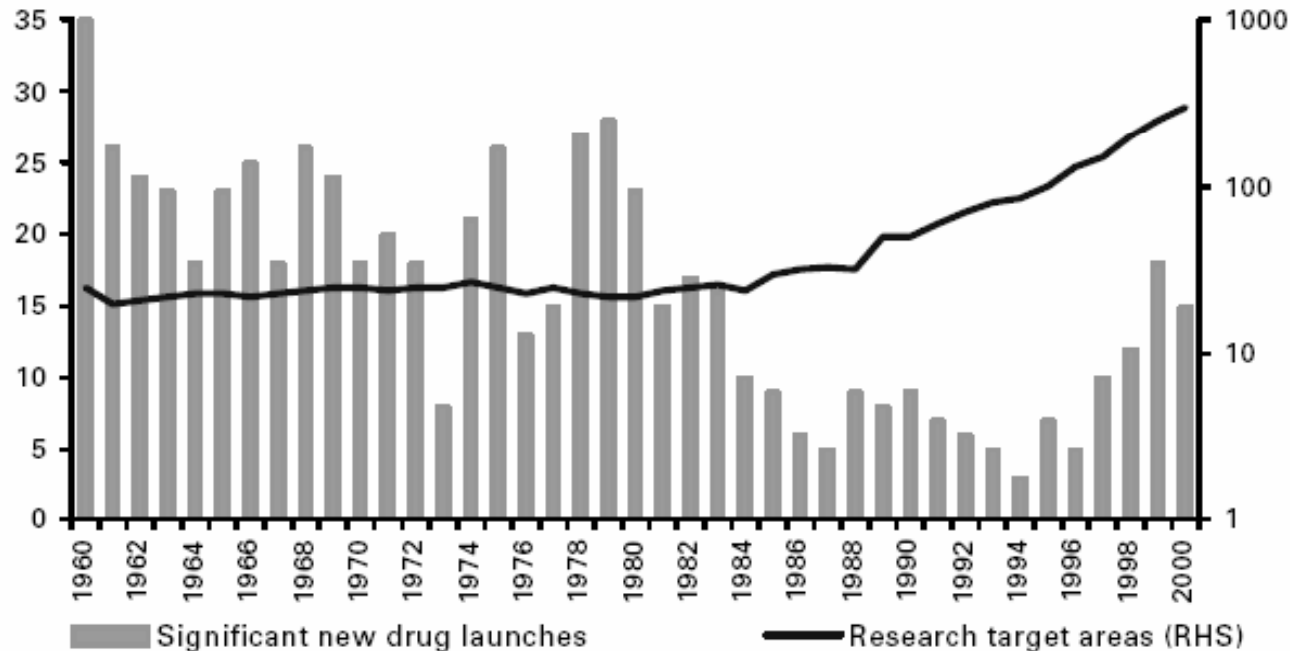
Zantac patent expiry (% sales lost, 1997)



Source: Deutsche Bank, Global Pharmaceuticals, 2005, p.9-10, 66

Research & Development

The number of drug receptor targets is increasing rapidly



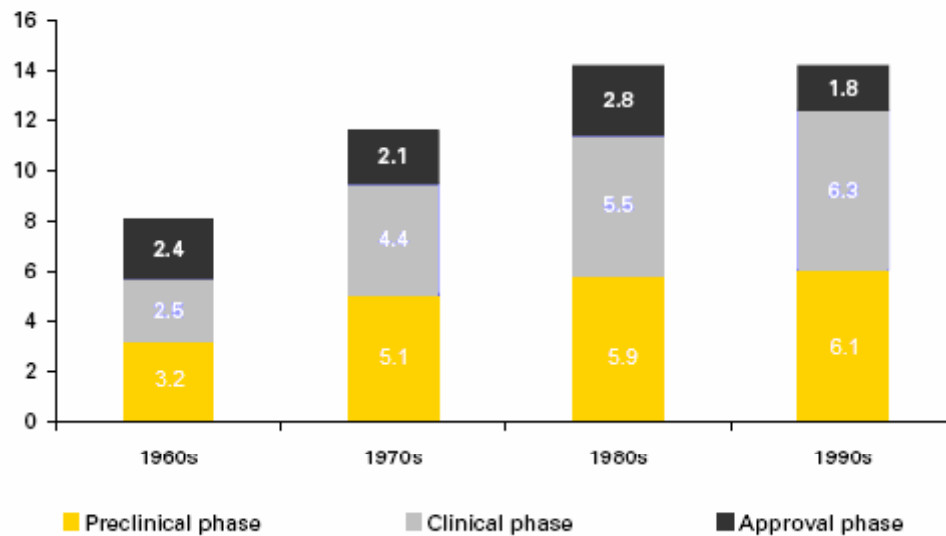
Source: Company data, Deutsche Bank estimates

- ▶ realization gap: research target areas vs. new drug launches
- ▶ more molecules than ever before are entering the research pipelines
- ▶ high increase in research target areas expected by understanding the era of genomics

