

1 Introduction

The Innovative Medicines Initiative (IMI) is a unique pan-European public and private sector collaboration between large and small biopharmaceutical and healthcare companies, regulators, academia and patients. The aim of IMI is to support the faster discovery and development of better medicines for patients and enhance Europe's competitiveness by ensuring that its biopharmaceutical sector remains a dynamic high-technology sector. The Innovative Medicines Initiative will ensure that Europe's biopharmaceutical sector receives targeted strategic support for the benefit of patients, as well as the scientists and citizens of Europe.

IMI proposes a number of clear, practical paths that will accelerate the discovery and development of more effective innovative medicines with fewer side-effects. IMI will implement innovative Patient Centred Projects that address the principal causes of delay or bottlenecks in the current biomedical R&D process. These bottlenecks have been identified as predicting safety, predicting efficacy, bridging gaps in knowledge management and bridging gaps in education and training. The Strategic Research Agenda (SRA) describes the recommendations to address these bottlenecks and a plan to guide their implementation.

1.1 The Strategic Research Agenda

The bottlenecks were identified through extensive consultation with stakeholders in the biomedical R&D process and from the literature. For example, data on product attrition rates indicate that the probability of a drug candidate passing from pre-clinical stages (i.e. the first GLP toxicity study) to market is 6% or less³. The most common factors resulting in project failure have been reported as either a lack of efficacy (25%), clinical safety concerns (12%) and toxicological findings in pre-clinical evaluation (20%), as illustrated in Figure 1 below. Reducing the risks associated with project failure is dependent upon a concerted and collaborative effort to address these bottlenecks in the drug development process. The biopharmaceutical industry's greatest need is for failure to be predicted at the earliest possible stage of the drug development process. Advances in basic biomedical science within the entire European research community could, potentially, make a significant contribution to improving the predictability of the biomedical R&D process. The vision for the future would be to possess the ability to identify lack of efficacy as soon as possible, even when a drug has promising pre-clinical data, and the potential for adverse drug reactions and pre-clinical toxicity.

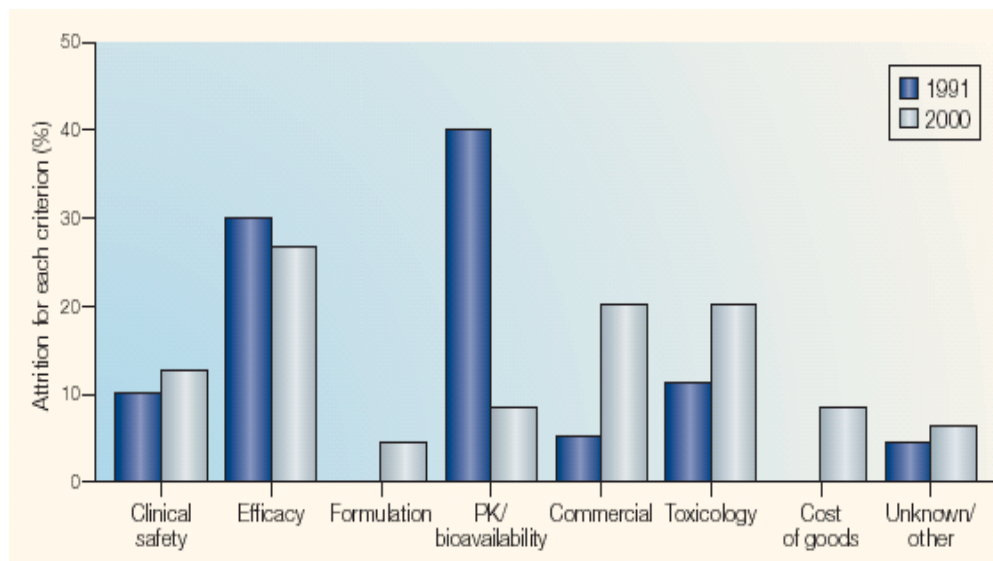


Figure 1 : Reasons for Attrition³

³ Kola I and Landis J (2004). A Survey of Pharmaceutical Companies Comparing Reasons for Attrition. *Nature Reviews Drug Discovery*; 3: 711–715.

The most significant advance in the drug development process between 1991 and 2000 was the optimisation of drug design through the improved predictive value of drug metabolism studies. This advance was possible because *in vitro* absorption and metabolism screens have been validated by correlation with clinical data. The Innovative Medicines Initiative aims to achieve similar clinical correlations within the different scientific disciplines described in Figure 1 above. It also aims to expand on the advances already made with the aforementioned *in vitro* screens through scientific synergies created by unique pan-European public and private sector collaborations. These collaborations conduct pre-competitive research projects, i.e. research where companies are not adverse to their competitors having equal access to the results. An example of a pre-competitive research project would be research that is aimed not at producing products, but rather at providing the: tools, information and data that enable all competing companies to develop and register future products and services.

As illustrated in Figure 2 below, the pre-competitive barriers or bottlenecks in the current biomedical R&D process are the predictivity of pre-clinical studies to anticipate clinical safety and clinical efficacy, as well as the overall assessment of patient benefits and risks with regulatory authorities. Regulatory processes need to reflect new knowledge and incorporate this new knowledge into an improved regulatory framework that supports the faster discovery and development of better medicines. This will increase patient access to new medicines, and decrease the escalating cost of drug discovery and development. Leveraging scientific and technological advances around these bottlenecks could, potentially, boost Europe's biomedical R&D base, and accelerate the discovery and development of better innovative medicines.

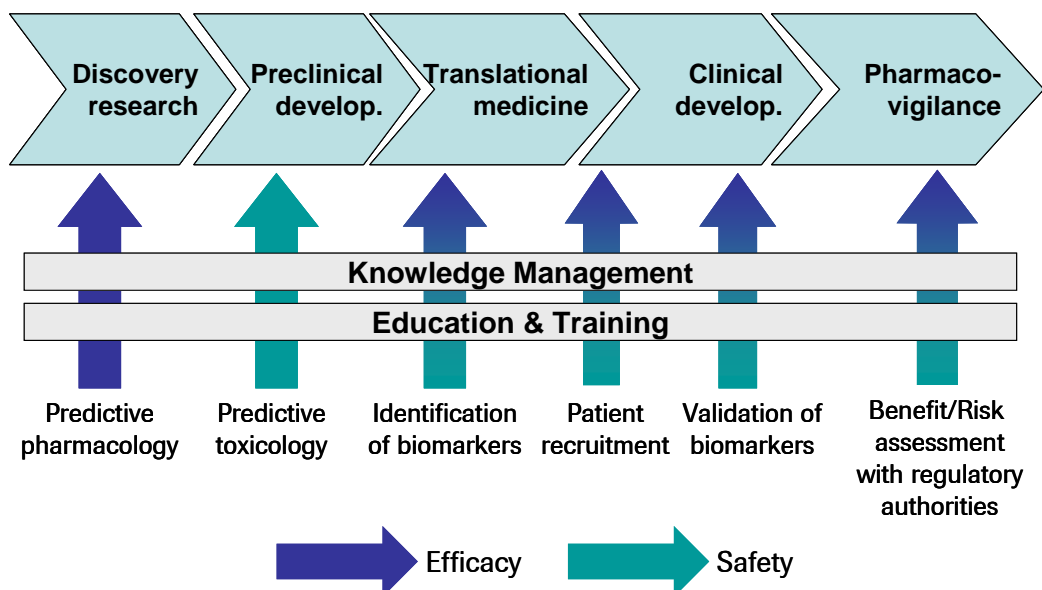


Figure 2 : Key Bottlenecks in the Pharmaceutical R&D Process

The Strategic Research Agenda addresses issues in all of the areas where pre-competitive bottlenecks exist, and proposes specific areas of research to improve the overall efficiency of medicine development in Europe. This is an ambitious aim, but one that is not considered to be beyond the collective capabilities of Europe's biomedical sector. The sector has recognised the urgent need to revolutionise the conventional drug development paradigm to support the faster discovery and development of better medicines.

