efpia

European Federation of Pharmaceutical Industries and Associations

Revising the Pharmaceutical Landscape in the EU

The Industry Perspective

Dr. Christine-Lise Julou

June 2008

Revising the pharmaceutical landscape in Europe

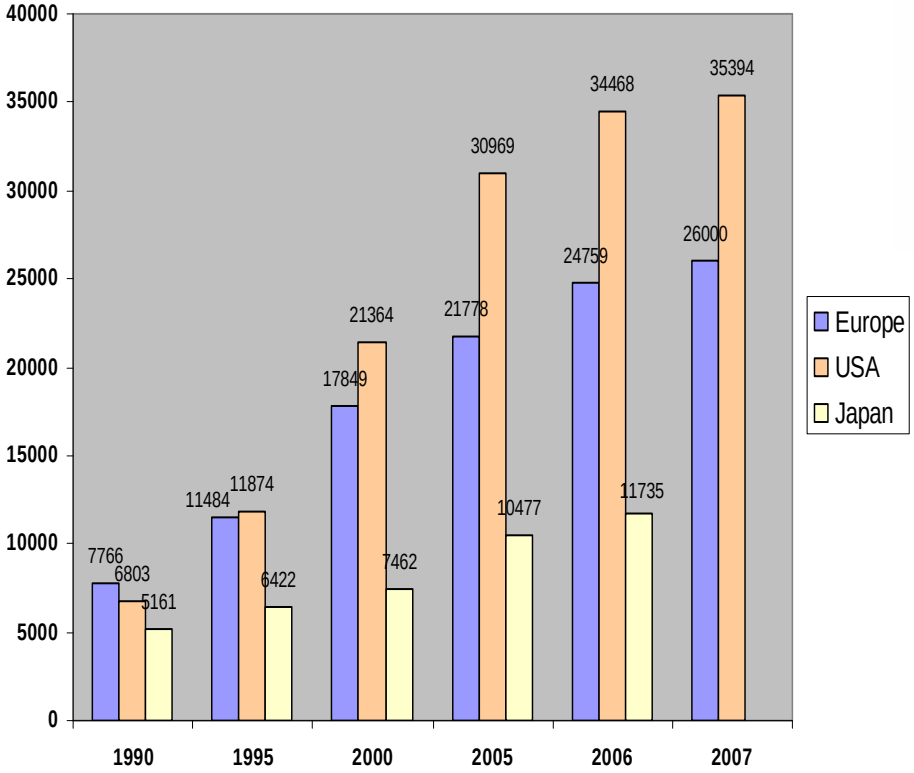
- Preamble
- New Legislation
- Other regulatory initiatives including harmonisation initiatives (harmonisation)
- Considerations in relation to other legislation

EFPIA’s mission and priorities

- Improving the competitiveness of the pharmaceutical industry in Europe by setting up a regulatory and political environment, which above all stimulates R&D and rewards innovation.

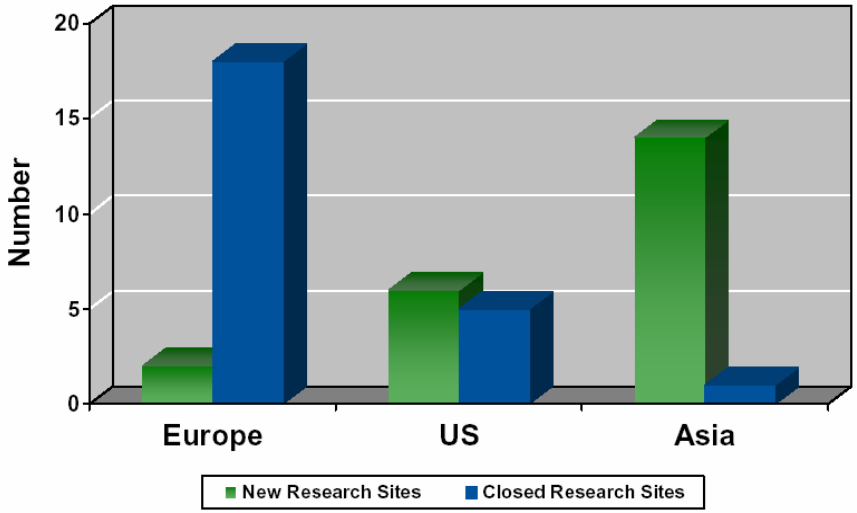
  This will guarantee industry’s continuous quest for better therapies and enable it to meet the growing healthcare expectations of today’s and tomorrow’s patients.

Pharmaceutical R&D expenditure 1990-2007 (million national currency units*)