Source: Deutsche Bank, Global Pharmaceuticals, 2005, p.9-10

Research & Development

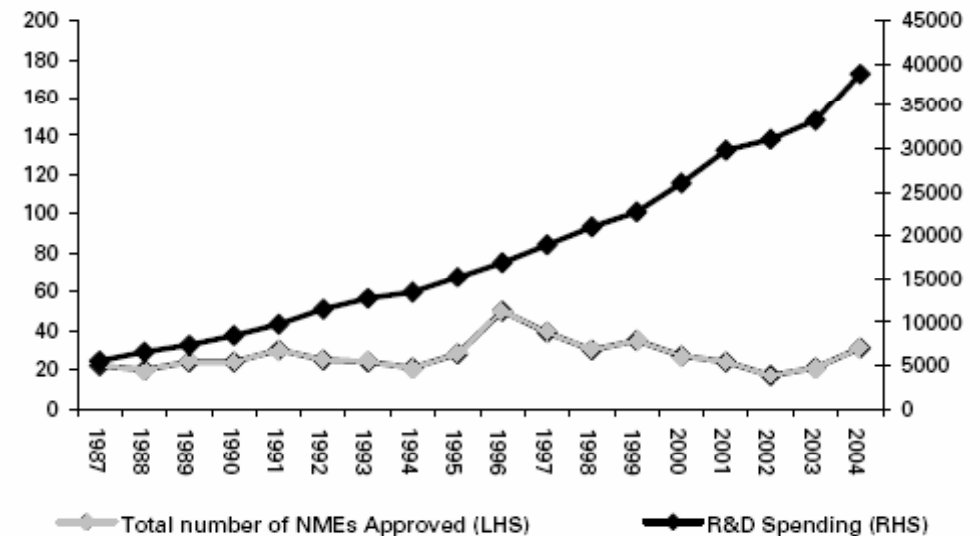
Time to get a new drug to market



Source: Deutsche Bank

- ▶ Average time to market increase over the past 20 years to almost 15 years (a near 20% increase)
- ▶ Effect: Protected patent time is reduced

R&D spend vs. drugs approved

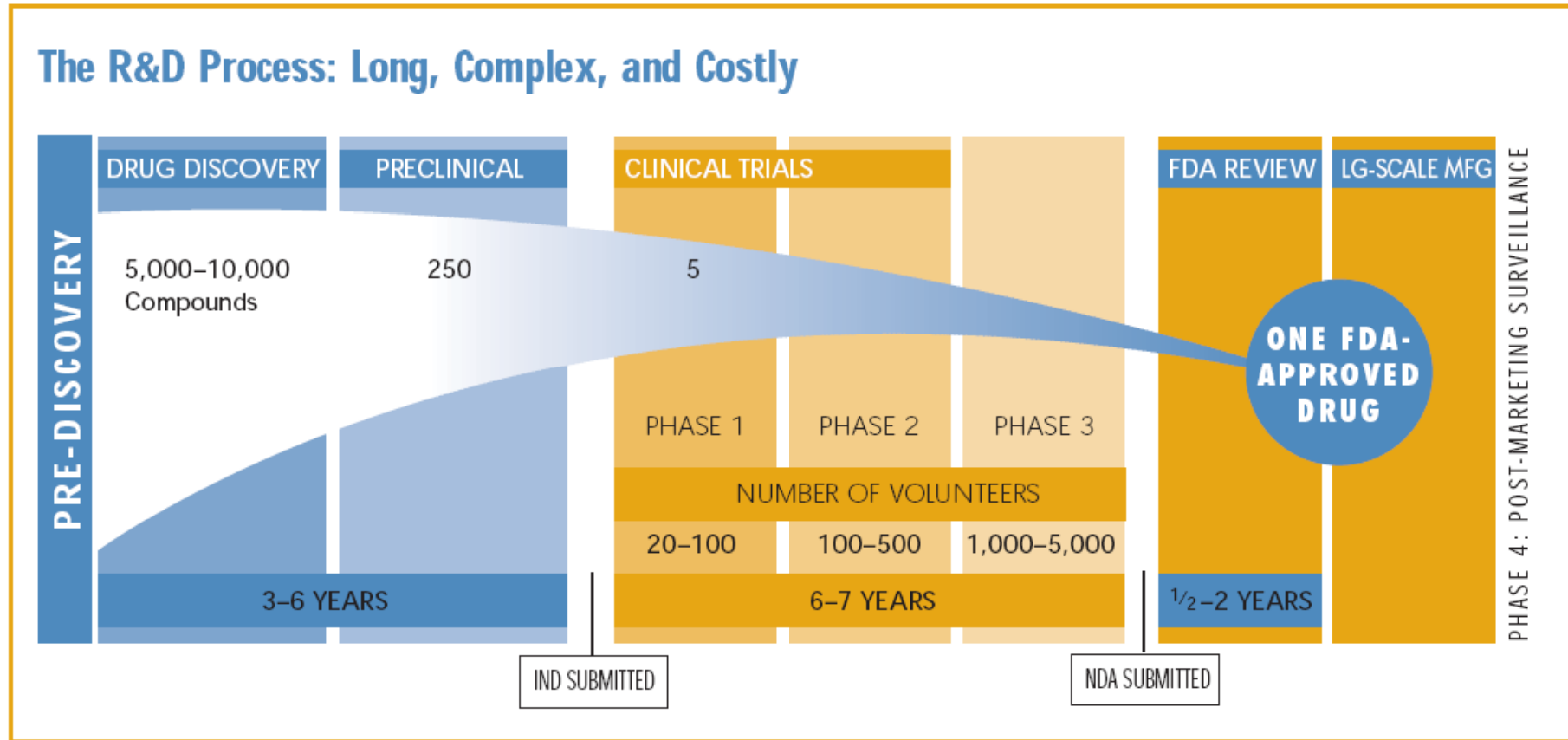


Source: Deutsche Bank

- ▶ Researched cost increase
- ▶ No significant increase of NMEs (New Molecular Entities)