The development of a new drug is a long, complex and resource-intensive process. Various estimates have placed the costs between \$400 mn and \$900 mn during the period 1994 to 2000⁴. There is a high possibility that a new drug will fail to reach the market because projects may fail for different reasons at different points in the overall process. During the previous 10 years, global R&D expenditure in the pharmaceuticals and biotechnology sector has steadily increased, without a corresponding increase in output of new medicines, as illustrated in Figure 3 below.

The data presented in Figure 1 and Figure 3 demonstrate that radically different initiatives are urgently needed to reduce the rate of attrition during the downstream phases of the drug discovery and develop-

⁴ DiMasi JA, Hansen RW, Grabowski HG (2003). The Price of Innovation: New Estimates of Drug Development Costs. *Journal of Health Economics*; 22: 151–185.

ment process. Such initiatives would support the faster discovery and development of better medicines, and provide a boost to Europe's biomedical R&D base. This would enable Europe to become a preferred location for biopharmaceutical industry investment. In recognition of this opportunity, the Research Directors Group of EFPIA has identified the pre-competitive barriers in the drug discovery and development process on which the biopharmaceutical industry, as well as other stakeholders in the biomedical R&D process such as academia, can collaborate.

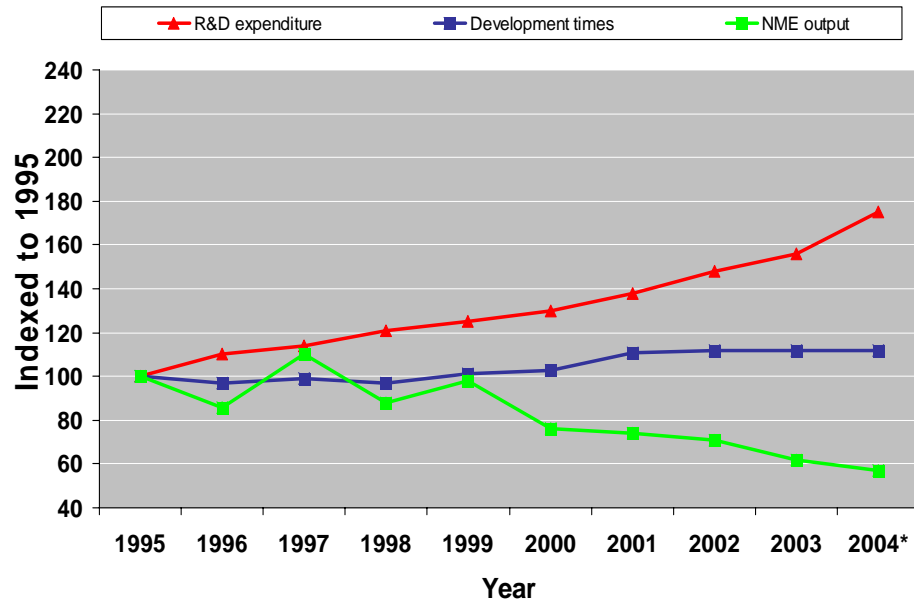


Figure 3 : Global R&D Expenditure, Development Times and NMEs 1995–2004⁵

The SRA includes recommendations that encompass the entire biomedical R&D process from discovery to launch and beyond i.e. pharmacovigilance. These recommendations address the bottlenecks in the conventional drug discovery and development process, and also include important regulatory considerations. To accelerate the discovery and development of more effective innovative medicines with fewer side-effects that reach patients faster, both the safety and efficacy evaluation of new molecular entities (NMEs) across the entire drug development process need to be improved, as well as knowledge management and education and training capabilities.

The SRA is organised around four strategic areas, or Four-Pillars, as described below:

- **Predictivity of Safety Evaluation (Pillar I):** This addresses bottlenecks related to predictivity in safety evaluation and benefit–risk assessment with regulatory authorities;
- **Predictivity of Efficacy Evaluation (Pillar II):** This addresses bottlenecks related to predictive pharmacology, the identification and validation of biomarkers, patient recruitment and benefit–risk assessment with regulatory authorities;
- **Knowledge Management (Pillar III):** This addresses bottlenecks related to gaps in information technology, providing platforms to analyse large amounts of information in an integrated and predictive way. This pillar will be key to maximising the potential of new platform technologies such as genomics, and in analysing data generated by IMI in a consistently integrated manner;
- **Education and Training (Pillar IV):** This addresses the bottlenecks related to gaps in expertise in biomedical R&D knowledge and skills. This pillar will identify and address specific gaps in knowledge and capabilities: a bottleneck which must be resolved if the safety and efficacy pillars of the SRA are to be supported effectively. The education and training pillar will also ensure that Europe's biomedical education landscape is enhanced to provide maximum support in revolutionising the conventional drug discovery and development paradigm.

The strategy of IMI is to co-ordinate and leverage the joint public–private investment within each of the Four-Pillars of the SRA, thereby creating synergies between the new scientific knowledge and capabilities

⁵ Centre for Medicines Research International Ltd. CMR International 2005/2006 Pharmaceutical R&D Factbook (2005).

in each of them to support the faster discovery and development of better medicines. The interdependencies between the Four-Pillars of the SRA are illustrated in Figure 4 below.

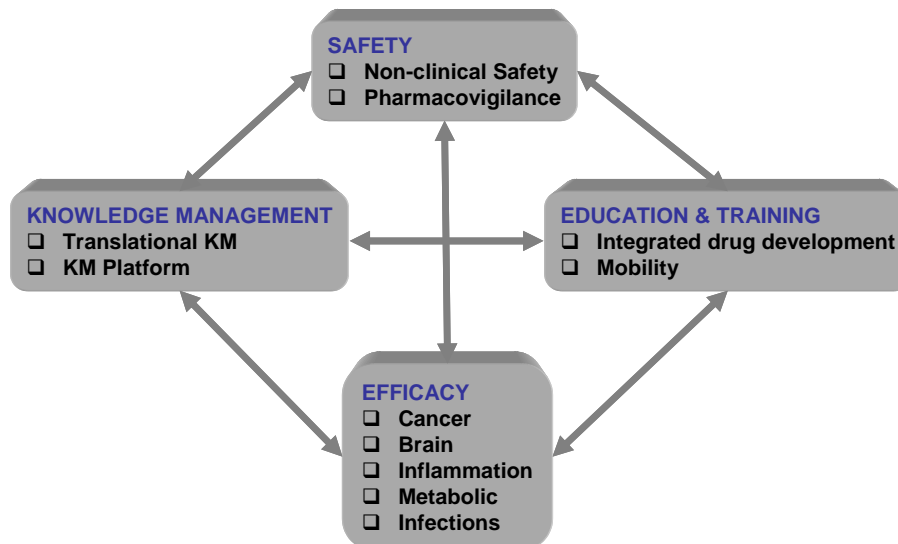


Figure 4 : Interdependencies between the Four-Pillars of the Strategic Research Agenda

Improved Predictivity of Safety Evaluation

To improve the predictivity of safety evaluation and address the current high attrition rate in drug development, the following nine recommendations have been agreed:

- Create a European Centre of Drug Safety Research (ECDSR) to identify and co-ordinate research needs in safety sciences;
- Establish a framework to develop biomarkers that will indicate the human relevance and regulatory utility of early laboratory findings;
- Study the relevance of rodent non-genotoxic carcinogens;
- Develop *in silico* methods for predicting conventional and recently recognised types of toxicity;
- Explore the implications of intractable toxicity in animals for human risk;
- Optimise data resources and strengthen the evidence base in pharmacovigilance;
- Develop and strengthen methodologies and networks for pharmacovigilance;
- Develop novel methods of risk prediction and benefit–risk assessment;
- Train and educate health care professionals and patients.