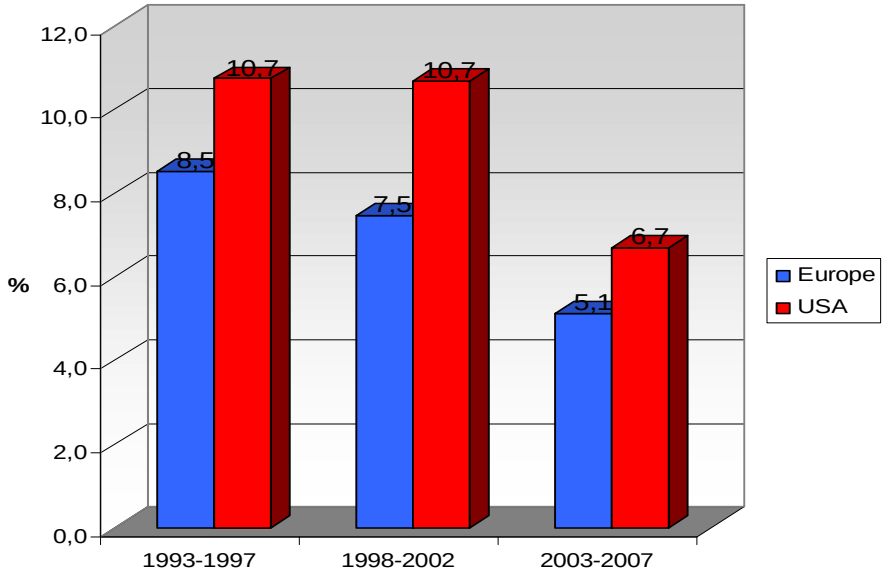
* National currency units: Europe: € million; USA: $ million; Japan: ¥ million x 100
Data 2007: estimate EFPIA & P*h*RMA
Source: EFPIA member associations, P*h*RMA, JPMA

Changes in Research Sites (2001 – 2006)

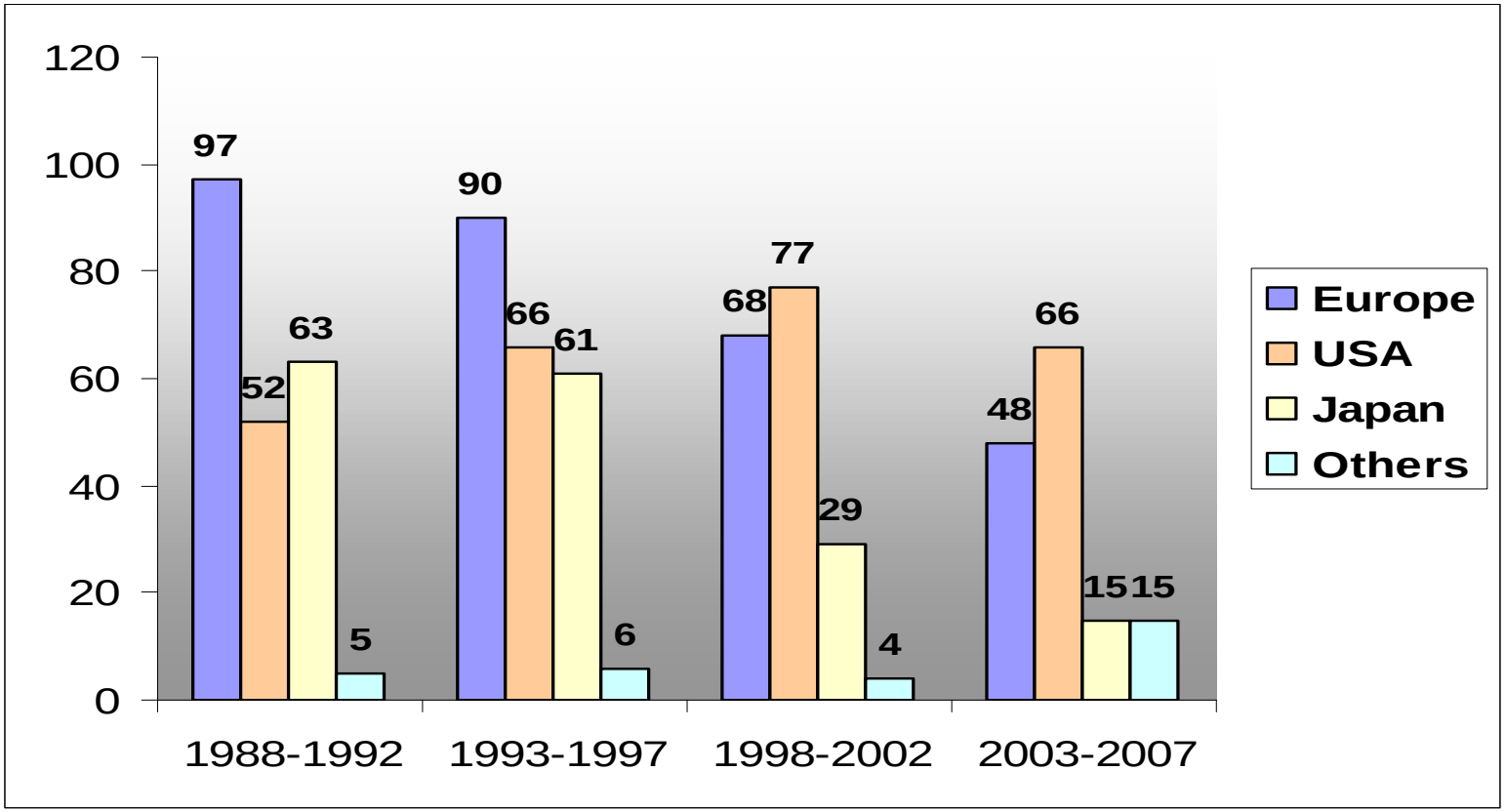


Changes in research sites: data relate to 22 global companies –
Source: IMI (EFPIA Research Directors Group & IFPMA)

R&D expenditure – Annual growth rate (%)