Source: Deutsche Bank, Global Pharmaceuticals, 2005, p.12

Product Lifecycle



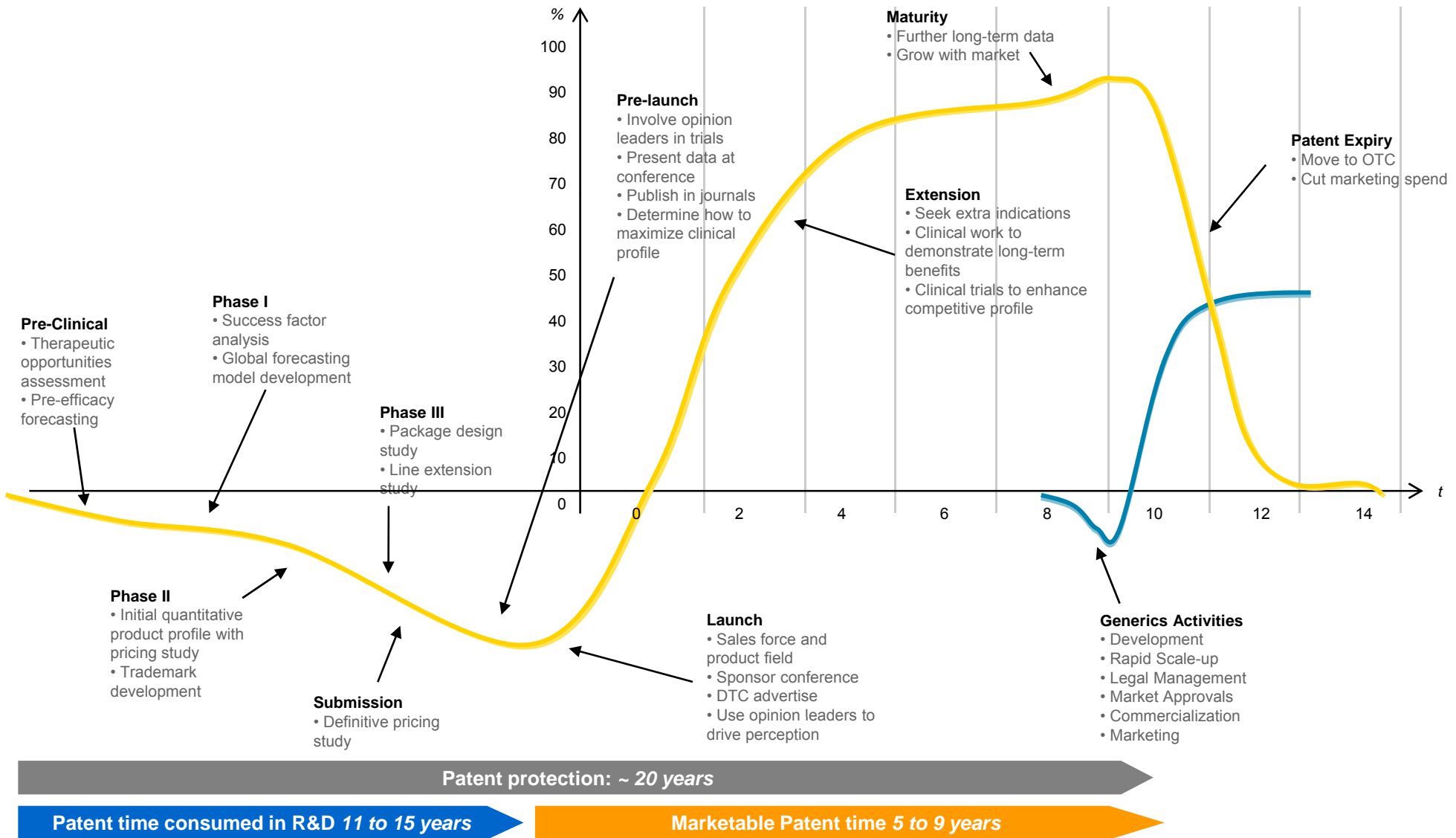
Patent protection: ~ 20 years

Patent time consumed in R&D
11 to 15 years

Marketable Patent time
5 to 9 years








Source: PROFILE 2008, PHARMACEUTICAL INDUSTRY, PhRMA, p. 4

Lifecycle & Generics impact



Cost Cutting: Global industry trends require significant improvements to cost performance

