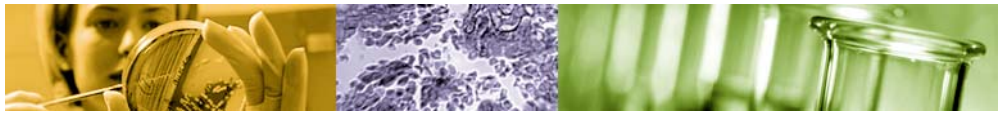

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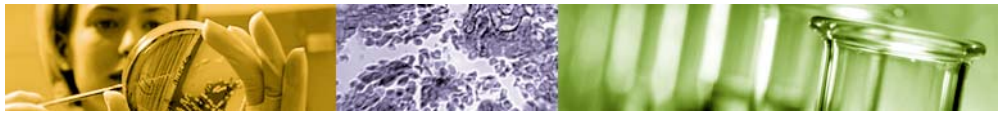
Innovation or Stagnation - Perspective of Pharmaceutical Industry

AGAH Annual Meeting 2006
21 February 2006

Dr. Siegfried Throm
Director Research, Development, Innovation
German Association of Research-Based Pharmaceutical Companies (VFA)



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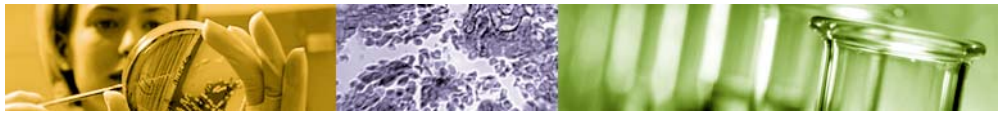
Bright side of R&D - Innovation

a lot of innovation enabling technologies

- Ultra high throughput screening
- combinatorial chemistry
- pharmacogenomics
- pharmacogenetics
- proteomics
- bioinformatics
- microarrays
- in-silico techniques
- system biology (artificial liver etc.)
- nanobiotechnology



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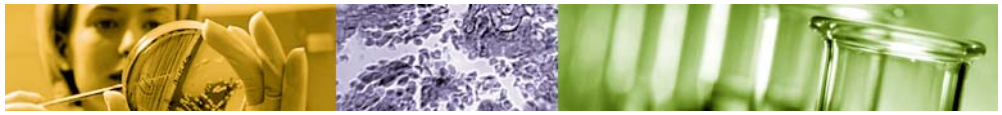
Bright side of R&D - Innovation

New or upcoming therapies – first registration

• Recombinant products	1982: human insulin
• Monoclonal Antibodies	1986: Muromonab
• Nanobiotech products	1994: liposomal surfactant
• Tissue engineering	1996: cartilage
• Antisense products	1999: Fomivirsen
• Pharmacogenetically enhanced products	2000: Trastuzumab
• Genomics-derived products	2001: Imatinib
• Gene therapy products	no registration, except 2003 in China
• Cell therapy products	medical devices: yes; no registration
• Viral cancer treatment	no registration, except 2005 in China
• RNAi products	no registration



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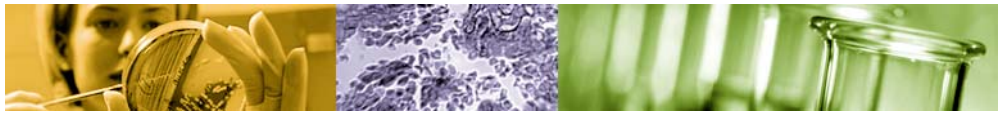
Bright side of R&D - Innovation

Innovation in treatment of many diseases

- heart failure
- cardiovascular diseases (drug eluting stents, statins, sartans)
- hepatitis C
- HIV/Aids
- breast, lung and colon cancer
- multiple sclerosis
- osteoporosis
- vaccines
- some orphan diseases, e.g. pulmonary hypertension



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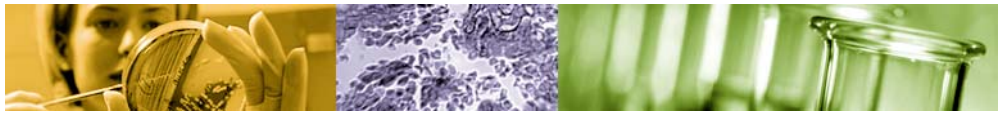
Bright side of R&D - Innovation