Improved Predictivity of Efficacy Evaluation

To improve the predictivity of efficacy evaluation and to address the current high attrition rate in drug development, the following nine recommendations have been agreed:

- Develop better understanding of disease mechanisms;
- Develop *in vitro* and *in vivo* models predictive of clinical efficacy;
- Develop *in silico* simulations of disease pathology;
- Stimulate translational medicine in an integrated fashion across industry and academia;
- Create disease-specific European Imaging Networks to establish standards, ensure imaging biomarkers are validated, and develop regional centres of excellence;
- Create disease-specific European Centres for the validation of omics-based biomarkers;
- Co-ordinate the development of national patient networks and databases to develop a true pan-European organisation for patient selection and clinical trial analysis;
- Form a European stakeholder consortium to address value demonstration, including quality of life issues, patient reported outcomes and the burden of disease;
- Develop a partnership with regulators to devise innovative clinical trial designs and analyses, to aid acceptance of biomarkers and to promote data sharing and the joint consideration of ethical issues.

Knowledge Management (KM)

To address the KM bottlenecks in discovering and developing new medicines, the following 15 key recommendations have been agreed:

- Set up a Translational KM team to support individual Safety and Efficacy projects, to define standards of compatibility across projects, and to promote the sharing of suitable KM technology;
- Set up a KM Platform team that, through partner consortium projects, conceives the overall architecture for an integrating biopharma / biomedical sciences platform;
- Set up an advisory Science Panel that supports the KM team in applied Information Technology matters, the ongoing evaluation of *prior art*, and the identification of complementary and synergistic technology R&D proposals;
- Set up task forces to evaluate cross-disciplinary aspects such as modelling and simulation of physio-pathological processes, validate specifications, and align priorities;
- Set up a cross-disciplinary task force to propose guidelines concerning non-KM issues related to data sharing, for example legal, regulatory, ethical and intellectual property;
- Evaluate the approaches and the investment required to build the core of a platform backbone ontology;
- Develop enhanced standards for data protection in a web services environment;
- Develop standards and models for exposing web services (semantics), scientific services, and the properties of data sources, datasets, scientific objects, and data elements;
- Develop enhanced knowledge representation models and data exchange standards for complex systems which, at present, are largely lacking, inconsistent, or incomplete, looking for synergies with current initiatives;
- Develop new, domain-specific ontologies, built on established theoretical foundations and taking into account current initiatives, existing standard data representation models, and reference ontologies;
- Develop advanced text mining tools for capturing implicit information about complex processes, as described in patents and the literature, beyond and above simple pair-wise relationships between entities;
- Develop innovative and powerful data exploitation tools, for example multi-scale modelling and simulation, considering and integrating from the molecular to the systems biology level, and from the organ to the living organism level;
- Build a core reference database of validated experimental data extracted from the literature;
- Design standards for and build an expert tool (ontology/schema/rules negotiator) for exposing the properties of local sources in a federated environment;
- Design standards for an expert tool (services/data negotiator) to guide users through the complexities of the data, data models, simulation and modelling tools and so on.

Education and Training

The SRA provides recommendations on new paradigms for conducting contemporary biomedical R&D which will have an impact on medical practice. To address the Education and Training bottlenecks in discovering and developing new medicines, the following five recommendations have been agreed:

- Establish a European Medicines Research Academy (EMRA), including a central co-ordinating unit and an advisory Education and Training (E&T) council;
- Establish programmes for integrated medicines development and for ethics committees and patient organisations;
- Establish programmes for safety sciences, scientists within pharmaceutical R&D and pharmaceutical medicine professionals;
- Establish regulatory affairs-based programmes;
- Establish programmes for biostatisticians, bioinformaticians and biomedical informaticians.

In summary, a total of 38 multi-disciplinary recommendations are presented within the Four-Pillars of the SRA. The complexity of contemporary biomedical R&D requires a combined multi-disciplinary approach to ensure patients benefit from advances in biotechnology. These advances, which include the decoding of the human genome, require a combination of both traditional and contemporary biomedical scientific excellence to create synergies between private and public sector capabilities. In essence, pan-European public and private sector collaboration and co-ordination is essential to ensure that patients benefit from advances in biotechnology, as the scientific challenges facing Europe are too complex for organisations to address in isolation.

This opinion is supported by *Nature Reviews Drug Discovery*:

*Greater collaboration between regulatory authorities, industry and academia is increasingly acknowledged as the answer to some of the thorniest problems in drug development, such as validation of biomarkers of efficacy and toxicity*⁶.

1.2 Stakeholder Involvement

1.2.1 Developing the Strategic Research Agenda

The Strategic Research Agenda (SRA) is the product of an extensive long-term consultation with stakeholders in the biomedical R&D process that commenced on the 5th and 6th October 2004, when the European Commission organised an initial consultation of stakeholders in Brussels. This consultation resulted in the following two main conclusions:

- The need for more information exchange between the different entities involved in biomedical research was identified as critical.
- The forum agreed with the list of issues to be addressed as proposed by the Research Directors from the pharmaceutical and biotechnology companies.

A report of this meeting can be found at:

ftp://ftp.cordis.lu/pub/lifescihealth/docs/tp_inmed_conclusions_meeting_5-6_oct_final1.pdf

Following this initial consultation, the European Commission and EFPIA organised a series of thematic workshops to develop the SRA. Since January 2005, a diverse and balanced group of 350 stakeholders, including R&D experts, regulators and patient group representatives from across Europe, have been consulted in the development of the SRA, and they have contributed to its recommendations. Figure 5 below illustrates that 48% of the contributors to the SRA originate from academia and SMEs. The characteristics of all contributors are presented in Figure 5, and they are listed individually in appendix 8.1 (page 123). This consultation culminated in an intensive discussion with all stakeholder representatives in Barcelona on the 21st and 22nd April 2005. A report of this meeting can be found at: http://www.eufeps.org/document/pdfs/nsmf_III_final_report.pdf

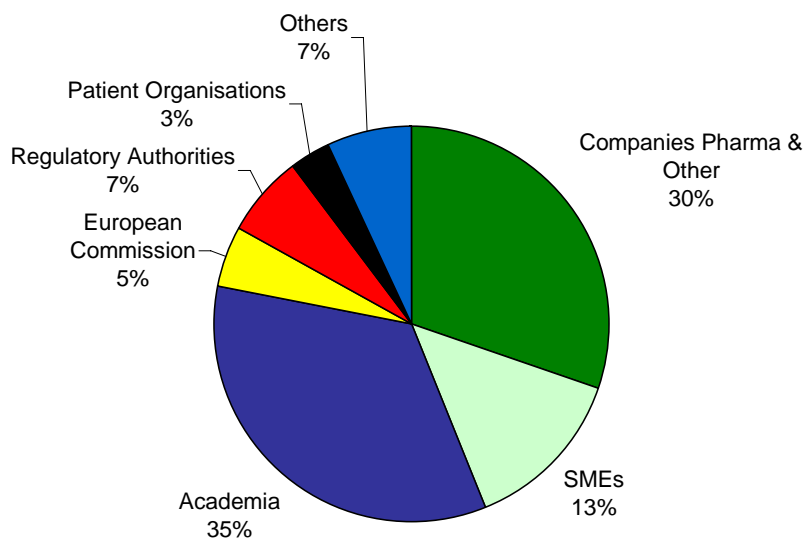


Figure 5 : Stakeholder Analysis of Contributors to the SRA

⁶ Editorial (2006). *Nature Reviews Drug Discovery*, 5: 267.