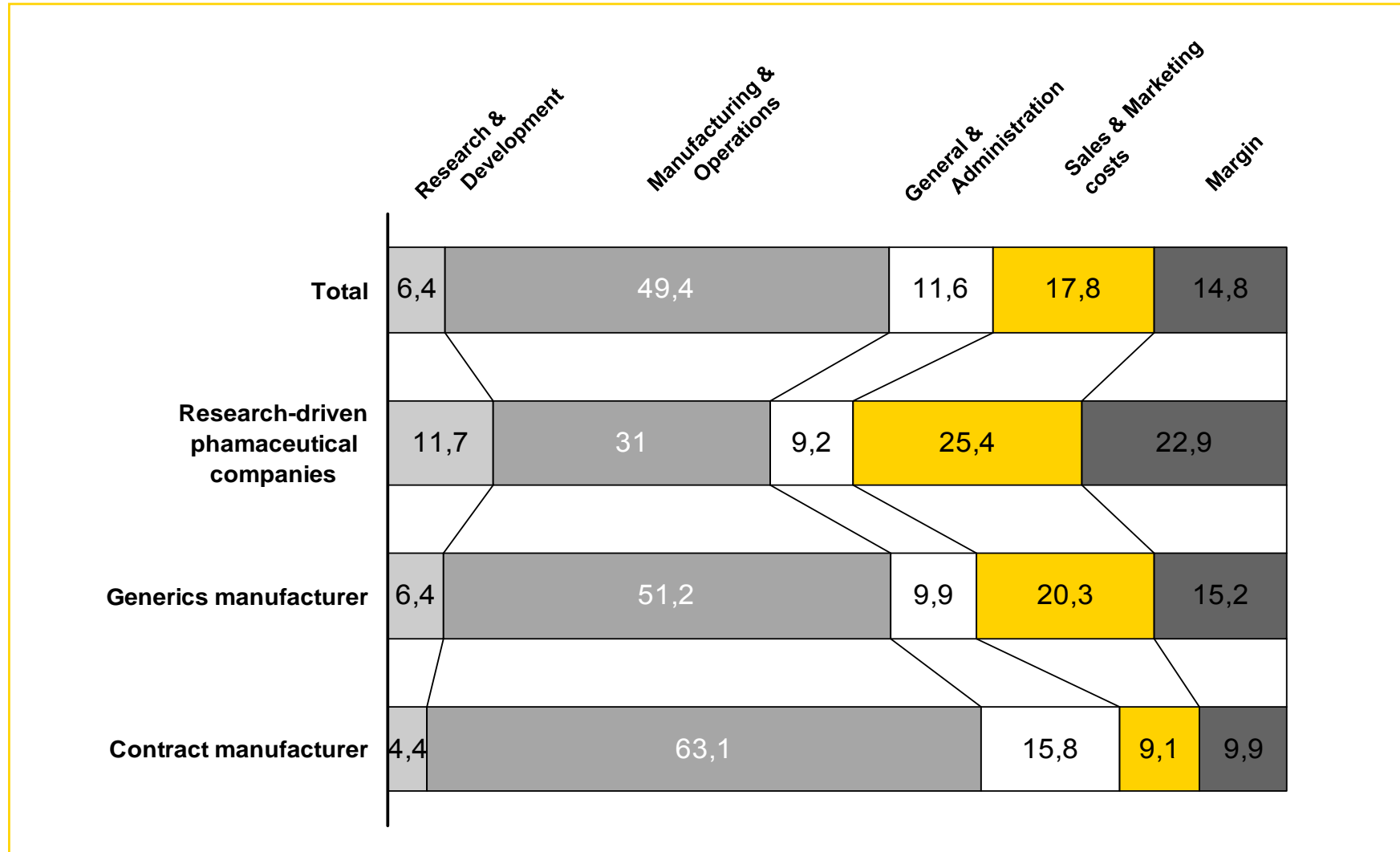
Major pharmaceutical companies are launching multi-year cost reduction programs, implementing global operating models and standardizing business processes to increase productivity

| | Revenue (in MM) | Annual Savings Estimate (in MM) & % of Revenue | Program Term | Key Initiatives |
|---|-----------------------|--|--------------|---|
|  | \$48,613 | \$4,500 - \$5,000 9.3 – 10.3% | 2005 – 2008 | Headcount reduction (10,000, 10%) Plant rationalization (48 of the 93 facilities) Procurement and supply chain cost reductions Simplify R&D and reorganize Pharma business |
|  | \$24,198 | \$3,500 - \$4,000 14.5 – 16.5 % | 2006 – 2010 | Headcount reduction (7,200, 12%) Plant rationalization (5 of the 31 facilities) |
|  | \$38,072 | \$1,600 4.2% | 2008 – 2010 | Headcount reduction (2,500, 3%) Global procurement and sourcing Plant rationalization and LEAN initiatives |
|  | \$61,095 | \$1,300 - 1,600 2.1 – 2.6% | 2007 – 2008 | Headcount reduction (4,800, 4%) Consolidate Pharma operations Integrate business model for Cordis franchise |
|  | \$19,348 | \$1,600 8.3% | 2008 – 2010 | Headcount reduction (4,300, 10%) Plant rationalization (27 facilities) |
|  | \$44,946 ¹ | \$1,400 3.1% | 2007 – 2010 | Improve the selling model Streamline global manufacturing Enhance R&D efficiency |
|  | \$29,559 | \$1,400 4.7% | 2007 - 2010 | Headcount reduction (7,600, 12%) Strategic procurement Simplify business support functions |

These initiatives alone target more than \$15 billion in annual cost reduction and 36,000 jobs by 2010