More than 320 biotech products in development
Worldwide: more than 1200 pharmaceutical products

- Big unmet medical need (e.g. Alzheimer‘s disease, cancer, depression, stroke, schizophrenia, new or re-emerging infectious diseases, e.g. HIV, SARS, TB, malaria, bird flu)

- Demographic development: prolongation of life expectancy by 3 months per year



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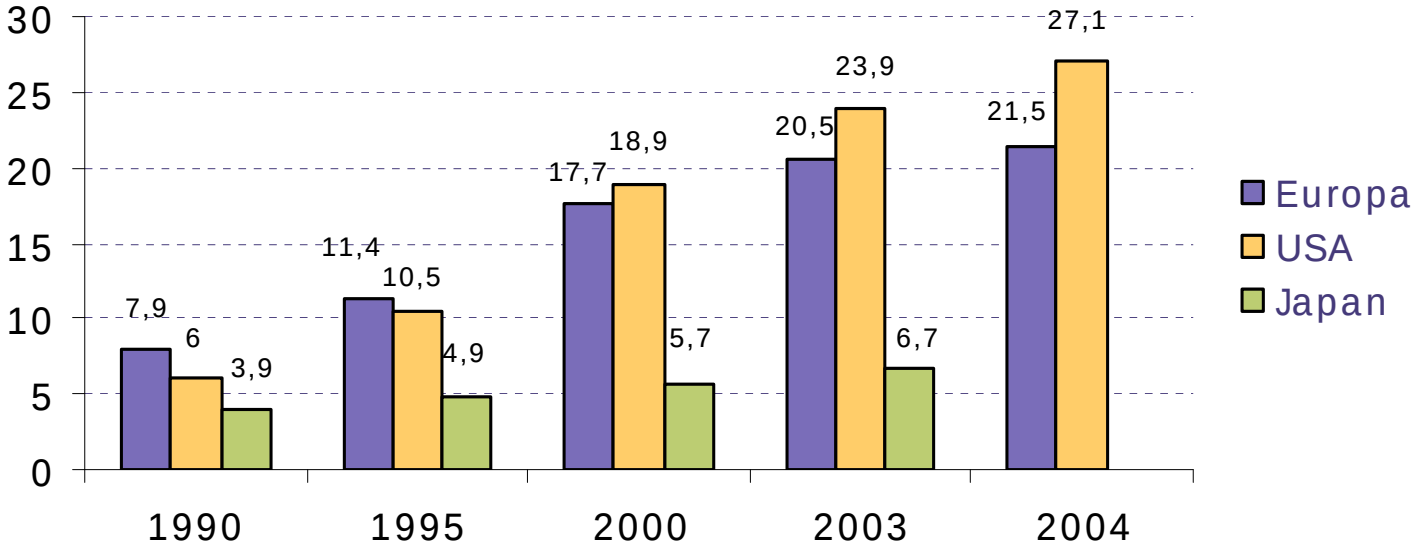
Dark side of R&D - Stagnation

Sharply rising total R&D ecpenditure

Pharmaceutical R&D Expenditure in Europe, USA and Japan
(€ Million, 1990-2004)