1.2.2 Updating the Strategic Research Agenda

In addition to their contribution to the preparation of the first versions of the SRA, all stakeholders have the opportunity to propose updates to the SRA based on new scientific or technological developments relevant to the objectives and scope of the SRA. The IMI Executive Office will define and communicate the detailed process for updating the SRA when the IMI legal entity is approved and operational.

1.2.3 Collaborating with other European Technology Platforms

European Imaging industry and public institutions have started to collaborate on the creation of a Strategic Research Agenda (SRA) for the NanoMedicine European Technology Platform. The vision paper was published in September 2005⁷. NanoMedical developments range from nanodiagnostics (lab-on-a-chip) and molecular imaging, through targeted drug delivery, controlled release and monitoring using carrier particles, to regenerative medicine. It is easy to envision a number of potentially successful collaborations within projects that originate from both IMI and NanoMedicine. In this context, both SRA teams have engaged in a dialogue, have agreed to exchange SRAs, to comment on them, and to inform and involve each other in calls for proposals and project work that involves disciplines such as:

- Molecular imaging modalities for both pharmacology and the clinic and disease specific imaging;
- Networks and communities of experts, standards setting for imaging in biopharmaceutical R&D;
- Development and validation of imaging biomarkers, targeted imaging contrast agents and tracers;
- A new and improved science-based regulatory approval process and healthcare delivery processes.

1.3 Contributions to Standards

IMI will not contribute to international standards *per se*, but by implementing the 38 multi-disciplinary recommendations described above it will enable new approaches to drug discovery and development to be evaluated and implemented more systematically and objectively.

The potential of IMI to create a new drug discovery and development paradigm is based on a more systematic use of biomarkers and on applying innovative technologies such as omics technologies and other types of data, in combination with appropriate knowledge management capabilities. One of the main objectives of IMI is to ensure all stakeholders are more closely involved in the enhancement of the biomedical R&D process. This includes discussion with representatives from regulatory authorities at an early stage of the biomedical R&D process and, therefore, IMI can be expected to facilitate a smooth transition of new basic scientific knowledge into regulatory standards.

In addition, the results of the implementation of the SRA recommendations will provide valuable input to the International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH) and thus have broad long-term international impact and benefit to society.

IMI may also contribute to further co-operation between the EMEA and the FDA, particularly as in March 2004 the FDA released a pivotal white paper entitled: *Innovation or Stagnation? Challenge and Opportunity on the Critical Path to New Medical Products*⁸. This document was intended to highlight the need for targeted collaborative efforts to modernise the tools, techniques and methods used to evaluate the safety and efficacy of drug products⁹. In March 2006, the FDA published the 'Opportunities List', which identified six areas of priorities. These are consistent with the Four Pillars of the IMI SRA. The topics are:

- Topic 1: BETTER EVALUATION TOOLS – Developing New Biomarkers and Disease Models to Improve Clinical Trials and Medical Therapy;
- Topic 2: STREAMLINING CLINICAL TRIALS – Creating Innovative and Efficient Clinical Trials and Improved Clinical Endpoints;
- Topic 3: HARNESSING BIOINFORMATICS – Data Pooling and Simulation Models;
- Topic 4: MOVING MANUFACTURING INTO THE 21ST CENTURY;
- Topic 5: DEVELOPING PRODUCTS TO ADDRESS URGENT PUBLIC HEALTH NEEDS;

⁷ European Technology Platform on NanoMedicine: Nanotechnology for Health. Vision Paper and Basis for a Strategic Research agenda for NanoMedicine. September 2005. ISBN 92-894-9599-5.

⁸ FDA (2004) Innovation Stagnation – Challenge and Opportunity on the Critical Path to New Medical Products.

⁹ Editorial (2006). *Nature Reviews Drug Discovery*, 5: 267.

- Topic 6: SPECIFIC AT-RISK POPULATIONS – Unlocking Innovation in Paediatric Products

If the use of biomarkers is generalised for pre-clinical and clinical investigations, IMI will contribute to standards by generating intensive discussions within the proposed networks on agreeing new approaches and European standards to validate biomarkers, as well as to evaluate risk and benefit for the patient.

This approach will also favour cross-functional collaboration between pre-clinical and clinical scientists, and promote the development of translational medicine. In addition, a main focus of IMI is to change the way the different stakeholders work together, establishing a new type of collaboration between industry, academia, clinicians, patients and, indeed, regulators. This would represent a true paradigm shift in culture as illustrated by the following quote:

Perhaps the biggest sociological divide in pharmaceutical sciences – the gap between academic and industry scientists. Put bluntly the sooner academic and industry scientists destroy the stereotypes they hold for each other, the more likely that drug discovery and development will truly evolve to succeed in the 21st century.⁹

1.4 Impact of IMI on the Use of Animals in Research and Development

The problem with drug discovery is simple to state – too many projects flounder because the medicines being developed either do not work well or are unsafe (Figure 1). A considerable proportion of the enormous expense of drug discovery is a result of the cost of attrition along the path from basic research to approval and marketing. To this financial cost can be added the use of animals which has borne little benefit if the compound does not become a medicine. Increasing the success rate of drug discovery through IMI would, therefore, have an impact on animal use. The development of new technologies in drug discovery may increase the use of animals in research as described below. In the medium term, application of new technologies should refine and reduce the use of animals and help replace their use. This is an example of how EFPIA fully supports the concept of the '3Rs'. In addition, EFPIA along with its members is an active participant in the European Partnership for Alternative Approaches to Animal Testing¹⁰. EFPIA's position paper on animal research and welfare can be read in appendix 8.2 (page 133). These principles include: Replacement (i.e. to substitute animals with valid non-animal techniques), Reduction (i.e. to use methods that allow the necessary information to be obtained from fewer animals) and Refinement (i.e. to use methods which cause the least possible distress).

The IMI makes several recommendations which have implications for the 3Rs. First, the increased use of *in vitro* and *in silico* techniques to predict and profile the behaviour of drugs in animals could replace some current *in vivo* tests. This may also refine the use of animals in the identification of compounds with undesirable properties as they are more likely to be screened-out prior to animal testing. For some compounds, this high-throughput screening may reduce the animal data required to select suitable candidates for clinical trials. Second, the development of biomarkers which predict clinical efficacy or safety issues could promote reduction of animals in the long-term through more predictive animal tests with measures that provide more meaningful data, as well as decreasing the number of compounds tested as a result of earlier detection of unsuitable candidates. Furthermore, biomarkers for early indications of serious toxicity (i.e. using premonitory markers to identify a surrogate endpoint) could benefit Refinement by minimising animal distress. However, it should be recognised that the evaluation and validation of biomarkers could lead, in the short term at least, to an increase in animal research. The rigorous application of all 3Rs is, therefore, essential. Third, a major issue in toxicology is the relevance of some common rodent findings to toxicology in man. For example, while rodent models are the only reliable way for experimental investigation of non-genotoxic carcinogenicity risk of compounds to humans, interpretation of findings is often difficult. Understanding the mechanistic basis of genotoxic carcinogenicity could lead to the replacement of existing long-term tests with *in vitro* assays or short-term testing in animals. There are several other similar issues, collectively termed 'intractable toxicities', which will be investigated by the IMI, all of which could have profound 3Rs implications. Fourth, the development of more predictive animal models of disease will result in fewer molecules and concepts failing in the clinic on the grounds of efficacy after they have been extensively tested in non-GLP and GLP animal studies in order to get them to this stage. Fifth, successful pre-competitive data sharing through the IMI could—and should—lead to faster drug development and reduced attrition, with consequent implications for the reduction of the number of animals used.

