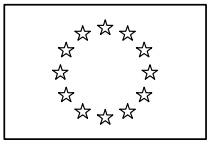

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Accompanying document to the
Proposal for the Council decision on the setting up the Innovative Medicines Initiative Joint Undertaking

Analysis of the effects of a Joint Technology Initiative (JTI) in the area of INNOVATIVE MEDICINES

European Commission, DG Research, Health Directorate

IMPACT ASSESSMENT

[COM(2007) 241 final]
[SEC(2007) 569]

TABLE OF CONTENTS

1. PROCEDURAL ISSUES AND CONSULTATION OF INTERESTED PARTIES

This document presents the impact analysis of the Joint Technology Initiative on INNOVATIVE MEDICINES, in brief IMI JTI. It is in accordance with the Commission's guidelines for ex-ante impact assessments[1].

The Seventh Framework Programme (FP7; 2007-2013)[2] introduces the concept of **Joint Technology Initiatives** (JTI) as a response to the real needs of industry and other stakeholders. JTIs are conceived as public-private partnerships (PPP) and have been identified by the European Commission[3] to support a limited number of European Technology Platforms in reaching their objectives[4]. With the introduction of JTIs, the Community will for the first time offer a legal and organisational framework that allows the effective pooling of resources across all R&D undertakers in a specific area, both from the public and the private sector. JTIs should pursue activities that are of common European interest[5] and their establishment should contribute to the achievement of the Lisbon competitiveness objective and the Barcelona targets for research spending[6].

The Innovative Medicines Initiative (IMI) has been identified by the Commission as one of the potential areas for the establishment of a JTI (resulting from the work of the "Innovative Medicines for Europe" Technology Platform[7]) during the implementation of FP7[8]. This was recently confirmed by the Competitiveness Council[9].

The present impact assessment of the IMI JTI is based on two reports. The first report, entitled "Assessment of Economic and Societal Effects" of the IMI JTI, was prepared by an independent expert group (hereinafter referred as the "Expert Group") that was established under a contract of the European Commission. This Expert Group met at four occasions over a period of 5 months, from September 2006 – January 2007. This group focused on an analysis of the current situation for the European pharmaceutical sector, the identification of different policy options and an in-depth assessment of the economic and societal effects of the proposed Joint

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1 Impact Assessment Guidelines, SEC(2005) 791, European Commission, 2005.

2 Decision of the European Parliament and of the Council on FP7 N° 1982/2006/EC of 18 Dec. 2006.

3 COM(2004) 353 "Science and technology, the key to Europe's future – Guidelines for future European Union policy to support research".

4 SEC(2005) 800, European Commission, 2005*Report on European Technology Platforms and Joint Technology Initiatives: Fostering Public-Private R&D Partnerships to Boost Europe's Industrial competitiveness*.

5 SEC (88)1882

6 {COM(2005) 488 final}"More Research and Innovation - Investing for Growth and Employment :A Common Approach" Impact Assessment

7 Commission publications: "Technology Platforms: from Definition to Implementation of a Common Research Agenda", September 2004 - EUR 21265, "Status Report on the Development of Technology Platforms", February 2005 – ISBN 92-894-8985-5 and "2nd Status Report: Moving to Implementation", May 2006 - ISBN 92-79-01019-0

8 Council Decision on the Specific Programme "Cooperation" implementing the Seventh Framework Programme (2007-2013) of the European Community for research, technological development and demonstration activities; 2006/971/EC, 19 Dec. 2006.

9 Council press release 15717/06 on the Competitiveness Council meeting on 4-5 December 2006

Technology Initiative. For their analysis, the Expert group screened public domain data, in particular OECD and EUROSTAT data and statistics, and used all documents related to the IMI Technology Platform (EFPIA vision paper, IMI Strategic Research Agenda, etc.).

The second report, entitled "The Innovative Medicines Initiative – Keys for Success", was submitted by the European Federation of Pharmaceutical Industries and Associations ("EFPIA"). This report was prepared as response to a letter from the Commission asking for the pharmaceutical industry's view on four specific items: Market Failure, Additionality, Governance and Role of Member States. This document expresses the opinion of 24 major pharmaceutical companies represented at the Research Directors Group of EFPIA (EFPIA RDG): AstraZeneca, Bayer-Schering Pharma, Boehringer Ingelheim, Chiesi, Eli Lilly, Esteve, Genzyme, GSK, Johnson & Johnson, Lundbeck, Merck, MSD, Novartis, Novo-Nordisk, Organon, Pierre Fabre, Pfizer, Roche, Sanofi-Aventis, Serono, Servier, Solvay, UCB and Wyeth.

This impact assessment equally reflects the results of extensive consultations with stakeholders in the biopharmaceutical sector. The consultations were conducted upon the creation of the "Innovative Medicines for Europe" Technology Platform in May 2004, which is driven by EFPIA[10]. Nine dedicated workshops, involving more than 300 people representing all stakeholder groups within the drug development process, have been organised to elaborate the Strategic Research Agenda (SRA). Additionally, more than 20 meetings were held within dedicated Task Forces (in particular on Governance and IPR issues) between stakeholders, experts, Commission staff and EFPIA representatives.

The Strategic Research Agenda and the IMI Joint Technology Initiative have also been publicly presented and discussed in major events such as the EURO DIA Annual conferences (Paris 2005, Vienna 2006), the Annual meeting of EUFEPS (Barcelona 2004, Nice 2005) and the BIO Congress (Philadelphia 2005, Chicago 2006). Finally, five meetings with national public authorities represented in the "Member State Group" gathering representatives from 28 Member States and Associated Countries[11] took place. These meetings covered the entire range of issues related to the content and the implementation of IMI and the Commission proposal on establishing IMI as a Joint Undertaking reflects the comments and input provided by Member States and Associated Countries.

2. PROBLEM DEFINITION

2.1. The Pharmaceutical Industry: An Important Industry for Europe

The research-based biopharmaceutical industry provides an important contribution to European health and economy. The industry has grown steadily over the last 10-15 years (Table 2.1) with increased production and with growing contribution to

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10 Formal launch of the "Innovative Medicines for Europe" TP at the EFPIA 2004 annul meeting (26 May Dublin).

11 Members of the Group are AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GR, HU, IC, IE, IL, IT, LT, NL, NO, PL, PT, RO, SE, SI, TR, UK.

Europe's balance of trade as well as to employment. The industry thus continues to make a strong contribution to the European knowledge-based economy.

Table 2.1 The Pharmaceutical Industry in Europe Key data

INDUSTRY (EFPIA Total) (*)	1990	2000	2004	2005
Production	60,220	121,471	160,769	170,000 (e)
Exports	23,180	90,935	165,003	178,000 (e)
Imports	16,113	68,841	132,853	144,000 (e)
Trade balance	7,067	22,094	32,150	34,000 (e)
R&D expenditure	7,766	17,849	21,106	21,700 (e)
Employment (units)	500,879	538,317	612,114	615,000 (e)
R&D employment (units)	75,760	88,524	102,222	103,000 (e)
Pharmaceutical market value at ex-factory prices	43,005	86,812	120,007	127,500 (e)

Values in € million unless otherwise stated
(*) Data relate to EU-25, Norway and Switzerland since 2004
Source: EFPIA Member associations (official figures) – (e): EFPIA estimate
Eurostat (EU-25 trade data 1995-2005)