Quelle: EFPIA member associations; PhRMA, JPMA

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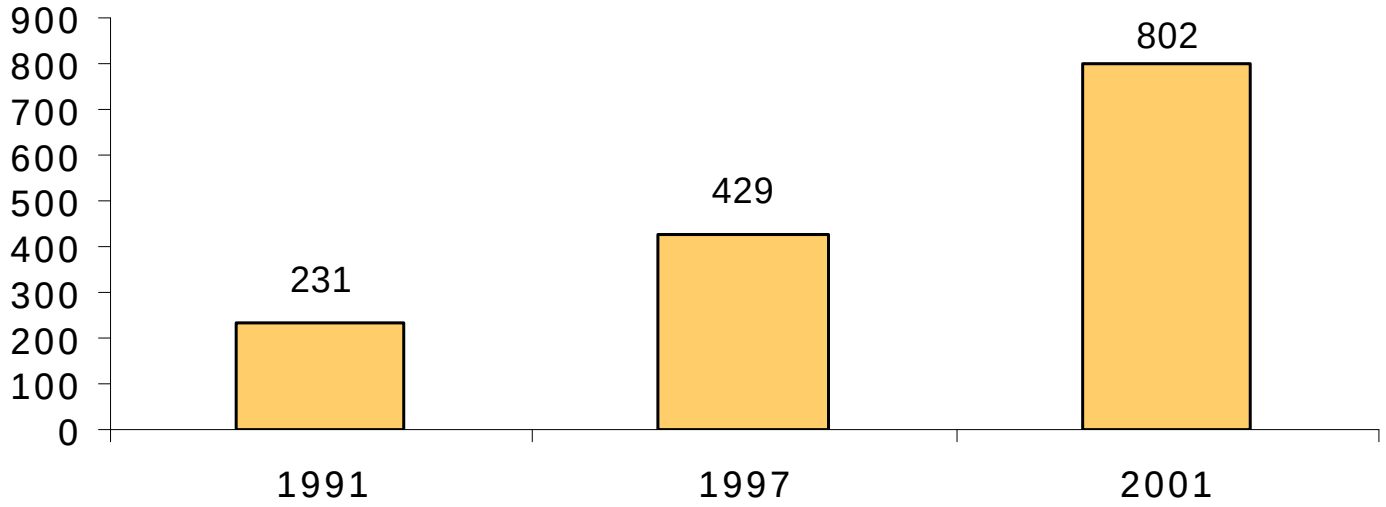
Dark side of R&D - Stagnation

Sharply rising costs for a NME

Estimated full cost of bringing a new chemical or biological entity to market (million US-$)



Quelle: VFA Statistics, 2005, DiMasi/Tufts University

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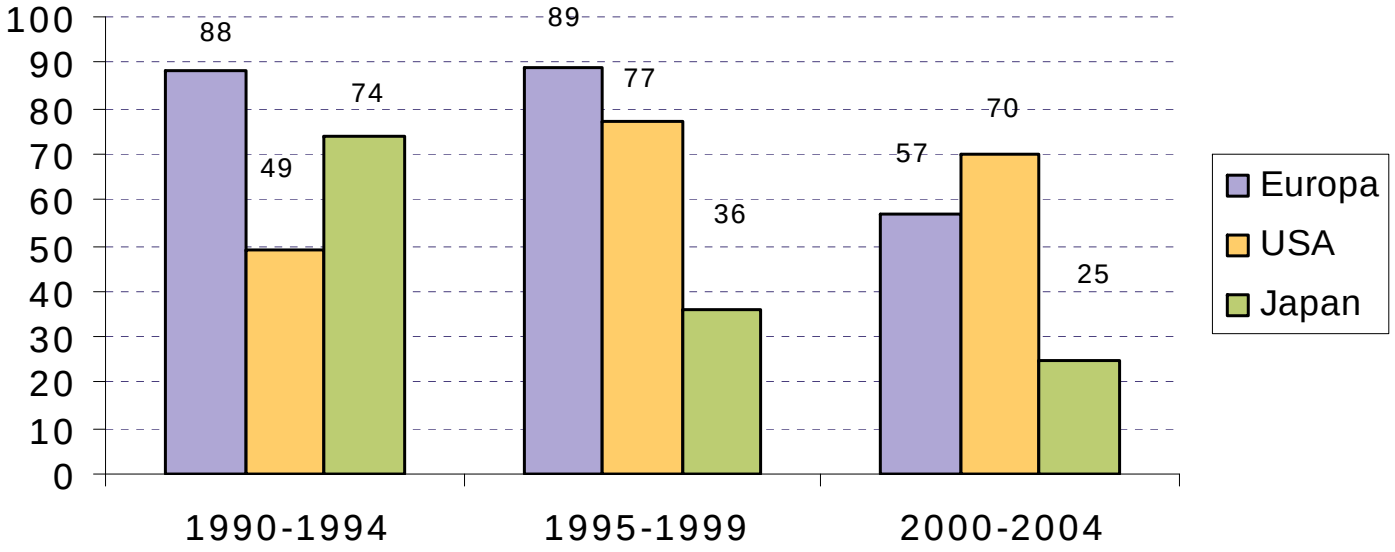
Dark side of R&D - Stagnation