Pharma's cost structure

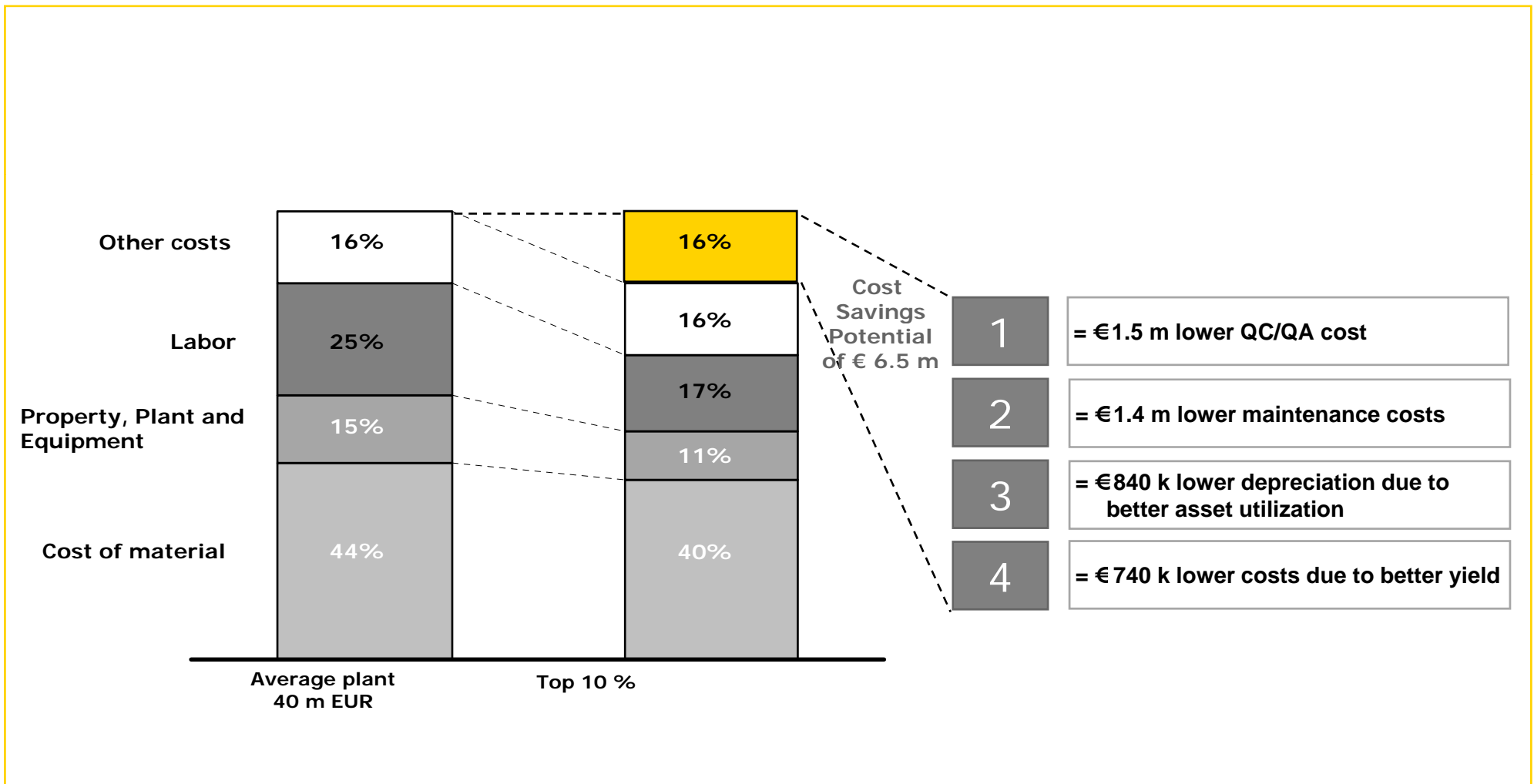
typical pharmaceutical mid-sized plant



Source: University of St. Gallen, International Benchmarking Study, Operational Excellence in the Pharmaceutical Study ,p. 6

Opportunity for significant savings

“Asset utilization, Maintenance efficiency, OPEX”



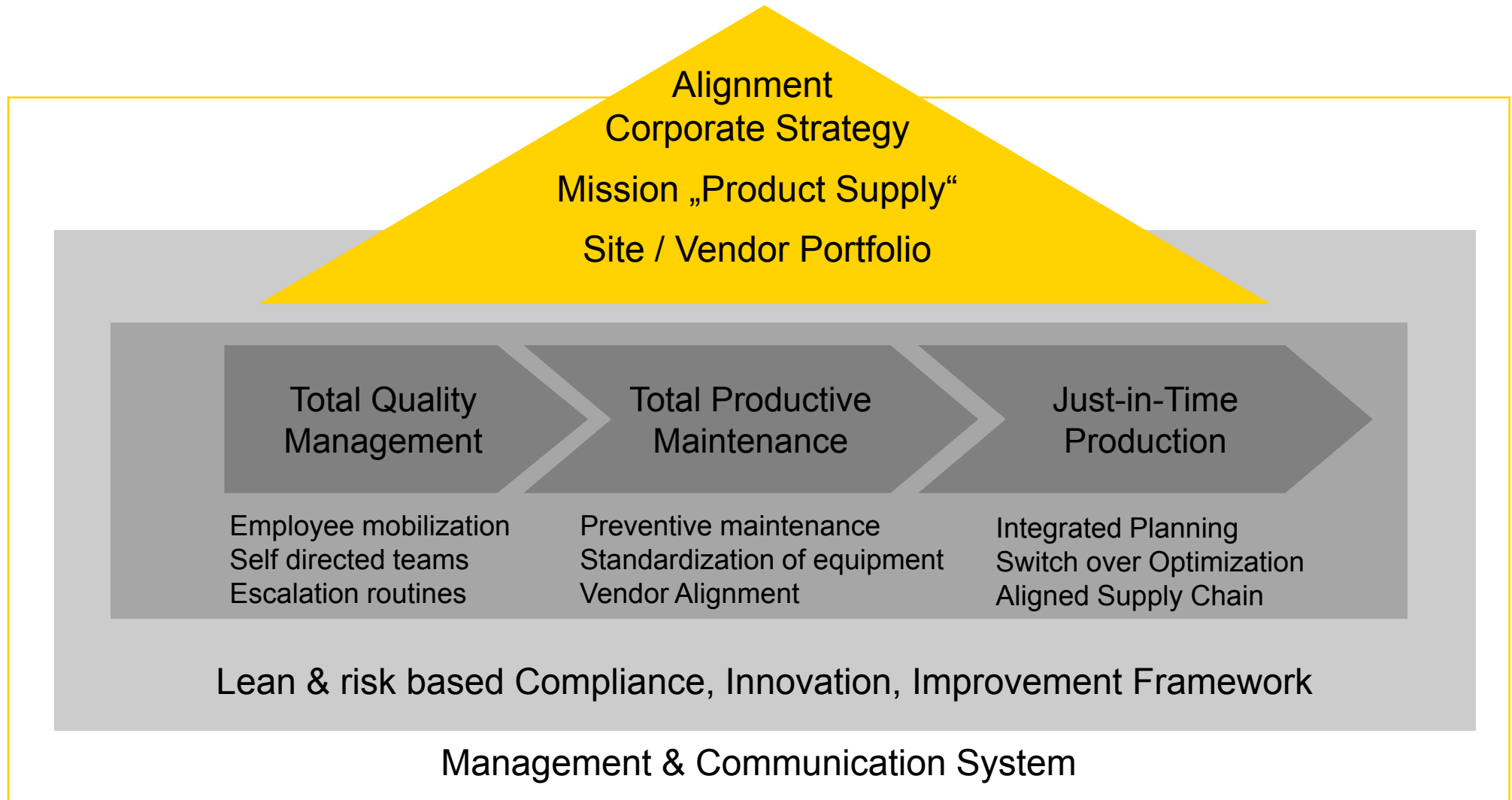
Source: University of St. Gallen, International Benchmarking Study, Operational Excellence in the Pharmaceutical Study ,p. 6