2.2. Private R&D Expenditure in Europe Is Lagging in the Biotech segment

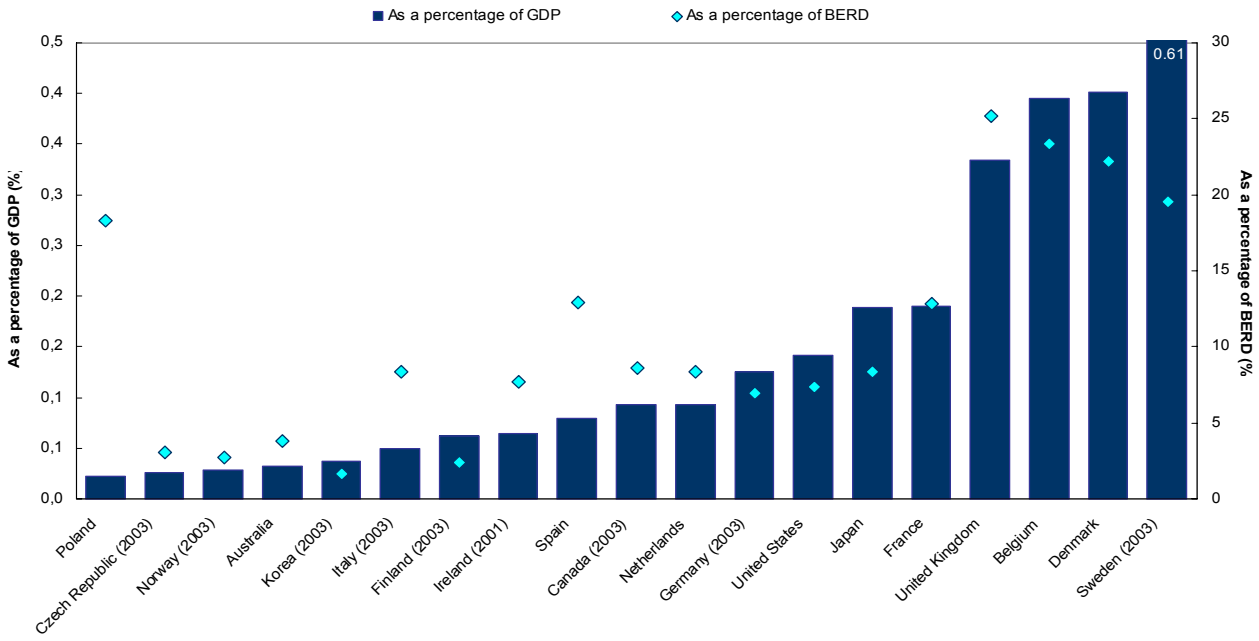
The picture regarding R&D expenditure by the biopharmaceutical industry in Europe versus the US is somewhat confused by terminology. Using standard statistical terminology[12] for the pharmaceutical industry, there seems to be little difference between the EU and US. Business R&D expenditure in the EU rose from a level of 9,6 Billion USD in 1996, to 16,8 Billion USD in 2003, while the equivalent expenditure in the US rose from 9,8 to 16,0 Billion. According to these figures[13], the EU, at least until 2003, had been keeping up with the US in terms of business R&D expenditure. And businesses in a number of European countries are relatively specialised on pharmaceutical R&D (Figure 2-1). However, these figures underplay

[12] ISIC, Revision 3 (ANBERD R-3)

[13] OECD ANBERD Database, 2005/6 - Analytical Business Enterprise Research and Development Database. Expenditure adjusted for PPP. It should be noted that there are methodological difficulties associated with international comparisons of BERD data – particularly relating to the US in industries that attract a high degree of federal funding.

the increasing role of smaller biotech companies (SMEs) and the rebranding of part of the industry as the "biopharmaceutical" industry. This is a vital distinction since activities in the fast-evolving biosciences will often comprise the high end of knowledge-based activities. For biotechnology related activities, the US remains a significant outlier in terms of R&D expenditure[14] and venture capital availability[15]. The US thus accounts for 74% of all VCs available across 23 countries sampled between 2001 and 2003 (see [OECD, 2005][Ernst & Young, 2006][Critical I, 2006].

Figure 2-1 - R&D Expenditure in the pharmaceutical Industry, 2002, as percentage of GDP and BERD[16] Source



Source : OECD Science, Technology and Industry Scoreboard 2005 [OECD, 2005]

2.3. European Public Support for Pharmaceutical R&D Is Lagging

By any measure, US public expenditure on health R&D is in excess of Europe, both in absolute terms and as a proportion of GDP. Government expenditure on health related R&D (GBAORD) in the US is some 0,26 % of GDP, while Europe in comparison spends much less, at around 0,04% of GDP (Figure 2.7). Similarly, the average growth rate (2000-2004) of health-related GBAORD is about 10% in the US, but only around a third of that in the major European countries (e.g. UK 3%, France 2,6%, Germany, 4%: see Fig 2-2). The gap therefore seems to be growing.

This, in combination with very attractive market conditions (one patent, free pricing, etc.), has made the US the most attractive location for R&D investments of biopharmaceutical companies.

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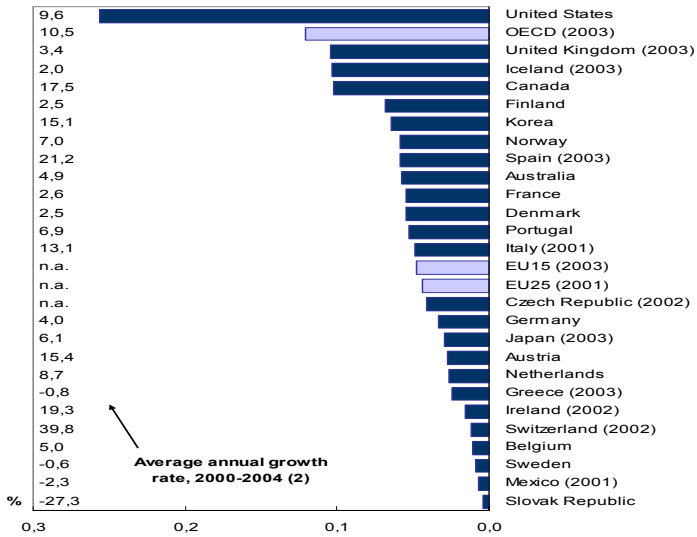
14 OECD Biotechnology Statistics 2006 (and reproduced as fig. 2.11 in the "Assessment of Economic and Societal Effects" report

15 Ibid (and reproduced as fig. 2.12 in the "Assessment of Economic and Societal effects" report

16 BERD – Business enterprise expenditure on R&D

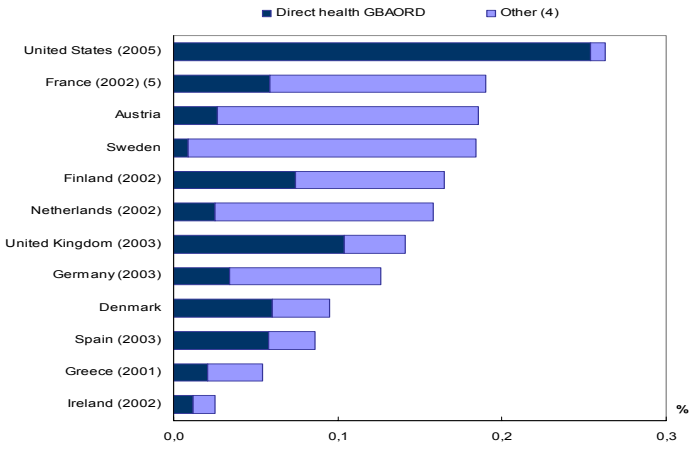
Figure 2-2 - Health Related R&D (%GDP) in Government Budgets (GBAORD[17]), 2004



Source : OECD Science, Technology and Industry Scoreboard 2005 [OECD, 2005]

The GBAORD data for health related R&D in government budgets suggests that the USA is a very significant outlier. If other health related public expenditures (NABS)[18] are taken account of (fig 2-3), the relative positions of countries become closer, though the US is still significantly ahead of even the highest spending of the European countries (let alone Europe as a whole).

Figure 2-3 - Effect of including other health related NABS categories in health-related GBAORD, 2004



Source : OECD Science, Technology and Industry Scoreboard 2005 [OECD, 2005]

On medical research, the US government has doubled the funding for the National Institutes of Health (NIH)[19] since 1998 to reach the current annual amount of

17 Government Budget Appropriations for R&D in PPP terms.

18 NABS (Nomenclature for the Analysis of Science Budgets) Analysis of net R&D expenditure – further broken down into biotechnology, information technology, international collaborative projects and payments to firms.

19 NIH – National Institutes of Health, www.nih.gov

approximately € 23 Bn. Direct health R&D funding fell in the late 1990s in a small number of European countries and the major countries have not kept pace with the US. For comparison, the combined contribution of key European research institutions and funding agencies (i.e. MRC UK, MP Germany, INSERM France, Karolinska Institute Sweden, CNRS Italy and the European Framework Programme part) only amounted to approximately € 4.2 Bn. This clearly indicates that there is a difference in the magnitude of public investment in the sector on the two sides of the Atlantic.