¹⁰ http://ec.europa.eu/enterprise/epaa/index_en.htm

The Strategic Research Agenda aims to accelerate modern advanced experimentation, to constructively challenge practices in toxicology, to emphasise the use of surrogate end-points in research and clinical development, and place more emphasis on man as the experimental model of choice. Its successful implementation will, inevitably, have positive consequences for the 3Rs.

1.5 Key Benefits of IMI

It is important to appreciate that IMI will not—and is not expected to—deliver new medicines *per se*. However, it is expected to deliver powerful new multi-disciplinary tools to improve the innovation process and thus establish a new drug development paradigm.

Establishing a new drug development paradigm will support the faster discovery and development of better medicines, providing faster access of patients to new and innovative medicines.

The research currently being performed in the FP6 InnoMed Integrated Project which encompasses predictive toxicology (PredTox), and the discovery and validation of new biomarkers for diagnostics, disease progression and therapeutic efficacy in Alzheimer's Disease (AddNeuroMed) demonstrates the unique contribution that European Public-Private Collaborations can make in improving the biomedical R&D process.

The main benefits of IMI for patients, scientists and Europe are:

- Faster discovery and development of better medicines for patients;
- More attractive professional environment for scientists, addressing the 'brain drain';
- Better European expertise and know-how in new technologies to attract biomedical R&D investment in Europe;
- Stronger competitive advantage for small and medium-sized enterprises, spin-offs and start-ups to enhance Europe's economy.

1.6 The Biopharmaceutical Sector's Contribution to the Lisbon Agenda

The pharmaceutical and biotechnology sector impacts upon the daily lives of citizens, but also accounts for a large proportion of Europe's GDP¹¹. Europe's (EU-25) biopharmaceutical industry produced a trade surplus of €24.1 bn in 2004, a significant amount, which has been growing at 11.4% per year since 2000 (4Y CAGR 2000–2004). On this basis, it can be estimated that the trade surplus of Europe's biopharmaceutical industry reached approximately €27 bn in 2005, as illustrated in Figure 6 below.

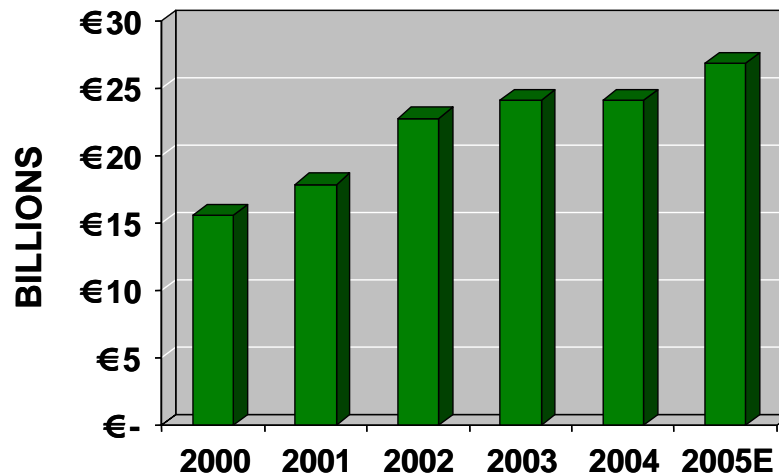


Figure 6 : Trade Surplus of Europe's Biopharmaceutical Industry 2000–2005¹²

¹¹ Aho E, Cornu J, Georghiou L, Subirá (2006). Creating an Innovative Europe – Report of the Independent Expert Group on R&D and Innovation Appointed Following the Hampton Court Summit, European Commission, Luxembourg.

¹² European Commission, Eurostat, SITC 54, Luxembourg.

The biopharmaceutical sector has Europe's largest high-tech sector trade surplus, and provided employment for more than 500,000 people in 2004 (Figure 7). A high proportion of these perform highly skilled knowledge-based R&D roles. Employment in biopharmaceutical R&D has been growing at 4.2% per year since 2000 (4Y CAGR 2000–2004). The trade surplus and employment statistics (both total and R&D only) can be considered to be conservative as they do not include data from Switzerland.

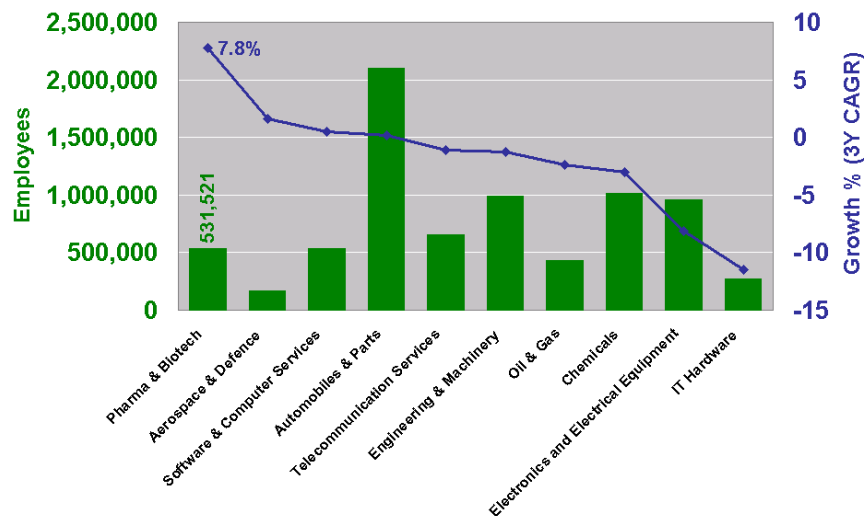


Figure 7 : R&D Employees of Europe's Biopharmaceutical Industry 2004¹³

According to the 2005 EU Industrial R&D Investment Scoreboard¹³ the pharmaceuticals and biotechnology sector invested a total of €17.7 bn in R&D in 2004, making it Europe's second-highest R&D investing sector after Automobiles and Parts. However it is the leading sector in terms of R&D investment growth which reached 11.9% between 2001 and 2004 (3Y CAGR)¹³. Over the same period, employment in the pharmaceuticals and biotechnology sector grew by 7.8% (3Y CAGR 2001–2004). These statistics demonstrate that the biopharmaceutical industry is Europe's most dynamic R&D sector, and a key contributor to the Lisbon Agenda.

Europe is seen as a less attractive R&D investment location in terms of market conditions and incentives for the creation of new biotech companies¹⁴. In 2005, the US biotechnology industry invested a total of €12.8 bn in R&D, which represented 79% of global biotechnology R&D investment, and a positive growth rate of 2.3% (3Y CAGR 2003–2005). In comparison, as illustrated in Figure 8 below, the European biotechnology industry invested a total of €2.7 bn in R&D in 2005. This represented 16% of global biotechnology R&D investment, and a negative growth rate of -10.9% (3Y CAGR 2003–2005). On average, European-based public biotechnology companies invested €22 mn per company in R&D in 2005, whereas their US counterparts invested €39 mn per company in R&D¹⁵.

¹³ European Commission (2006). The 2005 EU Industrial R&D Investment Scoreboard, Luxembourg

¹⁴ EFPIA (2006). The Pharmaceutical Industry in Figures, 2006 Edition, Brussels.