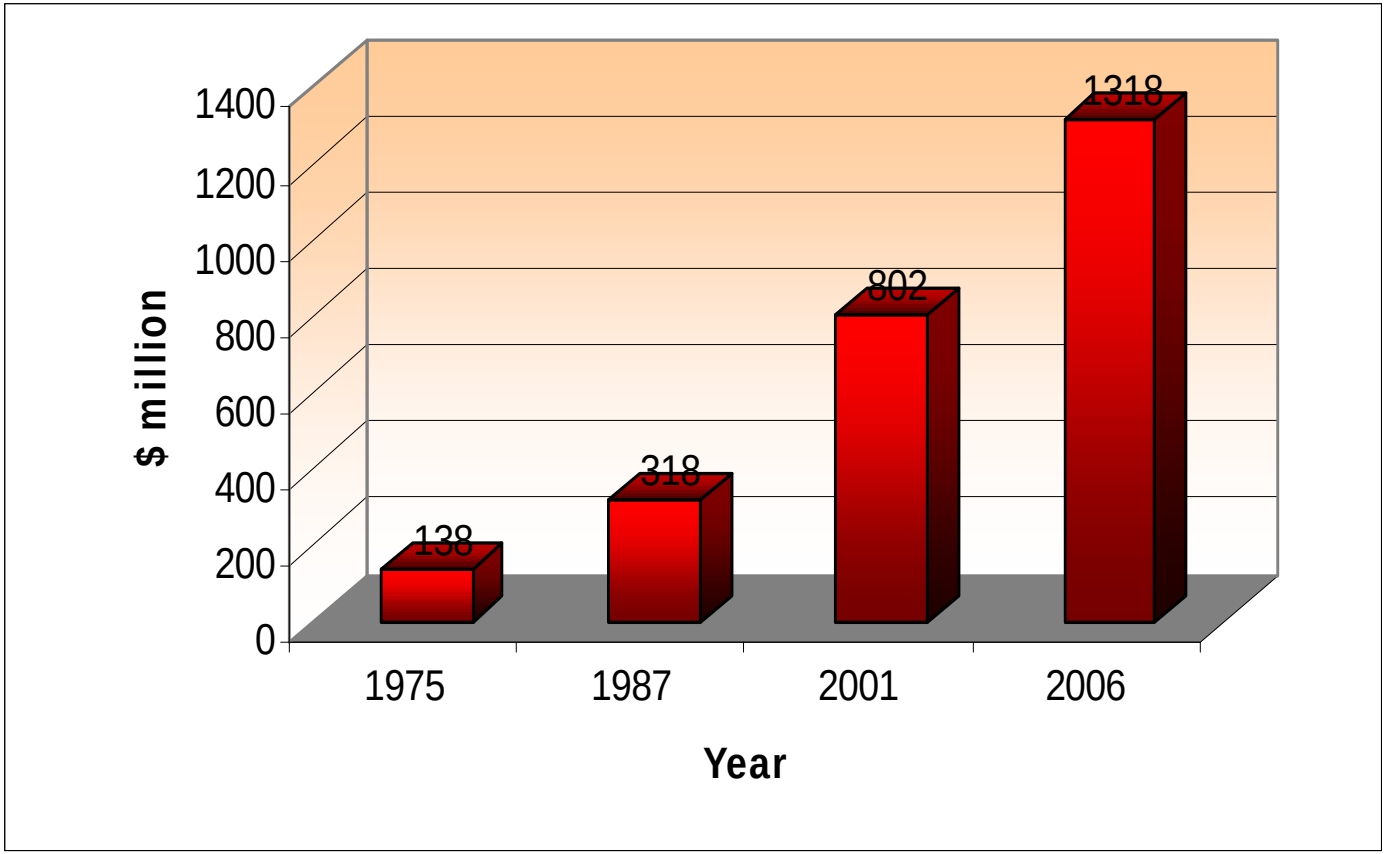


New Molecular Entities 1988-2007



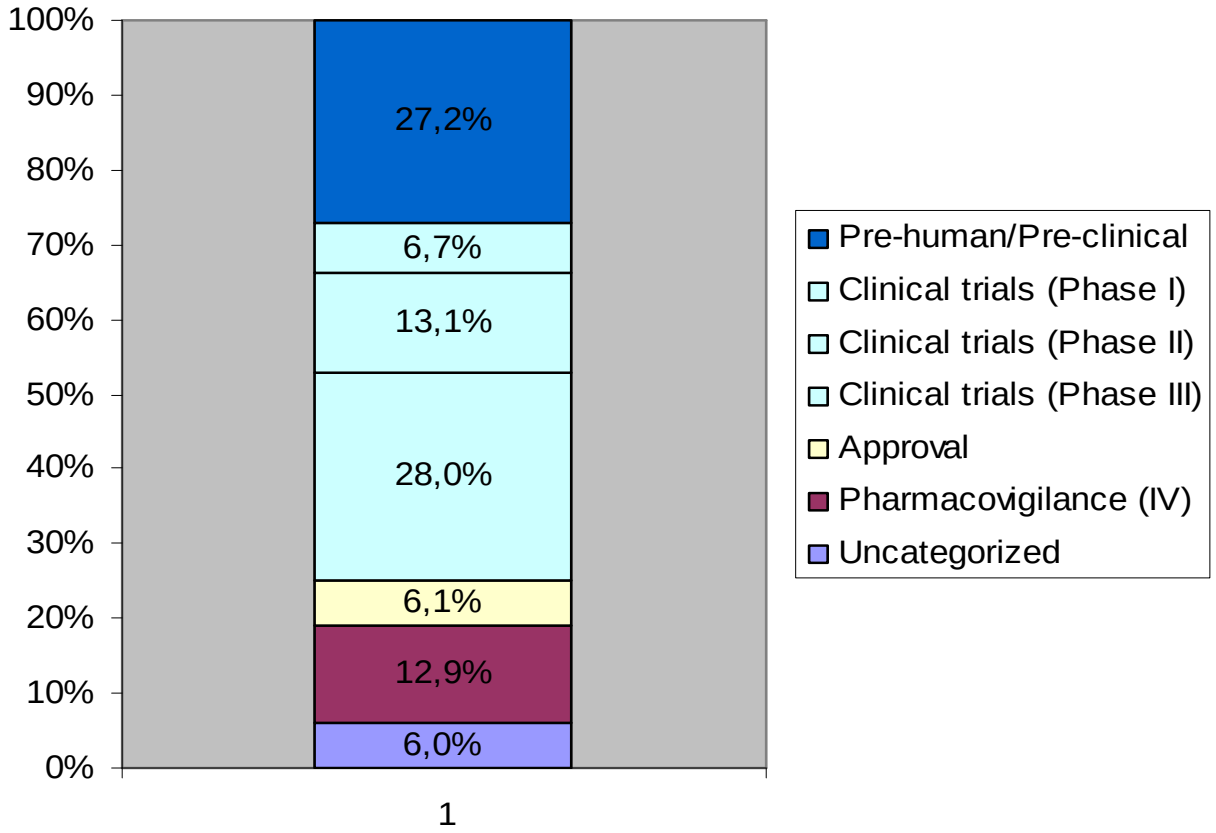
Source: SCRIP - EFPIA calculations (according to nationality of mother company)

Estimated full cost of bringing a new chemical or