Operational Excellence?!

... Whenever a pharmaceutical company changes any part of its manufacturing processes, new approvals and extensive documentation are required. So it often makes more sense to throw batches away than try to figure out what went wrong...

Source: Manufacturing Business Technology Volume 24, Issue 2, special Report 02.2006

Operational Excellence



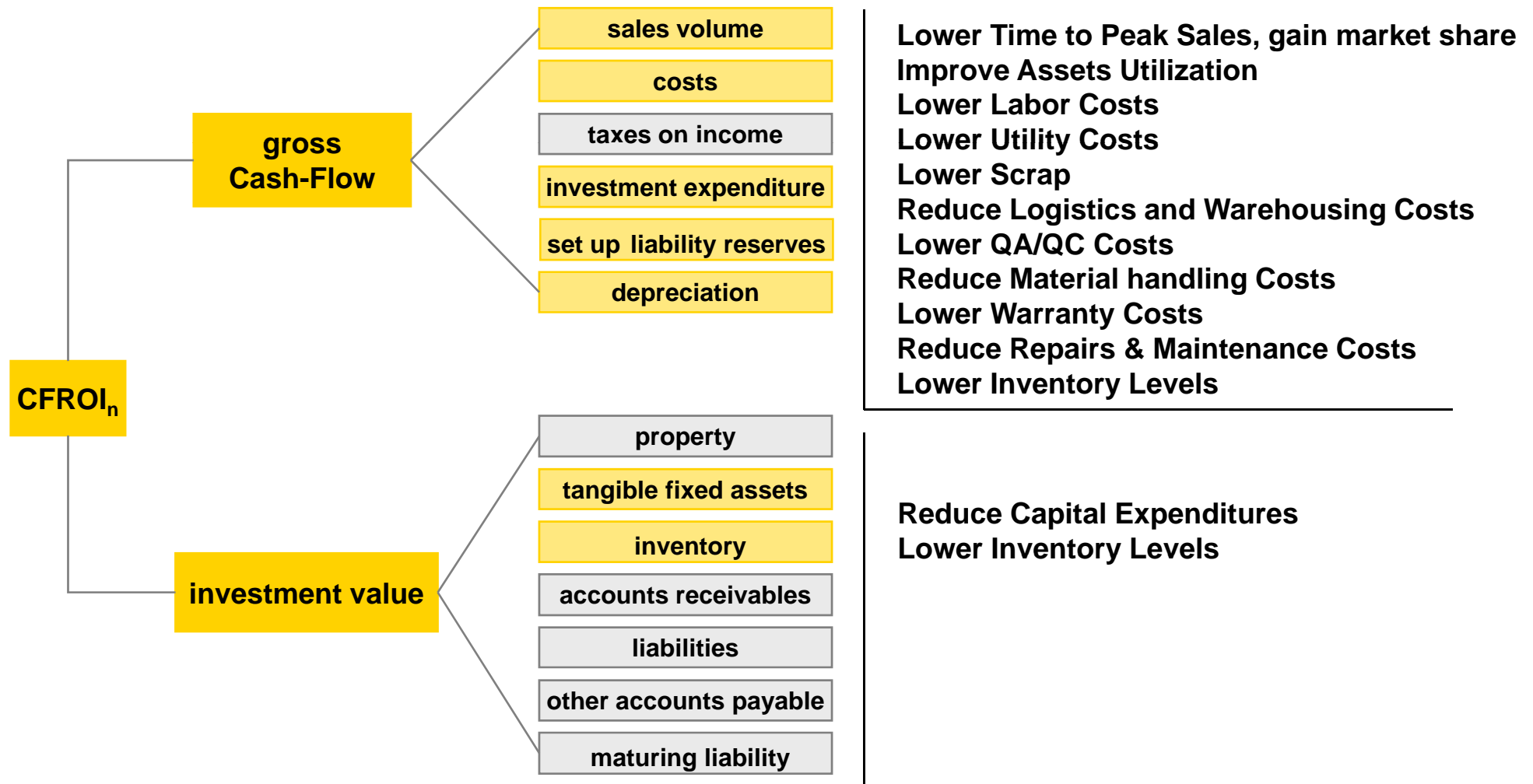
Source: adapt from University of St. Gallen, International Benchmarking Study, Operational Excellence in the Pharmaceutical Study ,p. 6-8