2.4. Pharmaceutical R&D Is Moving out of Europe

Over the past 10-15 years, Europe's pharmaceutical research and development basis has gradually eroded. Whereas R&D investment in the United States grew by 4.6 times between 1990 and 2005, the corresponding increase in Europe was only 2.8 times[20] In 1990, major European research-based companies thus spent 73% of their worldwide R&D expenditure on the EU territory, while the figure was only 59% in 1999. According to the biopharmaceutical industry [EFPIA, 2006], companies are increasingly transferring leading-edge technology research units out of Europe, mainly to the United States and recently also to Asia. The industry thus frequently refers to Europe losing the "R&D race". The loss of leading edge technology units could be extremely serious for European competitiveness, as several lines of evidence[21] points to the pivotal role of innovation and cutting edge technologies for long-term economic growth.

The relocation of R&D investment also means that Europe will have weakened scientific environments to nurture and retain talented researchers. This may fuel a European "brain-drain" with loss of skills and experience. In combination with the modest public research spending, this could make Europe even less attractive for pharmaceutical research activities in the future. There are already indications that industry regards Europe as a decreasingly attractive place to locate its key knowledge intensive operations. In 2002, pharma giant Novartis said it would "move the headquarters of its worldwide research organization from Basel, Switzerland, to a new $250 million, 255,000 square-foot laboratory and office facility in Cambridge, Massachusetts." In November 2006, Novartis announced that it would further expand its R&D headquarters in the U.S. by adding as much as 500,000 square feet. Another example is in the EFPIA report to the Commission, where it is clearly mentioned that 5 pharmaceutical companies have recently opened new R&D Centres in China, whereas the associated investments could have been made in Europe.

A key factor for the relocation is the trend of large pharmaceutical companies to move research activities to countries or regions with a high availability of researchers and access to specialised R&D knowledge and results[22]. Targeted and intelligent public investments in pharmaceutical R&D, including training and human capacity building activities, could thus be an important step towards the re-establishment of Europe as a highly attractive place for research activities. Increasing public financial

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20 EFPIA (2006): The Pharmaceutical Industry in Figures, Edition 2006. Brussels, European Federation of Pharmaceutical Industries and Associations.

21 OECD (2007). Innovation, Growth and Eqsuity. Key Issues. Paris: OECD – Organisation for Economic Cooperation and Development.

22 2005 EU Survey on R&D Investment Business Trends in 10 Sectors

support (supply-side policy) may not alone be sufficient to improve Europe's attractiveness for private R&D investments in the pharmaceutical sector, but it may trigger activities that contribute to an improvement of the product, labour and fiscal market conditions and thus reverse the current relocation of research activities.

2.5. Escalating Drug Development Costs and Market Failures in the Biopharmaceutical Sector

The challenges facing biopharmaceutical research and development are significant. The development of a new drug is a long, complex and resource-intensive process. Various estimates have placed the costs between $400 million and $900 million during the period 1994 to 2000 and the current trend is for the cost to increase further, as the drug development process becomes increasingly complex and resource intensive. During the previous 10 years, global R&D expenditure in the pharmaceuticals and biotechnology sector has thus steadily increased, without a corresponding increase in new medicines reaching the market and the patients.

Increasing clinical development times and investment in drug candidates that fail during late stages of development drive the high cost of developing a new medicine. This raises the challenge of optimally predicting safety and efficacy early in the R&D process i.e. making sure that successful medicines can be identified with greater certainty early in the drug discovery and development process. Reducing attrition in late stage drug development will allow for more resources to be directed at early stage development, with the aim of increasing the number of promising candidates entering into clinical trials. However, this is currently hampered by the lack of efficient tools for predicting safety and efficacy at an early stage of the drug development process.

The amount of research needed to apply and validate new technologies successfully is very substantial. Therefore no single pharmaceutical company can fund this hugely expensive and extensive research that is needed. In addition, individual companies normally do not invest in research that benefits the whole sector. There is no market incentive for a single company to invest in generating knowledge that will benefit the entire sector (including competitors). In other words there is no commercial advantage for a single company to invest in this type of research; this is why public intervention is required.

Companies small and large, regulators, governmental institutions, academics and patients need to come together to share resources and expertise to address the challenges of modern drug discovery and development. Access to knowledge from multiple organisations/stakeholders will be a key factor to overcome the obstacles. Companies mostly focus on competitive research (e.g. research to deliver a new medicine) and are not used to share data and expertise in non-competitive areas. Thus data from failed trials are often not optimally used to improve the overall drug development process. Without public intervention as, this situation will only change very slowly and with difficulties.

The public intervention could act as a neutral mediator between the different companies and stakeholders in the drug development process. In this way, the public intervention could be a focus point that would attract interest, knowledge and

investment from the pharmaceutical industry, as well as other actors in the drug development process.

2.6. The Need to Collaborate

The application of genomics and other technologies offers a real opportunity to address the challenges of drug development. Better prediction of safety and efficacy of an investigational compound as early as possible in the drug development process can be achieved, for example, by applying advances in predictive toxicology (toxicogenomics, toxicoproteomics and metabonomics), or by developing a better understanding of disease mechanisms through the use of approaches such as system biology, modelling, improved animal models and experimental medicine. Such cross disciplinary efforts can only be done in collaboration with all stakeholders in society i.e. academia, regulators, governmental institutions, companies and patients.

Companies small and large, regulators, governmental institutions, academics and patients need to come together to share resources and expertise to address the challenges of drug discovery and development. To achieve this, a new system of research collaboration will be necessary that allows companies to collaborate between themselves and with other stakeholders in the biomedical world. Companies are mostly focused on competitive research (e.g. research to deliver a new medicine) and are not used to share data and expertise in non-competitive areas, and such a system is therefore unlikely to emerge without public intervention.

2.7. The Need to Provide Support at Community Level

The European pharmaceutical research suffers from considerable fragmentation due to a rigid compartmentalisation of the stakeholders in different countries and sectors (academia, established industry, bio-tech SMEs, clinicians, regulators, patients). This fragmentation limits the free exchange and pooling of knowledge and experience between actors. Furthermore, the growth of the pharmaceutical research sector, in particular highly innovative research-intensive SMEs is often hampered by limited availability of capital due to financial fragmentation.

There are currently several interesting research projects ongoing in various member states, but they are mostly fragmented (compared to the US). The impact of such projects could be much larger if they are coordinated at the European level. In this context it is important to remember that while governments mostly plan nationally, industry plans globally, as a result of this any larger region of the world that can coordinate its efforts is generally more attractive to the pharmaceutical industry. Large countries such as the US and China have a unified investment strategy that allows the biopharmaceutical industry to better plan and leverage its resources. In Europe it is instead necessary to use a lot of resources on coordination due to the fact that member states to not operate as one on their R&D investment.

The pharmaceutical industry in Europe has strongly expressed (e.g. EFPIA, 2006) that it would benefit significantly from a closer contact and collaboration with the regulatory authorities. The majority of new medicines are now approved through the centralised European procedure (EMEA) rather than national regulations. Action at a national level would therefore have limited effect, whereas community-supported actions could establish a convincing collaboration between EMEA and the industry.

To harness the scientific know-how and expertise that exists across the European Union in the pharmaceutical sector, action at community level has been called for by the G10 high level group on innovation and provision of medicines[23], and more recently by the "Aho report[24]". The Commission has, as a response, called for "A stronger European-based Pharmaceutical industry for the Benefit of the Patient" with emphasis on the strengthening of innovation in medicines' R&D as one of Europe's key policies.

Only Community legislation can establish an operational R&D framework to combine the benefits of European integration with fast adaptivity of industrial goals and policies and with flexibility in participation. Without a focused and coherent industrial R&D programme that is able to draw on all sources of R&D investment (public and private) at European level, efforts addressing the research bottlenecks in drug development will continue in a scattered and unstructured manner. Progress will be held back by lack of coordination of industrial R&D objectives, duplication of effort, unnecessary bureaucracy, and suboptimal use of limited research funding.

2.8. Objectives for a public intervention

The preceding sections have demonstrated that the European science-based biopharmaceutical sector is facing a number of obstacles. This includes scientific and technical problems such as escalating development costs; fragmentation of knowledge and high failure rates; but also a number of serious infrastructural challenges from pharmaceutical R&D moving out of Europe; limited public spending on health R&D ; and limited access to venture capital from investors.