biological entity to market ($ million – year 2005 $)



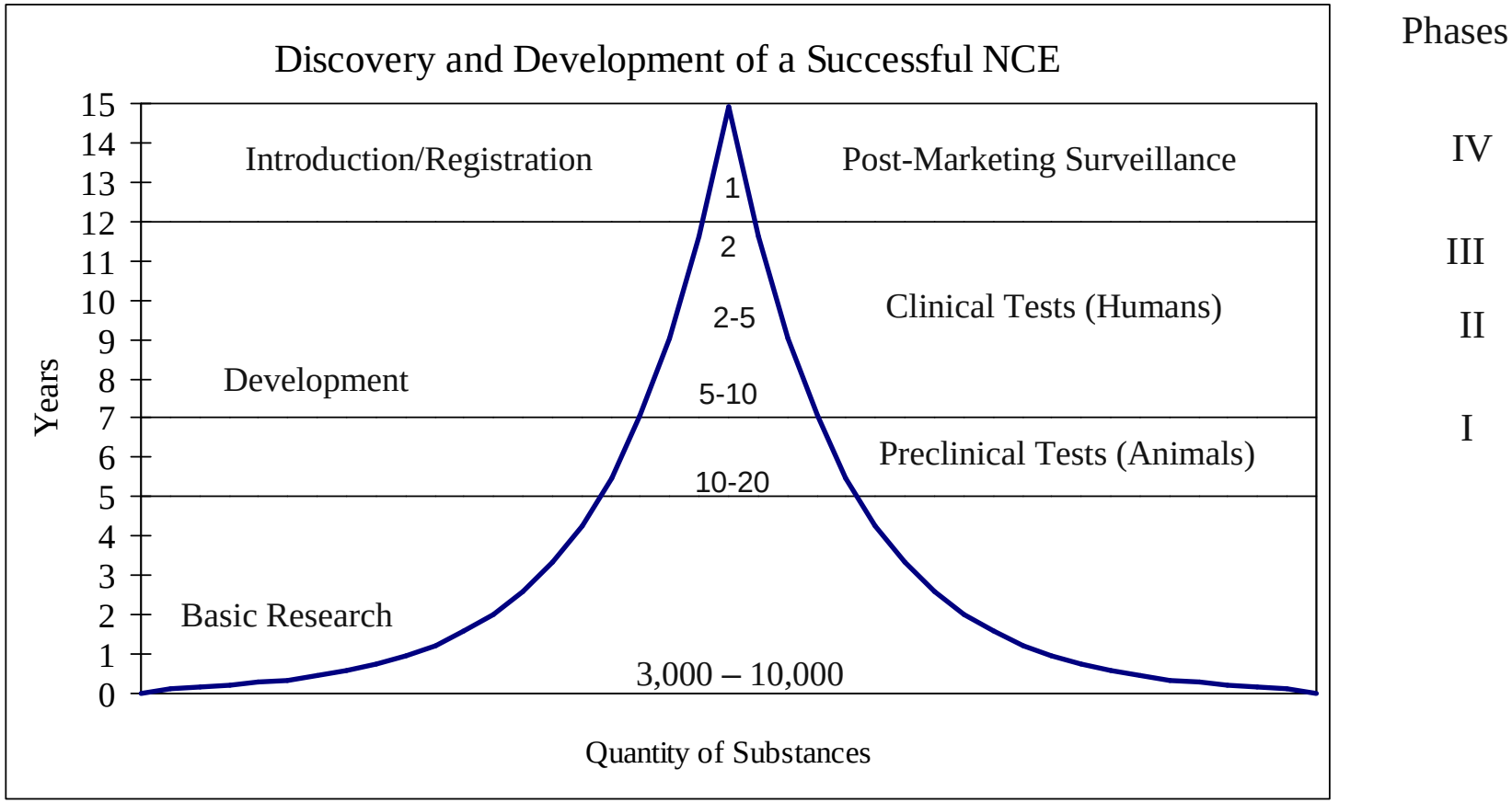
Source: J.A. Di Masi and H.G. Grabowski, 'The Cost of Biopharmaceutical R&D: Is biotech Different? Managerial and Decision Economics 28 (2007): 469-479