FDA Response

Final report: „pharmaceutical cGMP for the 21st century – a risk based approach“, September 2004

- **Risk Based Approach** “as a driving principle for current good manufacturing practices (cGMP) initiative”
- “..as **pharmaceutical manufacturing** evolves from an art to a science and engineering based activity, ... **improve the efficiency and effectiveness** of both manufacturing and **regulatory decision-making**“
- “**scientific framework** to find ways of **mitigating risk** while **facilitating continuous improvement** and **innovation** in pharmaceutical manufacturing is a key public health objective. ... will **encourage the implementation of new technologies**, such as **process analytical technology (PAT)**, and facilitate continuous manufacturing improvements **via implementation of an effective quality system.**”

Measures & Benefits



CFROI: Cash Flow Return on Investment

Drug Safety versus trustful Cost Take Out counterfeiting in the supply chain, diary (1/2)

14 Apr 2008 - [Heparin death tally worsens; FDA issues device warning](#)

The number of people whose deaths are associated with an allergic reaction to heparin has shot up as the US Food and Drug Administration (FDA) has updated ...

30 Mar 2008 - [China watchdog responds to heparin scare; AZ now affected](#)

China's drug regulatory authority is finally ... becoming a global heparin contamination, sparked ... has also urged heparin producers to source their raw heparin from registered suppliers only ...

25 Mar 2008 - [Heparin recall widens in US](#)

The heparin recall has widened after a lot of heparin sodium USP active pharmaceutical ingredient (API) produced by Scientific Protein Laboratories (SPL) was found ...

25 Mar 2008 - [Customer recalls product using Cambrex API](#)

Cambrex Corp, the US-based ... Associated Press inferred that the ingredient involved might be heparin. This was ... on 21 March. But heparin does not appear on ...

20 Mar 2008 - [FDA identifies heparin contaminant; confirms China link](#)

The US Food and Drug Administration (FDA) has now identified the contaminant found in samples of Baxter's recalled heparin and confirmed that it is indeed ...

18 Mar 2008 - [FDA makes progress in plans for China presence](#)

The US Food and Drug Administration (FDA ... scare over Baxter's blood-thinning drug heparin. Production of ... was suspended after heparin was linked to four ...

Source: <http://www.in-pharmatechnologist.com>

Drug Safety versus trustful Cost Take Out counterfeiting in the supply chain, diary (2/2)

11 Mar 2008 - [China-made heparin scare spreads beyond US](#)

The made-in-China heparin scare has now spread beyond the US, with Germany and Japan both recalling the drug. German manufacturer Rotexmedica was ...

07 Mar 2008 - [Heparin contamination emerges after FDA China investigation](#)

A US Food and Drug Administration (FDA) investigation into the recent Baxter heparin scare has uncovered a contaminant in the product that was sourcing the active pharmaceutical ...

04 Mar 2008 - [FDA 'concerned' after inspection of China heparin plant](#)

The US Food and Drug Administration (FDA ... the active pharmaceutical ingredient (API) for Baxter's heparin - ... in association with Baxter's drug products ...

28 Feb 2008 - [China tells drug importers to take responsibility for quality](#)

China's drug watchdog has revealed its ... case with the Chinese supplier of the API for Baxter's heparin that ... by one of Baxter's subsidiaries in ...

20 Feb 2008 - [FDA mix-up caused failure to inspect Baxter's Chinese supplier](#)

More details have emerged over the US Food and Drug Administration's (FDA's) failure to vet the Chinese manufacturing plant implicated in the Baxter ...

14 Feb 2008 - [China plant implicated in heparin scare "never" inspected by FDA](#)

Questions are hanging over the role of a Chinese manufacturing facility in the Baxter heparin scare after it has emerged that the US Food and Drug Administration (FDA) ...