Stagnation/decline of output

New chemical or biological entities (1990-2004)



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Dark side of R&D - Stagnation

Worsening of attrition rate:

1999: 4 out of 5 products reaching clinical development fail; 50 % in Phase III

2002: 9 out of 10 products reaching clinical development fail

„Low hanging fruits have been picked.“

For acute diseases excellent products available;
Problematic areas: nervous system, cancer, cardiovascular

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Dark side of R&D - Stagnation

- Many more potential targets – but are they valuable?
- Reduction of total pipelines by mergers and acquisitions
- Higher regulatory requirements: longer development times
- More hurdles: Cost-effectiveness required by payers; head to head comparisons/ superiority wanted; environmental risk assessments

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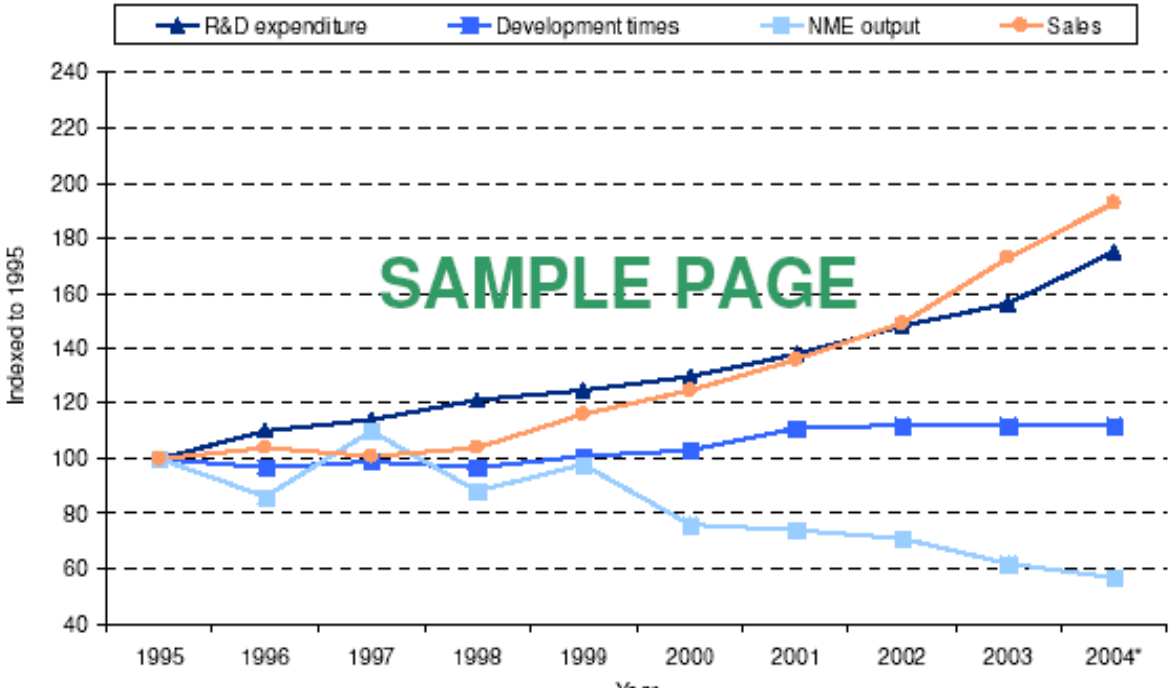
Dark side of R&D - Stagnation

Global R&D expenditure, development times, global pharmaceutical sales and new molecular entity output 1995-2004

CMR International
Perspective•Insight•Opinion



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The way forward

Aims of the FDA initiative critical path: to make the development of new medicines faster and more efficient

Safety:

Problem: Over the last decade liver problems have cost us 2 bn $ (Pfizer)

- better and earlier prediction in development process
- raising success rate by 10 % before the start of clinical trials would save 100 Mio $ development costs

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The way forward

Safety:

- better prediction for human immune response
- new techniques for the evaluation of liver toxicity
- use of pharmacogenetics, proteomics, toxicogenomics
- computer-aided predictive toxicology (up to 50 % reduction of development costs possible)
- new predictive safety models based on FDA-data
- non-clinical methods for assessing heart rhythm abnormalities, QTc-internal prolongations

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The way forward

Efficacy:

Problem: 25 % of the clinical projects fail due to lack of efficacy

- building a knowledge base for future paediatric trials by analysing the available paediatric trials
- identifying new biomarkers and surrogate parameters by screening available data
- promoting imaging technologies

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The way forward

Efficacy:

- amending the development process by model-based drug development
- accepting patient driven outcome measures
- using proteomics and pharmacogenomics for finding new biomarkers to target responders, monitor clinical response and assess drug effectiveness

Quality:

- amendment of manufacturing methods:
  more consistent and less costly production of high-quality

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The way forward

Quality:

- finding additional characterisation procedures and standards for “advanced therapies” (cell therapy, gene transfer, tissue engineering products)
- developing sound scientific standards such as Process Analytical Technologies (PAT)
- remove obstacles to adopting modern science-based characterisation/manufacturing methods

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The way forward

European Platform on Innovative Medicines

Objectives:

- remove bottlenecks hampering the efficiency of the development of new medicines
- strengthen research to increase competitiveness of the European pharma/biotech industry
- inclusion of all relevant stakeholders:
  EMEA, national regulatory agencies, patient organisations, health care providers, big pharma, SMEs, academia, member states

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The way forward

Innovative Medicines Initiative Strategic Research Agenda

Four cornerstones:

- Safety (predictive toxicology; risk assessment)
- Efficacy (predictive pharmacology; idenitfication and validation of biomarkers; patient recruitment)
- Knowledge management (management of huge amount of information generated by new technologies)
- Education and Training: (closing gaps in expertise; achieving excellence in EU; biomedical education)

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The way forward

Innovative Medicines Initiative Strategic Research Agenda – Main Recommendations

Safety

Aim: Improve predictability of toxicological observations

- create a European Centre of Drug Safety to identify and co-ordinate research needs in safety sciences
- establish a framework to develop biomarkers
- develop in-silico methods for predicting conventional and recently recognised types of toxicity
- develop toxicogenomics, toxicoproteomics and metabonomics

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The way forward

Innovative Medicines Initiative Strategic Research Agenda – Main Recommendations

Efficacy

Aim: Improve clinical performance and early access

- stimulate translational medicine
- create disease-specific European Imaging Networks for the establishment of standards, validation of biomarkers, development of regional centres of excellence
- develop partnerships with regulators: design innovative clinical trials and analyses, accept biomarkers; promote data sharing and joint consideration of ethical issues

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The way forward

Innovative Medicines Initiative Strategic Research Agenda – Main Recommendations

Knowledge Management

Aim: Manage and organise data to create knowledge to predict benefit and risk

- develop enhanced knowledge representation models and data exchange standards
- build core reference database of validated experimental data extracted from literature
- design standards/build expert tool for local databases in a secured environment

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The way forward

nnovative Medicines Initiative Strategic Research
genda – Main Recommendations

ducation and Training

m: Support interdisciplinary education essential to the
oscience sector

create a European Medicines Research Academy for education and
training

Map of existing activities in E&T; identify European centres of
excellence; develop programmes for critical areas

evaluate options to foster mobility between academia and industry

440 Mio. € each year for a period of 7 years required to implement

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Conclusions

- The research and development of innovative medicines and therapies is continuously becoming more difficult, time-consuming and costly; the attrition rate is rising, the output is declining
- Therefore the initiatives in the US and EU which aim at making the development process more efficient are highly welcomed.
- It is not only in our interest but especially in the interest of the patients that these initiatives will be successful.
- With so many new promising technologies and therapies the chances for a turnaround should be good.

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„Ich kann freilich nicht sagen, ob es besser wird, wenn es anders wird, aber soviel kann ich sagen, es muss anders werden, wenn es gut werden soll.“ (Georg Lichtenberg, Naturwissenschaftler und Philosoph)

[I can‘t say whether it will become better if it will change, but I can definitely say that it must change if it shall come to a good end.]