Allocation of R&D investments by function



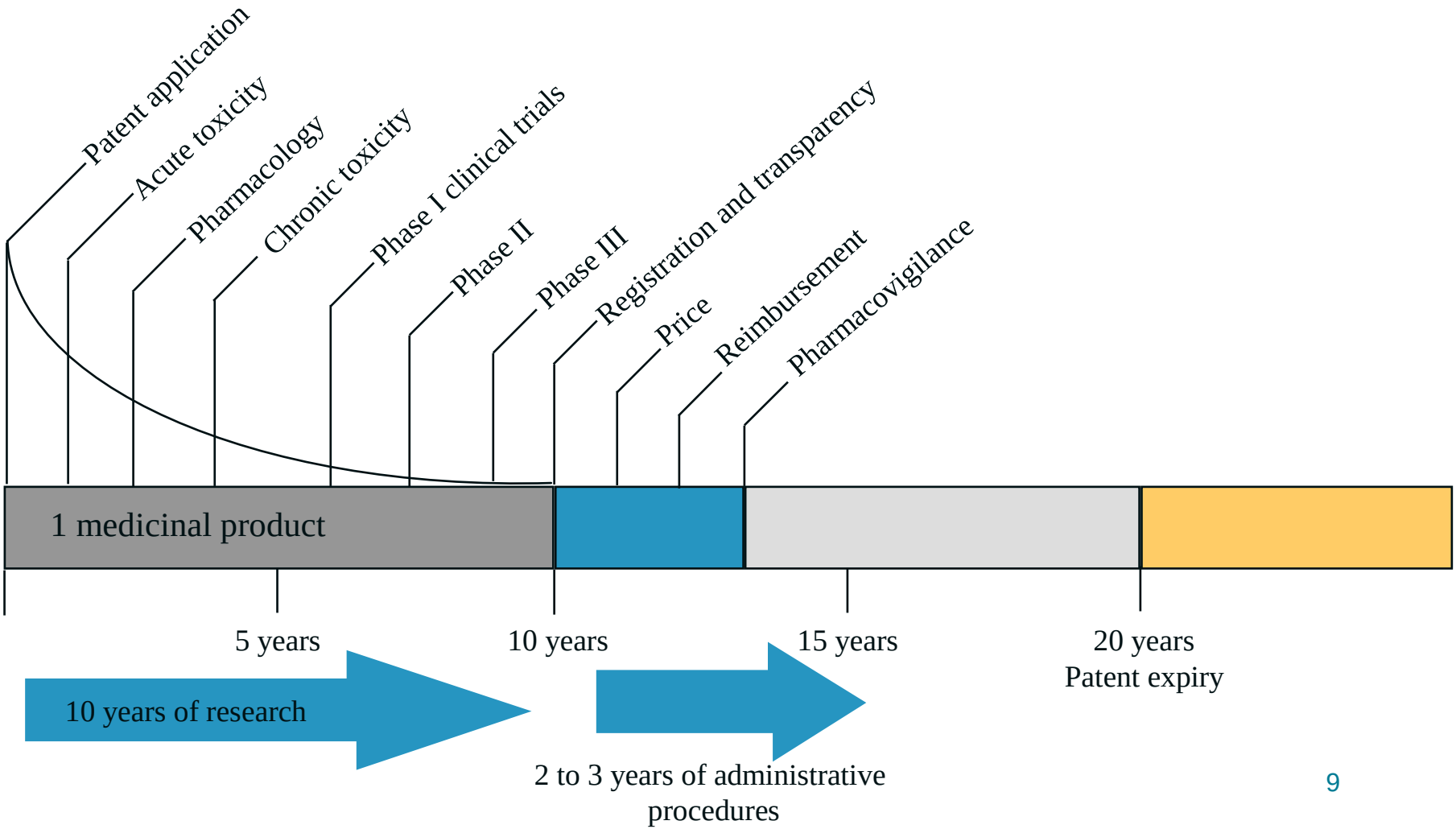
Source: P*h*RMA, Annual Membership Survey 2008 (percentages calculated from 2006 data)

R&D: Scientific Risk



Source: Based on PhRMA analysis, updated for data per Tufts Center for the Study of Drug Development (CSDD) database.

ROUTE OF A NEW SUBSTANCE FROM DISCOVERY TO PATIENT'S ACCESS



Better Regulation Initiative and Revision of the Legislation

- Regulatory framework on changes to medicinal products
- Legislative proposals to strengthen and rationalise the EU system of pharmacovigilance

EU System of Pharmacovigilance

- Overall EFPIA considers the draft proposals to be a valuable and important step forward in rationalising/simplifying and strengthening pharmacovigilance.
  - Particularly welcome a number of initiatives such as single point reporting to Eudravigilance, implementation of a Pharmacovigilance System Master File electronic submission of PSURs.