Source: <http://www.in-pharmatechnologist.com>

Drug Safety versus trustful Cost Take Out

Federal Agency Takes heparin from the market

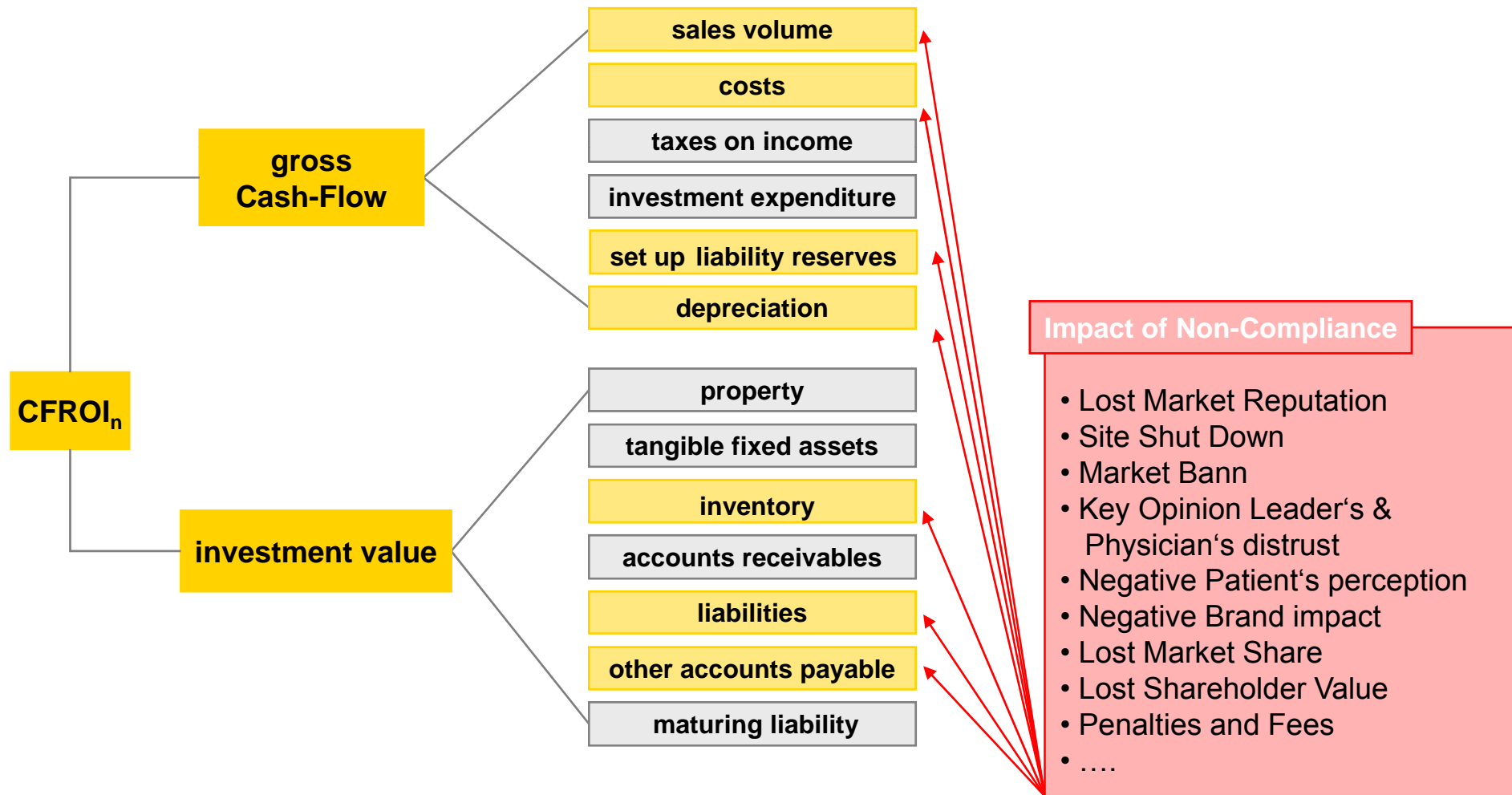
Die **deutsche Arzneimittelbehörde hat potentiell gefährliches Heparin vom Markt** genommen. Der **Blutverdünner war offenbar mit Substanzen aus China verunreinigt** - und **kann schwere allergische Reaktionen** auslösen. Der Skandal könnte internationale Dimensionen annehmen.

...Möglicherweise gibt es einen Zusammenhang zwischen dem deutschen Heparin-Rückruf und einem aktuellen Skandal mit dem gleichen Medikament in den USA. Dort sind **nach neusten Zahlen der US-Arzneimittelbehörde FDA 19 Menschen nach der Verabreichung der Arznei gestorben und 785 weitere ernsthaft erkrankt**. ... [Die FDA] forderte nun dennoch alle US-Hersteller des Medikaments auf, ihre Heparin-Vorräte auf Verunreinigungen zu prüfen....

... Die Behörde schließt nicht aus, dass es sich bei der Kontamination um **eine bewusste Medikamentenfälschung handelt**. Die gefährliche Substanz sei ein Molekül, das Heparin täuschend ähnlich sehe und bei den Standard-Tests nicht auffalle....

Source: Spiegel-Online, 7. March 2008, <http://www.spiegel.de/wissenschaft/mensch/0,1518,540094,00.html>, original title: "Bundesbehörde nimmt Heparin vom Markt"

Measures & Benefits



CFROI: Cash Flow Return on Investment

Wrap Up & Outlook

... it is about our health, safety & trust

- ▶ **Need to align & commit for “true innovation”**
 - ▶ Therapeutic approaches, Medicines & Health Care Systems
 - ▶ Value Chain & Risk Management

- ▶ **Cost Efficiency gets center stage**
 - ▶ Operational Excellence in Manufacturing, Supply Chain & Sales
 - ▶ Combat Counterfeiting

- ▶ **Ensure Corporate Responsibility**
 - ▶ Shareholder Value & Corporate Social Responsibility
 - ▶ Responsible Care in Sales & Marketing

- ▶ **New Business Models**
 - ▶ Changing Markets: De-Regulation of Market Access
 - ▶ New Value Networks, innovative & cost effective?

...it's never boring



Teamwork

personal responsibility

Multidisciplinary

Teams

Documentation

fun

international

Ernst & Young network

Direct

Training on

Client Contact

the job

Dealing with numbers

→ always new challenges

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