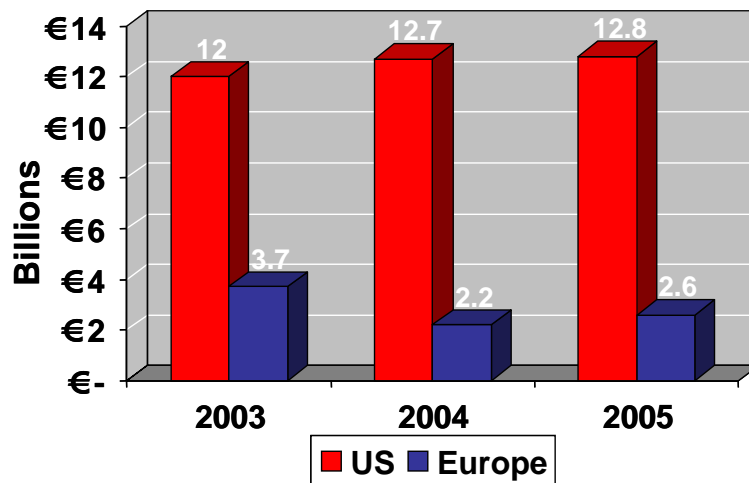


Figure 8 : Global Biotechnology R&D Investment by Company Origin 2003–2005¹⁵

Throughout the world, the biosciences rank prominently in the economic development agendas of governments because progress in microbiology and genomics hold the promise to make biotechnology the dominant economic force of the first half of the 21st century^{16 17}. At the Lisbon Summit in 2000, the European Council set a clear strategic objective: to transform Europe into the world's most competitive and dynamic knowledge-based economy by 2010 – an economy characterised by a R&D Intensity of at least 3%, and with two-thirds of its total R&D expenditure originating from the business enterprise sector¹⁸. The European Council regards R&D as the driving force behind economic growth, job creation and innovation of new products in general, as well as improvements in healthcare. However, while R&D Intensity for Europe has shown a positive growth rate in the six years up to 2003, it currently lags behind that of the US and Japan, and is being seriously challenged by China, as illustrated in Figure 9 below.

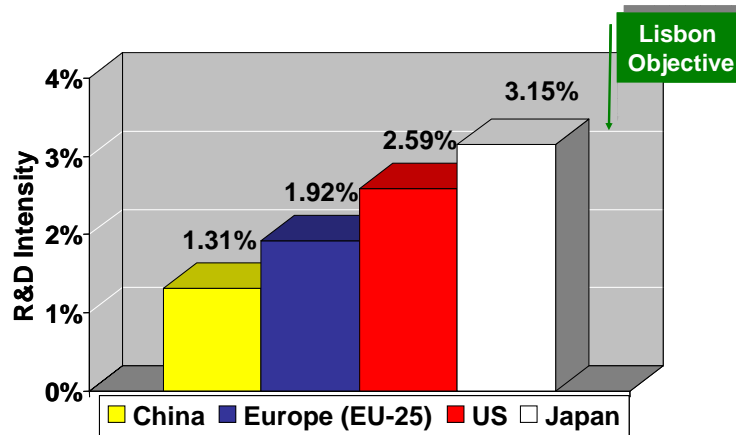


Figure 9 : Comparison of R&D Intensity¹⁸

Furthermore, Figure 10 confirms the argument above by demonstrating that the growth rate of China's R&D Intensity (4Y CAGR 1999–2003) out-performed all other leading economies, and was a staggering 17 times higher than that of the EU-25.

¹⁵ Ernst & Young (2006). Global Biotechnology Report.

¹⁶ Rinaldi A (2006). More than the sum of their parts?, *EMBO Reports*; 7, 2: 133–136.

¹⁷ DeVol R, Wong P, Ki J, Bedroussian A, Koepf R (2004). America's Biotech and Life Science Clusters: San Diego's Position and Economic Contributions. Santa Monica, CA, USA: Milken Institute.

¹⁸ European Commission (2006). Europe in Figures, Eurostat Yearbook 2005, Luxembourg.

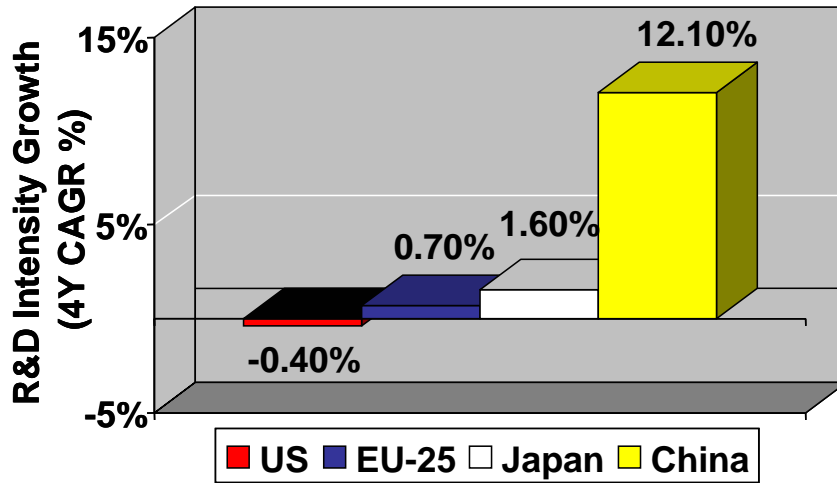


Figure 10 : Comparison of R&D Intensity Growth¹⁸

Recent data on the R&D Intensity of the EU-25 suggests that the Lisbon objective is in jeopardy without a significant injection of new R&D investment from both the private and public sector, as illustrated by the following quote from the recent Aho report:¹⁹

It is well known that the 3% target cannot be approached without a very substantial increase in business investment in R&D and innovation.

Government support for R&D in the EU-25, as measured by GBAORD, is lower than it is in the US, and only marginally higher than Japan, as illustrated in Figure 11 below.

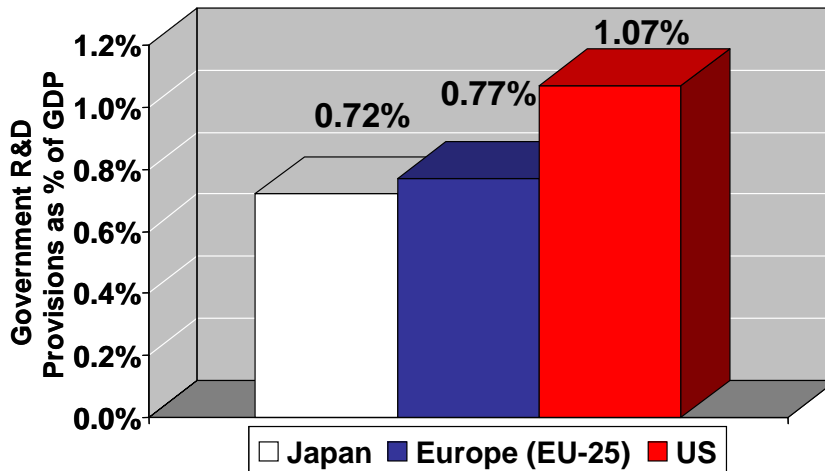


Figure 11 : Comparison of Government Support for R&D (GBAORD)²⁰

The overall pattern of R&D under-investment in the EU-25 described above is also true for biomedical R&D. This point is demonstrated in Figure 12 below, which highlights the fact that, in the US, a far greater proportion of GDP is directed to public sector sponsored biomedical research than in Europe (EU-15).