EU System of Pharmacovigilance

- Legislative proposals also raised several issues in particular in relation to
  - Proposal to establish a Committee on Pharmacovigilance (Role & responsibilities of this Committee)
  - Applicability of the requirements regarding the submission of PSURs (EFPIA does not believe this should depend on whether a marketing authorisation was granted based on a certain application type (e.g. generic, herbals, well-established use, biosimilar, etc.)
  - Addition of a new ‘key safety information’ section to the SmPC and Patient Information leaflet.

EU System of Pharmacovigilance

- Other issues raised by the proposals
  - Management and presentation of the proposed ‘European list of medicines under intensive monitoring; addition of specific text on outer box of medicines/package leaflet in this regards
  - Publication of list of QPs
  - Inclusion of ADR form within packages (EFPIA suggests that more efficient and possibly more effective alternatives are considered)

EU System of Pharmacovigilance

Need to dissipate concerns/clarify misunderstanding in relation to:

- Suggestion that **non-serious** ADRs that occur in the Community might have to be subject to expedited reporting
- Suggestion that adverse reactions that lack causality assessments might have to be reported
- Scope of definition of Post-Authorisation Safety Studies

EU System of Pharmacovigilance

- It will be crucial to ensure enforcement of submission to Eudravigilance **alone** throughout **all** Member States and a **single** Pharmacovigilance System Master File (No imposition of additional national requirements); also acceptability of a Single Risk Management Plan.
  - ***Striving for consistency through a single piece of legislation to allow industry to proceed with greater clarity, save time and deploy resources in a more efficient manner.***
- Safety Communication and transparency.
  - ***Consistency of the info made available in different databases***
  - ***Info assessed and made available in an appropriate manner (i.e. can be readily and accurately interpreted by the public including its limitations and constraints.)***

Variations Regulation

- Regulation has the potential to significantly lower the current regulatory burden for introducing changes and/or updating information.

  EFPIA particularly welcomes:

  - **Principle of consistency in requirement applicable throughout the EU**
  - **Grouping & worksharing**
  - **Concept of definition of principles based on which variations categories are laid down and development of guidelines on the details of the various categories to bring further predictability while making regular updates '*in the light of scientific and technical progress, taking in particular account of developments regarding international harmonisation*' easier.**

Variations Regulation

- Will need some reassurance in relation to implementation of Regulation
  - with respect to timelines (e.g. acknowledgement of receipt of a valid notification, information as to whether the variation is accepted or rejected, amendments to the decision granting the marketing authorisation, completion of the procedure provided for in Article 10)
  - Acceptance of minor variations of type IB
  - Use of the clause that a decision or approval cannot be recognised on grounds of a potential serious risk to public health

Variations Regulation

- Provisions on grouping and worksharing appear to be applicable only in cases where all concerned marketing authorisations are held by the same Marketing Authorisation Holder: this restriction will have an impact in cases of licensing agreement for same product or MA is held by different affiliates from same group of companies

Variations Regulation

- Guidelines on the details of the various categories of variations and on the operation of the procedures laid down in the new Commission Regulation will be of critical importance

Transatlantic Administrative Simplification

- Harmonisation between US and EU risk management plans for innovative medicines (single global RMP; harmonisation of the documentation to be submitted)
- Surrogate endpoints/biomarkers
- Aligning and sharing results from the Critical Path and Innovative Medicines initiatives.
- Parallel Scientific Advice
- Facilitating and streamlining global development of new paediatric indications (exchange of information and explore possible harmonisation of template requirements and timings in relation to PIPs and Paediatric Study Requests

Transatlantic Administrative Simplification

- Collaboration on inspections and acceptance of results
- Acceptance and planning of 3rd country inspections
- Possibility to avoid re-testing of medicinal products imported from the US (seek appropriate arrangement between EU and USA pursuant to Art 51.2 of Directive 2001/83/EC)

Transatlantic Administrative Simplification

- Certificate of Pharmaceutical Products
- Increase exchange of information on counterfeit medicines; harmonised approach to anticounterfeiting initiatives, including e-pedigree systems and technologies
- Common application format to facilitate parallel submission for orphan designation in EU and USA

ICH

- Adoption of important new guidance documents in the quality, efficacy/pharmacovigilance and safety area.

Upcoming legislation

- EFPIA submitted responses to public consultation on preparation of legal proposal to combat counterfeit medicines for human use (key ideas for better protection of patients against the risk of counterfeit medicines) and the key elements of a legal proposal on information to patients (detailed responses on ‘Pharmacos’)

Information to Patients

A few guiding principles

- Overcoming inequalities in accessing high quality information; improving public health
- Pharmaceutical companies have unique disease expertise and know their medicines better than anyone else
- The doctor/patient interaction remains crucial
- Information which is provided **unsolicited** to the public should be limited to general health information (e.g. prevention, awareness) but not mentioning specific medicines
- However **when citizens/patients actively seek information** companies should be able to provide high-quality medicines information

Counterfeit medicines

- EFPIA overall supports proposed principles
  - Tightening requirements for manufacture, placing on the market of medicinal products and inspections
  - Tightening requirement for the import /export/transit of medicinal products
  - Tightening requirements for manufacture, placing on the market of active substances and inspections
- EFPIA considers it is critical to ensure that the integrity of the original package is guaranteed throughout the entire supply chain, from manufacturer to end user.