On this background, 3 major strategic objectives for a public intervention can be identified:

- address the growing R&D gap (with the US in particular), by attracting more public and private R&D in the biopharmaceutical sector in Europe such as to sustain the competitiveness of the sector and in a wider sense contribute to achieving the Lisbon Agenda;

- foster Europe as the most attractive place for biopharmaceutical R&D; (re-)allocation of global research funds from the private sector to Europe.

- develop a network of relevant institutions, industries, stakeholder groups, etc. to increase the collaboration and coordination of research, in order to foster creativity, entrepreneurship and critical mass.

To reach the strategic objectives, the "Strategic Research Agenda" (SRA) outlines four key research bottlenecks in the drug development process that should be targeted with the aim to:

- improve prediction of *safety* evaluation (early indications of safety problems)

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[23] G10 Medicines report "Stimulating Innovation and Improving the UU Science Base", adopted 7 May 2002

[24] *Creating an Innovative Europe: Report of the Independent Expert Group on R&D and Innovation*, "The Aho Report", European Commission, 2006. http:europa.eu.int/invest-in-research/

- improve prediction of efficacy evaluation – (early indication of efficacy by use of biomarkers & clinical performance)

- bridge knowledge management gaps – collaborating to break information barriers at the interfaces

- bridge educational gaps – "*from bench to bedside*" preclinical and clinical research, and breaking barriers between disciplines

It is important to note that the SRA addresses the drug development process itself, rather than the development of new pharmaceuticals or vaccines. The main outcome should therefore be 1) new methods, tools and techniques that are generally applicable for predicting the safety and efficacy of new medicines, 2) better tools for managing and sharing research results and knowledge, and 3) increased competencies among the researchers in the sector.

3. POLICY OPTIONS

Different policy options can be considered to confront the European R&D gap in biopharmaceutical research. The best policy option should address the strategic objectives by improving the following key success parameters:

- *System or Market Failure:* the public interventions should overcome the identified system or market failures that create obstacles to the pharmaceutical industry in the EU. They should create an R&D programme with extensive collaboration and networking between different sectors (pharma industry, SMEs and public research institutes). The specific focus should be on solving research obstacles, as identified by the European pharmaceutical industry, in the pre-competitive phase.

- *Additionality:* the initiative must lead to research being done in Europe that would not otherwise be done; and to efficiency gain in the way resources are spent. The public intervention should thus provide an incentive to industry to increase their R&D expenditures in Europe. Public money should thereby act to leverage other investments in European pharma research – whether private capital or intellectual capital – in the targeted activity.

- *European Added Value*: there should be demonstrable added value from the fact that research is done at the European rather than national or other level.

Considering these criteria, the following four policy options have been evaluated and compared:

(1) '**Do Nothing**' option, and spend on other health related research within FP7.

(2) Address the identified pre-competitive bottlenecks at **national level.**

(3) Address SRA bottlenecks at EU level under **the traditional FP (7) programme**

(4) Establish IMI set up as **JTI,** (Joint Technology Initiative), a public-private partnership with the participation of the industry and a specific legal set-up, as a *"Joint Undertaking" model on the basis of Art, 171 of the Treaty.*[25]

3.1. Option 1: Do Nothing

The *simplest* option is to take no new policy initiative and leave the market to determine where and how much research funds should be spent. In this option, no new European public money is spent on the problems identified before, and the biopharmaceutical industry is left on its own. The "Do Nothing" option would neither address the productivity problems nor the European R&D gap in the pharmaceutical research sector, and it would therefore also not contribute to the Lisbon objectives. It consequently appears as a clearly undesirable option. This is even more true on a global perspective, as several countries outside Europe seem to be taking steps to support pharmaceutical research, including the establishment of Public-Private Partnerships (PPPs) or such as the Critical Path in the US. This means that if no action is taken, problems are likely to exacerbate, leading to an increasing Europe – US research gap.

The EFPIA position paper ("Keys to Success") clearly mentions that without significant and suitable public intervention, pre-competitive pharmaceutical research projects (and the associated pharmaceutical R&D investment) are very likely to take place outside Europe through other initiatives in the US and Asia. Europe's biomedical R&D base would therefore decline together with the attractiveness of Europe as a place for the biopharmaceutical industry to invest. This is likely to create a vicious circle with further re-location of the pharmaceutical industry's R&D activities outside Europe, which will further decrease Europe's ability to sustain a competitive research infrastructure to support cutting edge academic and clinical research. Ultimately innovative medicines will be discovered and developed outside of Europe. Long term this may result in delayed access to innovative medicines for European patients.

There are also other reasons to believe that action is necessary. Individual companies are unlikely to invest in pre-competitive research activities that may benefit other companies. And even if some actions would take place, they would probably do so in a very fragmented way and without addressing the systemic failures of the pharmaceutical R&D process. Based on this analysis, the *do nothing* option does not address the problems identified before (Chapter 2).

3.2. Option 2: Address problems at the national level

A *second* option is to take action at national rather than European level. This option would present the following difficulties:

- this option would not address the fragmentation problem; the problems to be addressed have been identified as Europe wide, and national intervention would not create a long-term structural improvement

[25] Article 171 The Community may set up joint undertakings or any other structure necessary for the efficient execution of Community RTD programmes

- actions at national level would be limited in terms of industrial and academic scientific expertise available in any country. This option would also lack coordination and risk duplication.

- actions at individual national level are likely to have less critical mass, than actions at European level.

- Individual national activities are unlikely to lead to a better EU regulatory framework for the pharmaceutical sector.

3.3. Option 3: Action at EU level within the traditional FP instruments.

The *third* option involves action at the European level to stimulate research on the SRA priority areas, using the traditional instruments for collaborative research within the framework programmes.

Former Framework programmes have given us some lessons concerning the participation of pharmaceutical industry in Framework programmes. As resulting from an internal review [European Commission, 2006]; out of the 608 projects funded under the FP6 health theme, 410 involved industrial partners (SMEs and large industries), and from those 97 engaged in 'pre-competitive' pharmaceutical research (18%). Even though there was some industry contribution to these projects, it was very limited. There are only 8 projects involving more than one major pharmaceutical company in the consortium.

Thus it seems that the traditional FP instruments are not well suited for attracting industry involvement, let alone collaboration and data sharing between two or more pharmaceutical companies. The main shortcomings of the traditional FP instruments seem to be that

- Bureaucracy: projects under FP6 had important tradeoffs and challenges (some real, some perceived) – lengthy call and evaluation procedures; a whole series of bureaucratic hurdles, and were lacking specific incentives for industry involvement.

- Call topics: projects and call topics were not well designed to support demand driven research based on initiatives coming from the pharmaceutical industry. It seems likely that with a different set-up, private contribution could be much higher, particularly with the requirement that public funds are to be matched by the private investment.

Based on past experience, it seems unlikely that option 3 will take full advantage of possible *additionality*. To elicit more industry participation and additionality, an alternative mechanism should be established that is superior to the traditional collaborative framework instruments in terms of effectiveness and efficiency.

3.4. Option 4 - Establish IMI set up as JTI

The *fourth* and final option is to do launch a Joint Technology Initiative (JTI) – the proposed Innovative Medicines Initiative (IMI).

The Seventh Framework Programme (FP7) (2007-2013) introduces the concept of **Joint Technology Initiatives (JTI)** as a major innovation to **give concrete answers** to the need for **greater strategic focus, for assembling a critical mass of research in key areas, for better coordination in research, and for tighter coupling between research and innovation**.

A JTI is **a public-private partnership**, mainly resulting from the work of European Technology Platforms (ETP) to implement (parts of) their Strategic Research Agenda. JTIs have been identified by the Commission[26] as part of the FP7 to support a limited number of European Technology Platforms in reaching their objectives[27]. As reflected in the FP7 text:

"In a very limited number of cases, the scope of an RTD objective and the scale of the resources involved could justify setting up long-term public private partnerships in the form of Joint Technology Initiatives. These initiatives, mainly resulting from the work of European Technology Platforms and covering one or a small number of selected aspects of research in their field, will combine private sector investment and national and European public funding, including grant funding from the Seventh Framework Programme and loan and guarantee finance from the European Investment Bank. "

JTIs are a new type of instrument to respond to the real needs of industry and other stakeholders in a way that is not possible under the 'traditional' FP7 instruments. For the first time, the Community will offer a legal and organisational framework that allows the effective pooling of resources from R&D undertakers, the Commission and potentially other stakeholders. In this way JTIs "transcends" the Framework Programme and national programmes, integrating both in an area where urgent action and industrial strategic focus is necessary. Setting up the JTI as an integral instrument to run alongside the Framework Programme is an essential step in achieving the Framework Programme's overall objectives.