¹⁹ Aho E, Cornu J, Georghiou L, Subirá (2006). Creating an Innovative Europe – Report of the Independent Expert Group on R&D and Innovation Appointed Following the Hampton Court Summit, European Commission, Luxembourg.

²⁰ European Commission (2006). Europe in Figures, Eurostat Yearbook 2005, Luxembourg.

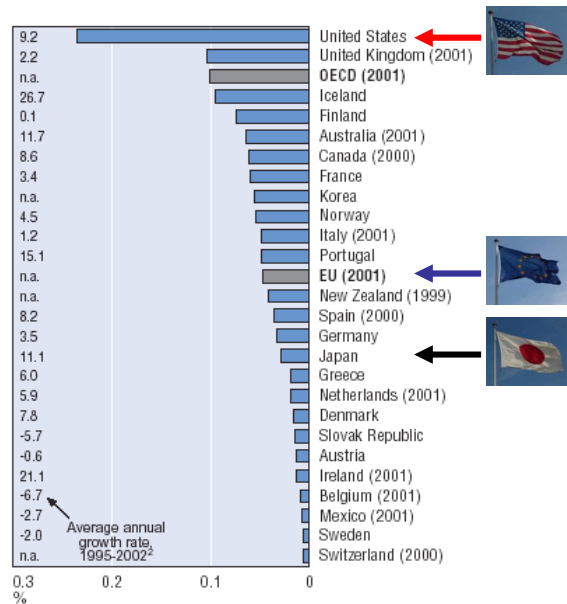


Figure 12 : Health R&D in Government Budgets as a Percentage of GDP, 2002²¹

Figure 13 below provides examples of national spending on biomedical research in selected Member States as well as the US. The total spending for the selected European organisations was € 3.6 bn in 2005. Although this does not represent the entire public biomedical research spending in Europe, it illustrates the level of under-funding in the EU-25 in comparison to the US. In addition, the fragmented nature of the biomedical research environment in Europe makes it difficult to optimise resources by creating pan-European synergies for the benefit of patients.

Research Funding Agency (Country)	Spending 2005 (€mn)
National Institutes of Health (USA)	23,000
Ministry for Science & Technology – Life Sciences (Japan)	3,015
Medical Research Council & National Health Service (UK)	1,750
Max Planck & Deutsche Forschungs Gemeinschaft (Germany)	778
FP6 ‘Life sciences, genomics & biotechnology for health’ (EU-25)	564
Institut National pour la Sante et la Recherche Medicale (France)	475
Karolinska (Sweden)	413
Consiglio Nazionale delle Ricerche (Italy)	174

Figure 13 : Examples of National Biomedical Research Funding in 2005

1.7 R&D Performance

Between 1998 and 2003, the US Government increased its funding of the National Institutes of Health (NIH) by 200% to \$27 bn. This fact can be interpreted as a commitment by the US government to winning the ‘R&D Race’. Should the US win this race, it would not only have serious repercussions for Europe’s economy but, more importantly, would exacerbate the serious issue facing Europe of delayed patient access to new innovative medicines. Based on NME approvals (which can be used as an indicator of innovation performance), US based biopharmaceutical companies are currently winning the ‘R&D Race’. This position is supported by the fact that US-based biopharmaceutical companies gained the highest number

²¹ OECD (2003). R&D Database, Paris.

of NME approvals between 1986 and 2005 – despite running second to Europe throughout the preceding decade (see Figure 14 below). Between 1960 and 1965, European-based companies invented 65% of new chemical entities (NCEs) placed on the world market. Forty years later, their share had fallen to 34%. The latest data available, for the period 2001–2005, show the dominance of the United States, which has now become the leading inventor of new molecules in the world²².

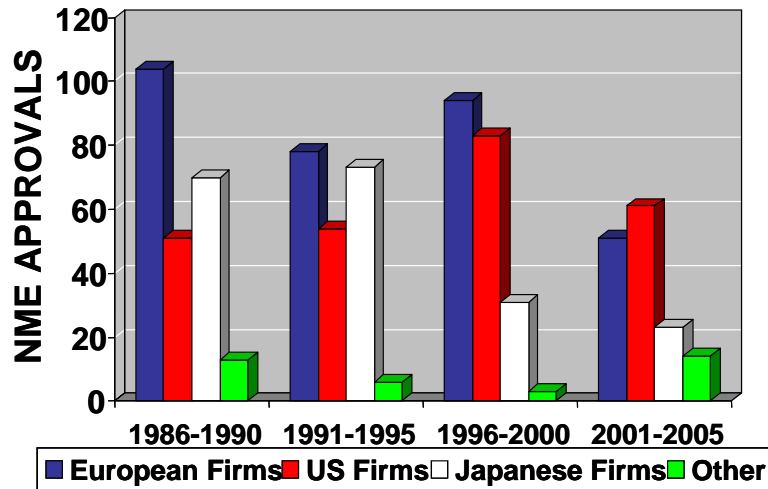


Figure 14 : Global NME Approvals 1986–2005²²

When comparing the innovative performance of European-based biopharmaceutical companies to those based in the US on the basis of FDA approved new cancer medicines (Figure 15), the innovation performance of Europe is even more alarming because oncology is an innovative therapeutic area that has produced breakthroughs in targeted therapy, such as Glivec® and Herceptin®.

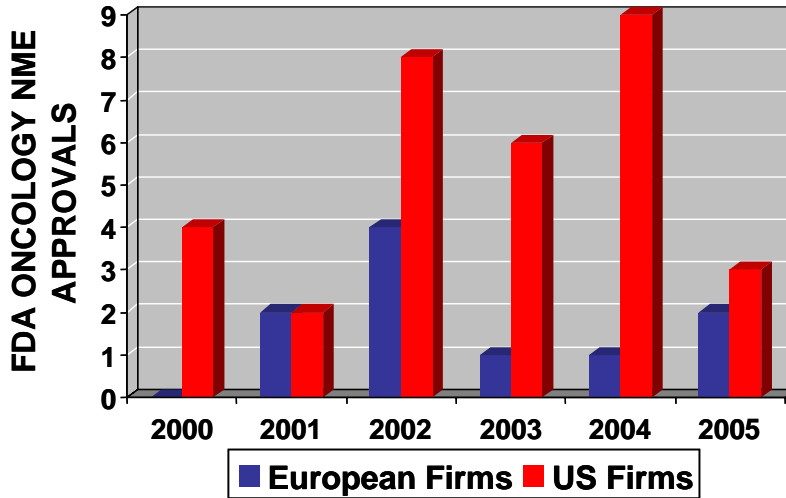


Figure 15 : FDA Oncology NME Approvals 2000–2005²³

Even more disturbing for patients with unmet medical needs is the fact that US patients are gaining access to better medicines faster than Europeans as the US remains the region of choice for first launches, accounting for almost 50% of all global NMEs first launched in 2004. This is illustrated in Figure 16 below.

²² EFPIA (2006). The Pharmaceutical Industry in Figures, 2006 Edition, Brussels.