Revising the Pharmaceutical Landscape

- **Other legislation**
- Regulation (EC) No 1901/2006 on medicinal products for paediatric use
- Regulation (EC) No 1394/2007 on advanced medicinal products
- Directive 2001/20/EC « Clinical Trial Directive »

Implementation of recently adopted legislation

- Paediatric Regulation: ongoing
  - Concerns in relation to the following matters:
    - Interpretation of the deadline '*end of pharmacokinetic studies in adults'* provided for in the Regulation
    - It has been suggested that obligations in relation to paediatric indications/PIP had no linkage with adult indications. Pragmatism and clarity are required in relation to linkage to adult indication
    - Compliance checks and linkage with national patent offices.

Implementation of recently adopted legislation

- Regulation on advanced therapy medicinal products:
  - Revision of Annex I to Directive 2001/83/EC as modified: overall welcomed however new definition of Gene Therapy product raises concerns (broadened scope)

Regulatory framework for clinical trial research

Key issues pertain to difference in interpretation of legislation in different Member States, national requirements, inconsistency of amendment notification, repeated assessment of the science and methodology by competent authorities , central and local institutional ethics committees

Recital 10 of Directive 2001/20/EC stipulated that delays and complications were detrimental to effective conduct of clinical trials in the Community

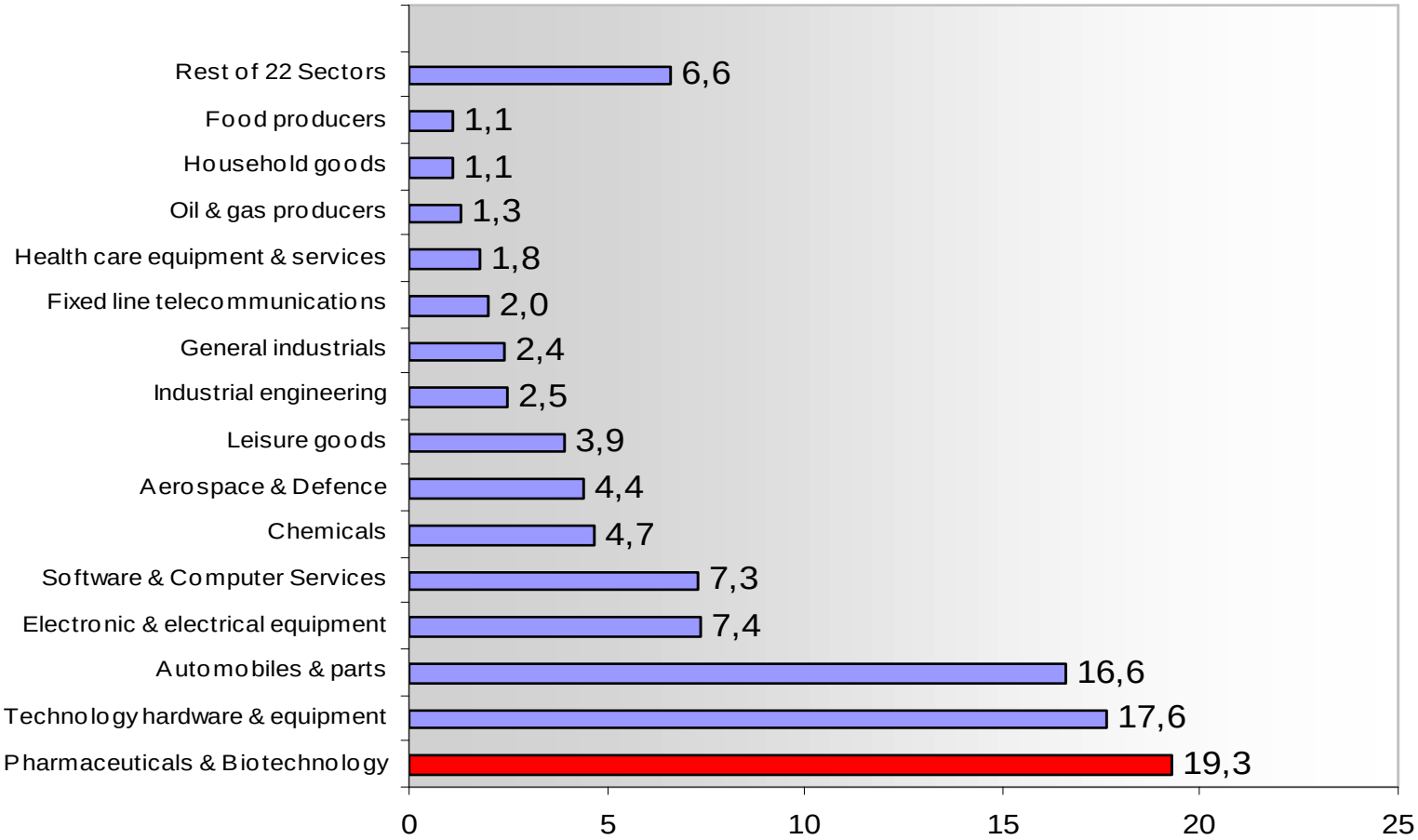
Europe needs a regulatory framework which is conducive of ‘effective conduct of clinical trials’ and trusted by all stakeholders

Conclusions

Revising the pharmaceutical landscapes is of critical importance; very encouraging steps have been taken; need to continuously improve and adapt to foster a favourable environment in Europe which encourages innovation and makes Europe attractive to invest in pharmaceutical R&D and production and serve public health.