As indicated by the FP7 impact assessment[28], the implementation of Joint Technology Initiatives will contribute to the achievement of the Lisbon competitiveness objective and the Barcelona targets for research spending, identifying areas critical for European competitiveness and supporting ambitious, research agendas, which will be strategic and long-term in nature; while involving the commitment of massive financial, organisational and human resources through public-private partnerships. The main advantage of a Joint Undertaken is that it creates a strong and efficient coordination mechanism, able to structure and handle contribution coming from different fields and sector.

A key feature of the proposed IMI is that public contributions will be equally matched by industry funds. The industry contribution will be based on research

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26 "Science and technology, the key to Europe's future – Guidelines for future European Union policy to support research", COM(2004) 353 of 16.06.2004

27 Report on European Technology Platforms and Joint Technology Initiatives: Fostering Public-Private R&D Partnerships to Boost Europe's Industrial competitiveness, SEC(2005) 800, European Commission, 2005

28 "More Research and Innovation – Investing for Growth and Employment: A Common Approach" Impact Assessment (COM(2005)488 final

investments in Europe (not world wide) done in addition to industry's normal R&D spending. The majority of the research tasks to be implemented will be on development and validation of *new techniques and methods* aiming to accelerate and enhance the prediction of *safety* and *efficacy* of medicines. This will demand additional research efforts from the industry because they must for example:

– do additional R&D in parallel with the practices of today (for example run new toxicology tests in parallel with those methods that are used today),

– adapt or replace their in house result and data collection systems to be compatible with those developed by IMI for the knowledge management and sharing of data from the biomarker and safety evaluations

– increase efforts for education and training to better bridge the existing gap between disciplines and to improve the understanding of the various stakeholder views.

The position paper from EFPIA provides several reasons to believe that the pharmaceutical industry would participate and contribute actively to the success of IMI:

∉ The funding allocated to IMI provides a level of predictability for industry which is absent in models in which projects compete for more general funding.

∉ The research priorities of IMI will be demand-driven. Public institutions will therefore orient their activities better for collaboration with the private pharmaceutical sector. This will create more interfaces between the public and private sectors, and will catalyze tighter and more efficient collaborations than traditional cooperation programmes. As industry gains access to efficient and focused collaborations, it is likely to engage more resources in such activities, thus leveraging the IMI investment.

∉ IMI permits companies to collaborate between themselves and with other stakeholders in the pharmaceutical world. The role of the European Commission as an "honest broker" in facilitating new partnerships is highly appreciated by the pharmaceutical industry.

∉ Industry thinks that IMI would provide easier possibilities to have closer interactions with EMEA and give EMEA early on a chance to give feedback on new development in the drug development process.

∉ The obstacles facing the drug development process are becoming so huge that no single company has the knowledge or resources to overcome them in isolation. Higher critical mass and impact can be reached through IMI to solve the complex difficult problem of predictability of safety and efficiency of drugs.

∉ Simpler financial and administrative procedures than in the cumbersome procedure of the FP contracts.

IMI will ensure private sector investment in the sector at equal level as the Community contribution, i.e. each € 1 of Community funds will leverage € 1 of

private sector investment. Due to this co-financing principle, IMI will anchor a minimum of 1 billion € of private R&D investment in Europe and generate research worth at least € 2 billion.

In-kind contributions from other industrial participants in the research activities (like e.g. Health Information Technology companies) and also complementary contributions from the participating SMEs (apart from the Community funds received via the IMI research projects) will add to the investments by the pharmaceutical industry, as these contributions are not included when calculating the matching funds from the pharmaceutical industry.

There is considerable econometric evidence that public funding of R&D carried out by enterprises leads to what is called a *crowding-in* effect on investment: it stimulates firms to invest more of their own money in R&D than without public intervention. Recent studies performed by the European Commission and others estimated that a €1 increase in public R&D investment induces overall on average € 0.7[29] - 0.93 of additional private sector investment[30].

Since, industry is heavily involved in setting the research priorities of IMI, a substantial *crowding-in* effect can be anticipated, likely to reach an even higher level than the average.

Furthermore, the establishment of IMI should also increase the general activity level of the pharmaceutical sector. This may have a positive effect on the behaviour of venture capitalists, leading to more investments in European biotech, and the potential creation of new companies.

Taken together, the total private investments mobilised by IMI will therefore be significantly higher than the matching in-kind contributions to be provided by the EFPIA member companies. It. It seems therefore clear that IMI can provide a much higher degree of *additionality* than any of the other options considered.

4. STRUCTURE AND GOVERNANCE OF THE IMI

The IMI JTI shall be implemented via the establishment of an independent legal entity, the Innovative Medicines Initiative Joint Undertaking (IMI JU) created under Article 171. The IMI JU will award research grants to support the implementation of the Strategic Research Agenda. All stakeholders will be eligible to participate in IMI projects, the only condition being that the research is performed in Europe.

The IMI governance structure has been developed by a governance taskforce comprising representatives of the Commission and EFPIA. The objective of this taskforce has been to ensure that the two partners funding IMI are aligned with the proposed governance structure.

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29 Guellec and Pottelsberghe (2003). "The impact of public R&D expenditure on business R&D", Economics of Innovation and New Technologies, 12(3).

30 SEC(2004)1397: European Competitiveness Report 2004

4.1. Decision-Making and Management Bodies

The governance structure of the IMI JU consists of one decision making body - the IMI Board, a management body - the Executive Office, and an advisory body - the Scientific Committee. In addition, a Member States Group and Stakeholders' Forum will ensure co-ordination with national activities and transparency of IMI activities towards all stakeholders (see Figure 4-1):

The governance structure reflects four basic principals of IMI: scientific excellence, collaboration, transparency and efficiency. In this context, industry has emphasised the strong need for a lean, streamlined governance/management with as little bureaucracy as possible.

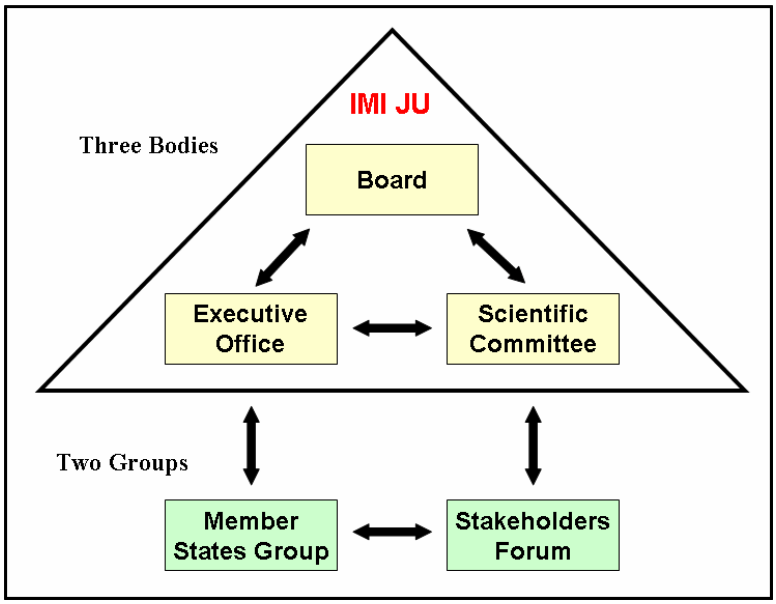

Figure 4-1: IMI JTI Governance structure

4.1.1. The IMI Board

The IMI Board will be composed initially of the Founding Members of the IMI JU, i.e. the European Commission and the European Federation of Pharmaceutical Industries and Associations. The Board will be responsible for the overall operations of IMI and implementation of the Strategic Research Agenda. To prevent potential conflicts of interest, Board Members cannot participate in Projects. The Board will be composed of five representatives of the European Commission and five representatives of EFPIA. It is proposed that the initial Board, composed of the EC and EFPIA representatives, shall aim at making decisions by consensus. Its Chairperson will rotate on an annual basis between the Founding Members. The IMI shall be open to new members, and the representation and voting rights of new members shall be proportional to their financial contribution to the IMI JU. The EC shall in any case maintain a veto right for any decisions concerning its contribution to the IMI JU.