²³ FDA <http://www.fda.gov/cder/cancer/approved.htm>

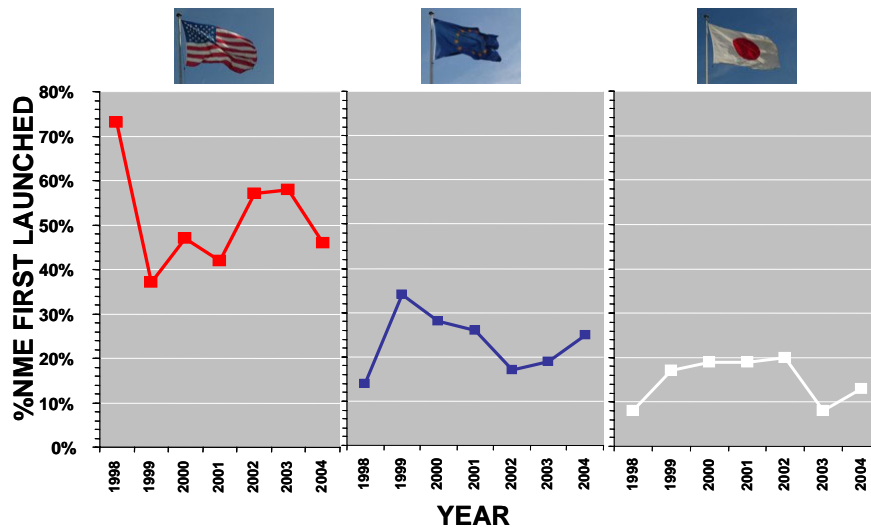


Figure 16 : Regions of First Launches of NMEs 1998–2004²⁴

Overall, the range of macro-economic indicators presented above support the conclusion that the biopharmaceutical industry is an essential sector for meeting the Lisbon objective of 3% R&D Intensity, and for Europe to continue to compete effectively with other economies in the future. However, Europe’s biomedical R&D base is actually diminishing in comparison with the US. Between 1990–2005 R&D investment in biomedical sciences in the US increased by more than 460% while, over the same period, R&D investment in biomedical sciences within Europe increased by just 280%²⁵. The pattern of relative underinvestment is illustrated with a sample of data from 2000–2005, described in Figure 17 below:

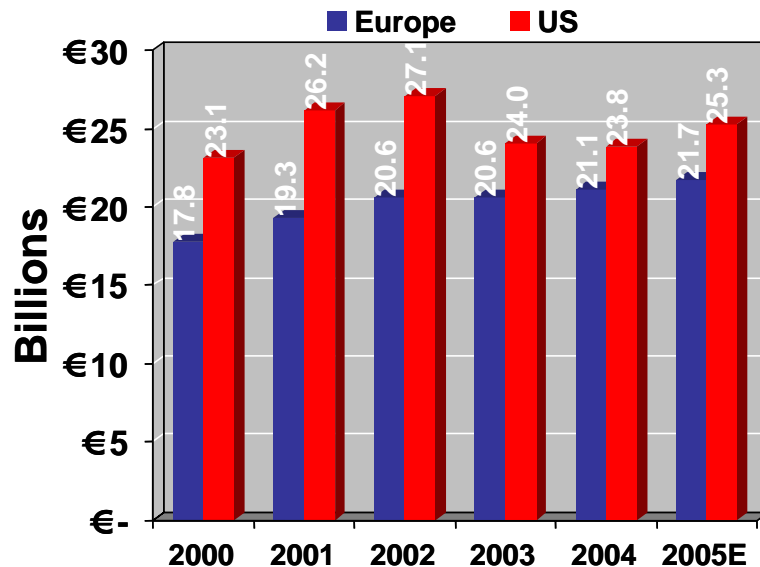


Figure 17 : Comparison of European and US Pharmaceutical R&D Expenditure 2000–2005²⁵

In 1990, the major European research-based pharmaceutical companies invested 73% of their global R&D budgets within Europe. By 1999, this amount had declined by 19% to 59%.²⁵ The US was the main beneficiary of this trend, evolving to become the preferred destination for the transfer of biomedical R&D assets in 2005. In addition, the biopharmaceutical companies have created R&D centres in Asia, predominantly in Japan, China and Singapore.

²⁴ Centre for Medicines Research International Ltd. CMR International 2005/2006 Pharmaceutical R&D Factbook (2005)

²⁵ EFPIA (2006). The Pharmaceutical Industry in Figures, 2006 Edition, Brussels.

Europe's research-based biopharmaceutical industry invested €21.1 bn on R&D in Europe in 2004²⁵, which can be divided into the four key areas listed below:

AREA	INVESTMENT (€bn)
Discovery & Pre-clinical Development	6.8
Phase I	1.5
Phase II	2.3
Phase III, Registration and Pharmacovigilance	10.5
Total	21.1

Should this trend of relative under-funding of biomedical R&D investment continue within Europe's pharmaceuticals and biotechnology sector, then it is clear that the European Union's Lisbon objective must be re-assessed, because R&D assets are widely recognised as the pipeline of technological innovation, and levels of R&D investment is a reliable indicator of innovation capacity²⁶.

Data contained in the 2005 European Innovation Scoreboard highlights the innovation gap between Europe and other economies, and reported that it would take 50 years for Europe to reach the US level of innovation performance²⁷. It can be concluded that, on the basis of this information, that the innovation capability of Europe and, thus, its competitiveness, is being weakened for the future by the current level of R&D investment. This position is supported by the following quote from the Aho report:

The current trends lead us to a position outside the world's top economic powers by 2030²⁸.

The Innovative Medicines Initiative seeks to address the economic issues described above for the benefit of patients and Europe. This is supported by the following quotes:

Europe and its citizens should realise that their way of life is under threat but also that the path to prosperity through research and innovation is open if large scale action is taken now by their leaders before it is too late²⁸.

Examples of areas of science and technology where Europe needs to invest today so as not to face a gap analogous to that what we see in ICT include biotechnologies, cognitive and neuro-sciences²⁸.

²⁶ DeVol R, Wong P, Ki J, Bedroussian A, Koepf R (2004). America's Biotech and Life Science Clusters: San Diego's Position and Economic Contributions. Santa Monica, CA, USA: Milken Institute.

²⁷ European Commission (2006). European Innovation Scoreboard 2005. European Trend Chart on Innovation. Luxembourg.

²⁸ Aho E, Cornu J, Georghiou L, Subirá (2006). Creating an Innovative Europe – Report of the Independent Expert Group on R&D and Innovation Appointed Following the Hampton Court Summit, European Commission, Luxembourg.

1.8 Signatures of the EFPIA Research Directors' Group Members

The Research Directors' Group of EFPIA consists of senior management responsible for R&D activities in the pharmaceutical industry in Europe. The group has the strategic leadership of IMI, and works actively to ensure its successful implementation.



P.H. Andersen / H. Lundbeck A/S



A. Busch / Bayer HealthCare



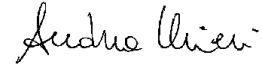
H. Buschmann / Esteve



E. Canet / Servier



D. De Chaffoy de Courcelles / Johnson & Johnson



A. Chiesi / Chiesi Farmaceutici S.p.A



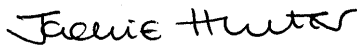
F. Gvillo / Schering AG



P. Herlling / Novartis AG



R. Hill / Merck & Co



J. Hunter / GlaxoSmithKline



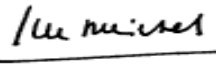
C. Incerti / Genzyme



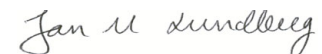
J. Knowles / F. Hoffmann-La Roche Ltd



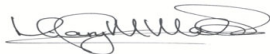
P. Kurtzhals / Novo Nordisk A/S



J. Kusmierek / Pierre Fabre Médicament



J. Lundberg / AstraZeneca



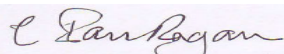
H. Malone / Wyeth



M. Pairet / Boehringer Ingelheim GmbH



A. Puech / Sanofi-Aventis



C. Ragan / Eli Lilly & Co



R. Rappuoli / Novartis Vaccines



D. Roblin / Pfizer



L. Turski / Solvay S.A.



F. Weber / Merck KgaA



N. Weir / UCB



T. Wells / Serono S.A.