Additional slides

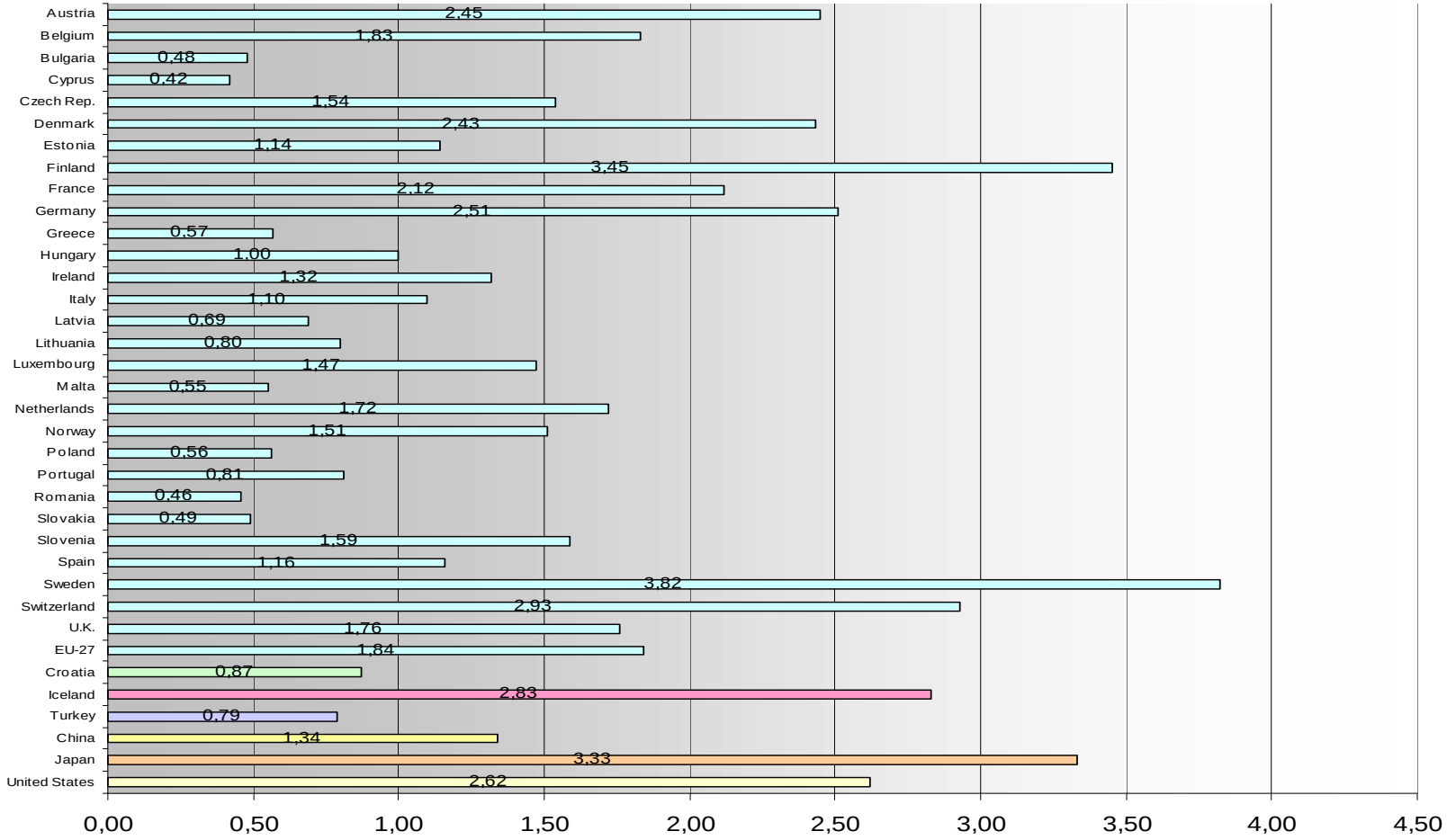
Sector R&D investment as % of all sectors



Note: Industrial Classification Benchmark set up by Financial Times Stock Exchange (FTSE) & Dow Jones
Data relate to the top 1,400 companies with registered offices in the EU, Japan, the USA and the Rest of the World, ranked by the size of their R&D investment (over € 23 million)
(over €24.91 million)

Source: The 2007 EU industrial R&D investment scoreboard, Joint Research Centre, Directorate General Research, European Commission

R&D Expenditure as a percentage of GDP (2006)



Note: Iceland, Switzerland: 2004 data; China, Italy, Japan, Portugal, Turkey, United Kingdom, USA: 2005 data; EU-27: estimate
Austria, Cyprus, Denmark, estonia, France, Germany, Greece, Luxembourg, Malta, Netherlands, Slovenia, Spain: provisional data
Source: EUROSTAT new release 342008, 10 March 2008; 'Science, technology and innovation in Europe', 2008 edition, EUROSTAT