4.1.2. The Scientific Committee

The Scientific Committee will be an advisory body to the Board and it shall conduct its activities in close liaison and with the support of the Executive Office.

The Scientific Committee is composed of a maximum of fifteen members. When members complete their term or resign, the Member States Group, working with the Scientific Committee, will be asked to produce a shortlist of replacements. After approval of the shortlist by the Board, final selection will be made by the Member States Group[31]. The Member States Group then makes the final selection, in accordance with specific selection criteria approved by the Board. This is to ensure a balanced representation of expertise across the IMI stakeholders e.g. academics, patients, regulatory authorities and industry. The chairperson of the Scientific Committee is elected from within the Scientific Committee and serves for a non-renewable 2 year term. The other members serve for a 3 year term, which is, subject to approval by the Member States Group, renewable once for an additional term of 2 years. The chairperson of the Scientific Committee may attend the Board meetings at the invitation of the Board.

4.1.3. The Executive Office

The Executive Office will be responsible for the day-to-day operation of IMI. It will consist of an Executive Director and supporting staff. Its activities will be set out in the 'Internal Regulation' document, which is approved by the IMI Board. The Executive office will play a key role in ensuring that the relevant stakeholders participate in IMI, by, among other things, planning outreach and communication activities to build awareness of IMI.

4.1.4. The Member States Group

The Member States Group will consist of nominees from all Member States and Associated Countries. It shall approve the composition of the Scientific Committee. It will facilitate rapid dissemination of information between IMI and Member State activities, and ensure co-ordination with Member State activities. In addition, it will play a leading role in the implementation of certain strategic parts of the Strategic Research Agenda, such as Education & Training.

The role of the Member States Group acting on behalf of Member States will be to facilitate communication between IMI and the EU Member States and Associated Countries.

The Member States Group shall include representatives from the: EU Member States and Associated Countries. The Member States Group will be invited to ensure an efficient communication between IMI and the relevant stakeholders and/or organisations within their respective countries. It shall in particular be invited to ensure the dissemination of information in their respective countries regarding calls for proposals, calls for experts or meetings organised by IMI.

The Member States Group shall be responsible shall be responsible for the implementation of some specific areas and/or topics of the Strategic Research Agenda, in particular concerning Education & Training, which falls within the rules for subsidiarity.

[31] Initially forty prospective members are short-listed by the Board

4.1.5. The Stakeholders' Forum

The Stakeholders' Forum will be an important communication channel to the European IMI stakeholders to ensure transparency and openness of IMI activities. Its role will be to disseminate the activities of IMI and to provide independent commentary on the progress of the implementation of the Strategic Research Agenda. Additionally the Stakeholders' Forum will be able to suggest proposals on the way forward for IMI. A Stakeholders' Forum will convene each year. There will quotas to ensure balanced representation of the different groups of stakeholders. As a guiding principle, representation should aim at reaching the following proportions:

∉	Universities, Hospitals, public research:	25%
∉	Large industry:	25%
∉	SMEs[32]:	25%
∉	Regulatory Authorities:	10%
∉	European Commission:	5%
∉	Patient organizations:	10%
∉	Member States Group Representatives	All Members

4.1.6. Funding Process

The proposed EC contribution to the IMI Joint Technology Initiative is €1 billion for the period of the 7th Framework Programme (FP7 2007-2013). EFPIA (in cash for management costs) and the pharmaceutical companies that are full members of EFPIA (in kind for research activities) shall contribute with resources at least equal to the EC contribution. The total resources available to the IMI JU shall therefore reach at least €2 billion for the FP7 period.

The EC contribution shall be earmarked for academic and SME participants in IMI projects, while biopharmaceutical companies (and other companies not being SMEs) shall fund their own contributions to 100%. With this structure, public money will therefore go exclusively to public sector participants and SMEs, and not to biopharmaceutical companies. The bio-pharmaceutical industry partner(s) will provide in-kind contributions to match the FP7 funds through R&D resources such as staff, laboratory facilities, materials and clinical research activities.

[32] Micro, small and medium-sized enterprises or SMEs are defined by the European Commission as: enterprises which employ fewer than 250 persons and which have an annual turnover not exceeding €50 mn, and/or have an annual balance sheet total less than €43 million32. IMI will apply the same definition.

The funding mechanisms of IMI are described in figure 4-2 below.

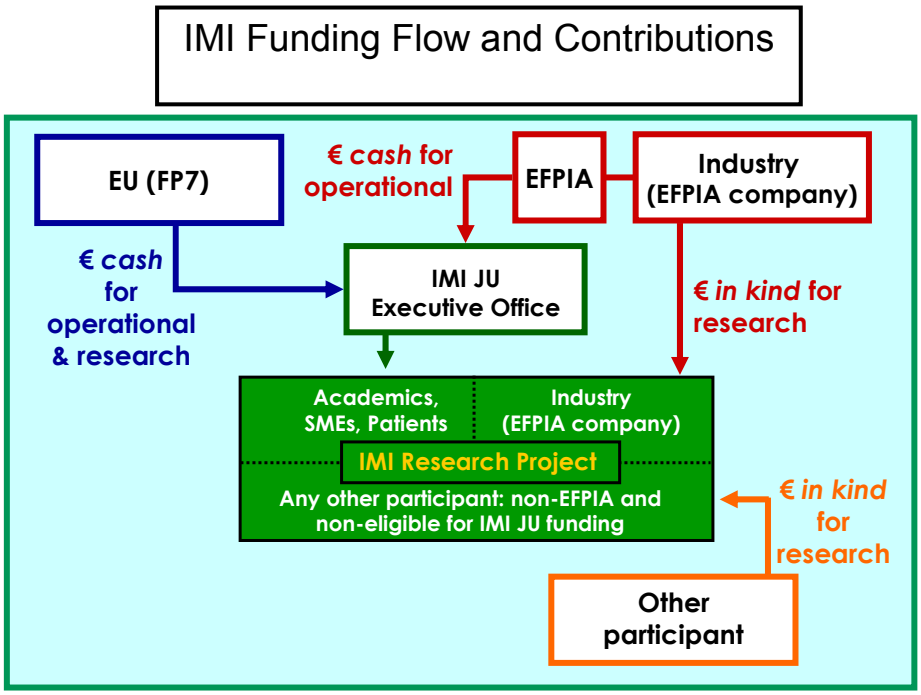

Figure 4-2: The overall principles of the IMI Funding mechanism

In order to ensure total transparency on the IMI costs, every year IMI's annual accounts and balance sheets for the preceding year shall be submitted for audit to ascertain that the biopharmaceutical industry has meet its commitment to match EU funds with in-kind contributions.

5. ANALYSIS OF IMPACTS

Given its size and duration, the potential impacts of IMI are likely to be manifold and substantial. This Chapter will review the expected economic, societal and environmental impacts of the IMI.

5.1. Economic Impact

In view of the lengthy and highly complicated nature of the drug development processes, many of IMI's expected impacts will be cumulative over time within the European pharmaceutical science base and industry, ultimately leading to **more** efficient and effective ways of developing innovative medicines.

Many of the *short term outcomes* (i.e. 2-3 years after IMI launch) will relate to improvements of scientific quality and enhanced knowledge production, network-based R&D capacity building, and human resources development. The *mid term impacts* (4-5 years after IMI launch) should include concrete results on biomarker validations and toxicology tests, along with shared IT facilities and other data-sharing infrastructure to improve communication and knowledge transfer. The *longer term* 'wealth and health' benefits will comprise improved economic performance,

such as increased competitiveness at the European level, securing employment in the pharmaceutical sector, and eventually new medicines and related medical treatments.

5.1.1. More efficient and effective research within the sector

R&D-intensive companies that actively participate in IMI may gain a range of longer-term competitive advantages. More specifically: cheaper, more efficient and effective drug development processes characterised by lower attrition rates, more compounds and promising drug candidates in the pipeline, less failures or withdrawals during clinical trials and post marketing stages. IMI will provide the organisational framework to ensure that dispersed research results are rapidly gathered and validated and, if appropriate, translated into practice.

Reduced R&D costs, less uncertainties and lower risks also help create new long-term investment options and to maximise investments.

Better cooperation and contact between industry and regulators may also be an important aspect of the IMI organisational structure that may result in faster approval of new drug candidates. The economic impact of the IMI objectives is difficult to quantify in exact terms, but simpler and quicker procedures will have a knock-on effect in terms of the productivity of the research process, allowing research results to be brought to market more rapidly. This *reduced time-to-market* is, potentially, one of the most significant of IMI JTI's benefits.

5.1.2. More efficient use of EU funds

A further benefit of IMI will be an **increased efficiency of EU-level disbursements** compared to the traditional spending or similar disbursements at national level. The Impact analysis for the Seventh Framework Programme[33] shows that in the long run (by 2030), FP-level disbursements will have 89% more impact on GDP per euro invested and a 20% greater impact on jobs than the same funding allocated at national level (Table 5.1). It is reasonable to assume that at least similar benefits could apply between the IMI JTI and the "Do Nothing" Scenario. Indeed, the expected €2bn of investments spent through the IMI JTI (matching the Commission's €1bn of national moneys) can be assimilated to EU disbursements since they will be allocated through common European procedures and focused work plans as in the Framework Programme, whereas in the "Do Nothing" scenario's this money is disbursed according to the different priorities of national programs.

[33] Impact Assessment and Ex-Ante Evaluation of the 7th Framework Programme, Commission Staff Working Paper, SEC(2005) 430, European Commission, 2005

Table 5-1: Comparison of Framework Programme disbursement versus national level disbursements

	Framework Programme disbursement	National disbursement	Ratio FP : national
GDP	0.51	0.27	1.89
GDP corrected for quality	0.82	0.35	2.34
Extra-European export	0.73	0.07	10.43
Extra-European imports	-0.35	0.21	-1.67
R&D intensity	0.061	0.058	1.05
Research employment	40 400	33 500	1.21
Total employment	492 600	428 400	1.15

Source: FP7 Impact Assessment

5.1.3. Increased Industrial R&D investments

IMI is expected to leverage a larger industry investment in research activities than the traditional EU funding mechanisms. The larger pharmaceutical companies will not receive any public funds, but will be committed to invest in-kind research at an equal level to the EC funds. This means in practical terms that R&D worth 2€ will be done for each 1€ invested EC funds. Industry's in-kind contributions to IMI will also act as a safeguard that the industry will be committed to longer-term objectives. This will potentially develop into new research infrastructures, R&D networks, and the creation of new companies and spin offs. IMI's anchoring of industry funds in European pharma research will increase the general activity level of this area in Europe. This will make the sector more attractive overall, and will increase the likeliness of additional research activities being brought to Europe.

5.1.4. Industry infrastructure and new business activities

By bringing together different actors from different areas of the pharma research sector, IMI is expected to create a critical mass of resources and shared facilities that can result in new business activities and creation of small dedicated companies. IMI also offers considerable benefits for existing SMEs in terms of lowering their costs of technology development and the risks involved when technology development is shared with industrial end-users (mostly the big pharma firms). Being an IMI participant, and benefiting from a clear-cut IPR regime to protect their assets and innovations, also entails less risk for venture capitalists, thus increasing access to venture capital funds. IMI projects may thus provide a low-risk seed bed for SMEs to develop new applications of existing technologies.

5.1.5. Employment, foreign investments and tax revenues

If IMI proves to be a successful platform for effective public-private cooperation and R&D coordination, it will contribute to maintain high skilled, high-income jobs in Europe - at first in the R&D undertakings and at a later stage in supporting industries. A more R&D intensive, competitive and innovative European pharmaceutical industry could lead to an influx of non-European research-intensive pharmaceutical companies and foreign direct investment in order to gain the benefits of improved value for money. Increased economic activity will also generate additional tax revenues through the production of new innovative drugs and maintained or increased employment.

5.1.6. Better cooperation and more effective research partnerships

The large biopharmaceutical industries do not have a history of pre-competitive collaboration and have never shared data before; this pooling of data between different companies does not exist today, but the FP6/InnoMed project has proved the principle, feasibility and willingness of industry to share such data [InnoMed Project, 2006].

IMI provides opportunities to (further) develop and shape dedicated European R&D networks focussed on closer cooperation between knowledge suppliers and users within the European pharmaceutical sector. IMI will address and facilitate the increased need for collaboration between private and public actors of biomedical research by providing an open platform for early involvement and collaboration with relevant partners and stakeholders. IMI will provide pre-competitive knowledge that was previously out of reach. IMI's joint agenda, and the planned quick dissemination of project results, will facilitate that insights from one project will feed into another project. This incentive system may stimulate firms to invest more resources within Europe and engage in sustainable collaborative arrangements with European public research organisations.

IMI-related cooperation and networking will also act as learning vehicle to increase the absorptive capacity of industry for accessing, accumulating and utilizing new knowledge, capabilities, techniques and skills. Successful cooperative arrangements will be characterised by commonly agreed research agenda's, shared ownership of research drivers (information, problems and expectations), and the willingness to reconcile different perspectives and (potential) conflicts of interest.

Another positive effect may be an increased awareness of a 'European knowledge market' in terms of (early access to) applicable knowledge, cutting edge technologies, expertise and top-level experts, and other valuable assets that are complementary to industry's own resources. IMI opens doors to this market by providing new potential partners for further research cooperation and co-development of drugs, and offering opportunities for recruitment and employment. IMI will act as an interface for access to relevant experts in other companies and research organisations. The transfer of skills and knowledge through people across national frontiers offers European-wide synergies that transcend the capabilities of individual Member States. This would also raise the overall profile of Europe as the most attractive location in the world for undertaking pharmaceutical research.

5.1.7. General Economic Impacts

Other aspects of the economic impact of IMI are summarised in the table below.

Table 5.2: Economic Impacts

Impacts on:	***IMI JTI impacts relative to the "Do Nothing" scenario***
Competitiveness, trade and investment flows	∉ IMI will promote *a greater efficiency of resource* allocation within industry and therefore a more efficient EU pharmaceutical sector, increasing its *competitive advantages of* (compared to non-EU rivals. ∉ It will have a key role in *leveraging private sector resources* within the EU and *attracting R&D investments* from *non-EU* owned pharmaceutical companies (including relocation of R&D activity) ∉ All this is likely to retain *high-quality high-income* jobs within the EU.
Operating costs and conduct of business	∉ Introduction of a new paradigm for drug R&D research - within collaborative arrangements (both public-private partnerships and inter-firm partnerships) ∉ Cost and time savings to industry through *efficacy* improvements ∉ Shared key results: available under non-proprietary/open source terms or under a IMI-specific property rights regime serve to all parties involved ∉ The *cost of running* IMI is small compared to its potential benefits.
Innovation and research	∉ It will contribute to the *development of new technologies* and *procedures*; improved efficiency and profitability of industrial R&D ∉ It will *strengthen Europe's global research position,* in particular in a well-defined *area of critical importance*, and by *pooling and coordinating research* in an integrated programme, and via an 'signalling effect', reorienting private and public European research agendas. ∉ Increase the propensity of research partners to *collaborate* in the future (structuring effect, behavioural additionality) and contribute to the pan-European embeddedness/connectedness and mobility of additional human resources in the area. ∉ Creation of *economies of scope*, through a 'centrally managed' research agenda and the planned prompt dissemination of project results. ∉ Serve as a basis for the establishment of *new research infrastructures and facilities;* create and also sustain for a longer period of time pan-European, cross-sectoral (firm, university, research institute), cross-size (large firms, small firms), inter-disciplinary networks between institutions and researchers. Via those networks allows

Impacts on:	*IMI JTI impacts relative to the "Do Nothing" scenario*
	for the pooling of financial and complementary specialised knowledge resources to achieve critical mass (economies of scale), quicker achievement of results, and enabling a more rapid dissemination of information and transformation of research results into new processes. ∉ Increase attractiveness of Europe to *foreign researchers and companies*.
Administrative costs on businesses	∉ Cost of running IMI will be small compared to the benefit ∉ Model foreseen is for a small and lean entity
Consumers and households	∉ IMI JTI results are expected, on the long run, to lead to a *wider availability of new and safer medicines*.
Specific regions or sectors	∉ Related to the *biopharmaceutical industry*, but may gradually impact on other related sectors such as the *wider medical sector.* Increased R&D cooperation between large pharmaceutical firms and *SMEs*.
Third countries and international relations	∉ Fostering of R&D collaboration with *companies and international partners globally active* and / or outside the EU. ∉ Contribution to the promotion of *new international standards f*or testing of new chemical/molecular compounds.
The macroeconomic environment	Addressing systemic failures within the biopharmaceutical industry, if successful, it will certainly impact the European *macroeconomic environment* through a combination of all the above.
Public authorities	∉ Funding of IMI will partly come from public money which will have a key role in leveraging private sector resources (leverage factor for Community contribution will be **higher** than 1:1)

5.2. Social and Environmental Impact

The IMI Strategic Research Agenda – and by implication the JTI – implies a variety impacts at the societal scale (IMI's environmental impacts are non existent or of minor significance). IMI's impact in terms of generating or maintaining high quality jobs was already mentioned above. Ultimately IMI-based results are expected to make a significant contribution to the production of new medicines with significant benefits to health care (preventing illness, treating diseases, reducing hospitalization), but many other effects and benefits are likely to occur during IMI's time-span. IMI's societal impacts are summarized below in Table 5.2. While a number of societal impacts are thus expected from IMI, no significant environmental impacts are foreseen. The wide variety of societal impacts can be classified under the following broad headings:

5.2.1. World-class science and specialized research facilities

IMI's calls of proposals are likely to be an effective way of promoting more intense competition between European universities and research centres, leading to higher quality. IMI's concerted efforts will not only contribute to the development of a pool of new industrially relevant knowledge, but also help create a high-quality knowledge base that is sufficiently broad and specialized to tackle a wide range of related R&D issues of industrial relevance. IMI's R&D projects will therefore not only contribute to European specialization in this area, but also leading to increased levels of R&D excellence. The participating universities and research institutions responsible for breakthrough discoveries and innovative technologies are likely to increase their European and global prestige, providing new opportunities to attract high-quality students and recruit top rate R&D staff (including those from outside the ERA). In the event of IMI projects opening up new areas of research and domains of application, it is likely that these developments will lead to the creation of new research facilities, further boosting the influx of skilled human resources and creating career opportunities for talented young researchers.

5.2.2. Transfer of knowledge and skills

The existence of sophisticated research infrastructures and high-quality teaching and training facilities tend to create significant mutually reinforcing and cumulative effects. IMI projects specifically devoted to teaching and training activities will boost the numbers of skilled professionals within the ERA and employed by European industry. IMI will contribute to Europe-wide education and training in this field of expertise; to better bridge existing gaps between disciplines, and to improve the understanding of the various stakeholder views. Dissemination and sharing of results is increasing the innovative value of research and maximizing the social return.

5.2.3. Health related impacts

Although IMI's main objectives focus on short term and medium impacts, the reduction in R&D costs and increasing the efficacy of drug discovery and development being the main aims, IMI's contribution's to strengthening application-oriented research within Europe's biomedical R&D environment will also benefit patients and society as a whole. Better research in biomarkers of safety and efficiency is likely to lower adverse drug reactions and improved patient safety and concordance.

The faster availability of drugs is likely to lead to better treatment for patients and thus to better health outcomes. More effective medicines lead to a better use of the national budgets devoted to purchasing and reimbursing the cost of innovative medicines. Such improvements of health systems is obviously a long term objective, and new methodologies should be developed to measure their health impact (see below).

5.2.4. General Societal Impacts

Other aspects of the societal impact of IMI are summarised in the table below. No major environmental impacts of IMI are expected.

Table 5.3: Societal impacts

Impacts on:	***IMI scenario relative to the 'Do Nothing' scenario:***
Employment and labour markets	∉ Leading to the *creation or at least anchoring of existing jobs* in the pharmaceutical sector in Europe as well as in the public research sector.
Standards and rights related to job quality	∉ Increase the *added-value of relevant existing R&D jobs* across a wide range of application domains.
Social inclusion and protection of particular groups	∉ Contribution to social inclusion by involving patient groups in the early stages of drug development
Equality of treatment and opportunities, non-discrimination	∉ Not relevant
Private and family life, personal data	∉ Improving availability of quality and safety medicines
Governance, participation, good administration, access to justice, media and ethics	∉ Creation of new working methods and structures for *cooperation and coordination* across industry, public research organizations, and other stakeholders from organized civil society. ∉ *Governance structure* fostering the participation of stakeholders: large industry, SMEs, academia, national public authorities, regulatory authorities, and the Commission. Each of these groups will participate to the decision-making process.
Public health and safety	∉ Contribution to the production of innovative medicines.
Crime, Terrorism and Security	∉ Not relevant
Access to and effects on social protection, health and educational systems	∉ As above, with regard to innovative medicines. IMI *knowledge management* will complement curricula within European educational systems.

6. INDICATORS, MONITORING AND EVALUATION OF IMI

6.1. Measurements and Indicators

European Pharmaceutical Industry agreed in their report to a set of performance indicators for IMI. These indicators are very similar to the ones proposed by the independent expert group. The expert group specially insist on comparable and measurable information that is gathered and analysed within a pre-specified

organisational structure with appropriate feedback mechanisms involving all IMI participants and stakeholders.

The experts propose a dual approach. Firstly, a quantitative approach on key measures on a large scale, which are conducted in a comparative and systematic manner and, secondly, a qualitative approach by conducting case studies and surveys done by expert panels and scientific committees. They advice also to perform a series of baseline studies which should focus on the state of affairs in the pre-IMI area (2005-2006-2007) in order to help assess IMI's additionality effects during its life time.

Some of the most important performance indicators as agreed by industry are the following:

1. To measure the impact of IMI on EU competitiveness:

The number of pre-competitive pharmaceutical collaborative research projects established in the EU as a proportion of those established globally;

The investment in EU pre-competitive pharmaceutical collaborative research projects as a proportion of the investment in these projects globally;

Number (and/or budget) of clinical projects performed in the EU: e.g. conduction of phase I, II and III clinical studies in Europe required to support safety and efficacy projects.

Per year, the number of pre-competitive pharmaceutical collaborative research projects established in the EU;

Per year, private investment in pre-competitive pharmaceutical collaborative research projects in the EU;

Over the duration of IMI, evolution of the private investment in pre-competitive pharmaceutical collaborative research projects in the EU;

Over the duration of IMI, evolution of the investment of the biopharmaceutical industry in R&D in the EU in comparison with the rest of the world;

2. To measure the impact of IMI Scientific Environment:

Per year, the number of validated biomarkers including chemical, toxicological and imaging that have been established and used in clinical trials.

Per year, the number of new or amended EMEA guidelines related to the use of new technologies in drug discovery and development;

Per year, the number of new EMEA guidelines including surrogate end points;

Per year the number of recalls and restrictions in use due to safety reasons

The change in median time to approval by therapeutic area.

6.2. Monitoring and Evaluation

The progress and efficiency of IMI is going to be closely monitored, via evaluating processes installed at different levels:

IMI's scientific progress is going to be monitored continuously through the central coordination performed by the Executive Office, which is going to be in charge of the operational tasks within the IMI joint Undertaking (as foreseen in IMI's governance structure). According to the four pillars of the SRA, equally four operational units are foreseen in the Executive office, thus ensuring a very tight follow-up of the projects selected and funded.
This close project follow-up will permit the Executive Office to draft its annual IMI progress report, which will include scientific, financial and managerial aspects and is to be presented at the annual Stakeholder Forum and further on to the IMI Scientific Committee and to the IMI Board. The Scientific Committee, consisting of high-level scientists, will give its view on the progress of the running projects and, based upon that as well as on advances of the field occurring in the global scientific scenery outside IMI, provide input and advice on potential changes to the content of the SRA and the strategic priorities to be set for the future calls.

Besides this "IMI-internal" monitoring, an annual reporting to the European Council will be performed by the Commission, in presenting the annual IMI implementation report that will include the IMI progress report together with an update on the implementation status and on the financial situation of the IMI Joint Undertaking.

At mid-term, an evaluation of the IMI Joint Undertaking is to be carried out by independent experts for the Commission. This evaluation shall cover the quality and efficiency of the IMI Joint Undertaking and progress towards the objectives set. The criteria for such an evaluation will be based upon the performance metrics and indicators mentioned in the section before, to the extent, as the output or impact is already comparable and measurable. In order to gather and analyse this information, a pre-specified organisational structure with appropriate feedback mechanisms involving IMI participants and stakeholders is to be set up (sort of semi-independent group). The Commission will communicate the conclusions thereof, accompanied by its observations to the Council.

At the end of 2013, the Commission shall conduct a final evaluation of the IMI Joint Undertaking. The results of the final evaluation shall be presented to the European Parliament and the Council.