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Innovative Medicine Initiative (IMI) – A New European Technology Platform for the European Pharmaceutical Research and Development

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Abstract:
Due to the fact that Europe has lost its major place as a global centre for biomedical research the European Commission has created Innovative Medicine Initiative (IMI) as a new European Technology Platform for developing the European pharmaceutical research and development. The European Technology Platform is an instrument under development by the European Commission to address major economic, technological or societal challenges enabled by Research and Development. IMI is one of the 25 Platforms. It addresses the future of biomedical research in the EU with the aim to develop safe and more effective medicines in Europe. Its main goal is to revitalize the European biopharmaceutical research environment and create a world leadership in this area. Its aim is to remove the obstacles that prevent drug development process identified by industry. The initiative was developed by different stakeholders in the form of Strategic Research Agenda (SRA). The basic concepts of the SRA are: 1) Prediction of safety, 2) Early indication of efficacy, 3) Knowledge Management and 4) Education and Training. There were recommendations developed for each of the concept. European Commission decided on substantial budget and financing of the initiative. Europe will highly benefit from IMI by increased economic value, creating new jobs, education and training, by creating healthier society and citizens. Patients and patient organisations, clinicians, health departments, research councils and general public will all benefit from this initiative.

Keywords: Innovative Medicine Initiative, biopharmaceutical research, European Technology Platform, Strategic Research Agenda, FP7

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1. Introduction

1. 1. Analysis of strength and weaknesses in Europe

Europe has an outstanding record of success in biomedical research. It has made innumerable contributions to every branch of medicine and the related sciences. There is an equal success in pharmaceutical R&D as well. Europe was the cradle of the pharmaceutical industry and dominated it for decades. Today the scene is very different. A number of countries outspend and outperform Europe.

Europe has lost its major place as a global centre for biomedical research. Despite a five-fold increase in the pharmaceutical trade surplus over the last five years investment in R&D has declined dramatically compared to the US. There are also new competitors emerging in China and India. Over the last decade US has invested far more in public sector sponsored biomedical research. Europe has not yet matched this **level of public sector investment.** This is affecting and will continue to affect the growth and development in Europe to the detriment of both patients and society.

Biomedical research not only improves health, it also contributes to the improvement of quality and quantity of life. Investment in biomedical research does not only lead to better health, it also creates wealth. The pharmaceutical industry benefits the EU every year by contributing over 25 billion Euros in net balance payments. It has the **most successful high-tech industry Europe** has ever had. The pharmaceutical industry is the fifth largest employer in the industrial sector, providing 582,500 highly qualified jobs, investing 19,8 billion Euro every year in research and developments and producing annually over 40 billion Euro trade surplus (McKillop 2004: 1).

At one of the forums organised by the European Union it was announced that Biomedical research is impending a revolution. Understandings of the human genome are **those unknown technological advances** that could lead to huge new developments. There is an immense scale of opportunities for developing biomedical research in Europe at present: from improving treatment for the 300 million people who suffer from atherosclerosis, to confronting the epidemic of obesity, to treating multi-drug resistant infection.

1. 2. Barriers in the way of developing biopharmaceutical research in Europe

Why is Europe lagging behind in pharmaceutical R&D, why it is giving up its position of enormous strength in biomedical R&D?

One factor is **underinvestment in** pharmaceutical products and healthcare, which is due to a fundamental difference in attitude to innovation in the US and Europe. **Innovation is estimated more in the US than in Europe** – the US is starving for it, while Europe has become precautious.

There are structural problems as well. Europe is full with laws and regulations therefore it is not functioning well. Across Europe there is very little facilitation of academic-industrial collaboration that was achieved in the US a decade ago.

A set of market distortions in Europe is an obstacle as well. Different European countries have introduced various mechanisms to control supply and demand of pharmaceutical products. According to the Treaty of Rome the free movement of goods and services across Europe means that if a country sets the lowest price for a product it becomes the major source of that medicine across Europe. Parallel trading causes lost of profit for pharmaceutical companies, much of which could be reinvested in R&D in Europe.

It is very costly to produce new d*rugs an*d introduction of them often goes all awry due to failure of the preclinical studies and to the **inadequate regulatory processes**. The main factors resulting in project failure are either lack of efficiency (25%), clinical safety concerns (12%) and toxicological findings in pre-clinical evaluation (20%). The greatest need for the pharmaceutical industry is to detect the possibility of failure as early as possible (Ismail and Landis 2004 cited in SRA 2005: 10).

Improvements of predictive biology and incorporation of new concepts into an improved regulatory framework would decrease the costs of drug development and speed up the delivery of new drugs to patients.

In most European countries there is still **a big gap between academia and industry** in case of government sponsored research and development that prevents coordination and joint efforts of these stakeholders.

2. Innovative Medicine Initiative: its aims and objectives

Innovative Medicine Initiative (IMI) is a proposal that deals with different issues connected with the future of biomedical research in the EU, and addresses ways of achieving exceeding development in the production of safe and more effective medicines, that aims to revitalize the European biopharmaceutical research (European Commission 2002).

The initiative suggests that **by pooling resources from all stakeholders** – academia, industry, small and medium sized enterprises, regulatory authorities, healthcare providers and patient authorities – a quicker access to new drugs may be achieved.

The overall objective of IMI is **to remove barriers that prevent the efficiency of the development of new medicines** to enable the European biopharmaceutical industry to become world leader where research is the first priority.

2. 1. Creation and Development of IMI

The European Commission is developing **European Technology Platforms (ETPs)** to promote innovation in Europe. They are an effective means of defining research and development priorities in a number of important areas of research where Europe has to become competitive both in the medium and long term. By means of ETPs Europe will achieve a better structuring of activities in one or another area of Research and Development. Europe is not capable at present to transform knowledge into commercial products and services. European Technology Platforms are assisting in increase of Europe's innovative capacity.

ETPs are bringing together stakeholders in key economic sectors in order to:

- Develop a long term vision of the sector,
- Create a strategy for delivery, and
- Establish a management structure to ensure maximum impact.

The Commission has recently initiated some 25 different Platforms in various areas of R&D. There are usually three stages of developing ETPs:

- getting together the stakeholders (in this industry plays an initiating role, the top executives of the leading companies are usually producing a vision document, which explains the strategic importance and outlines the development objectives)
- defining a Strategic Research Agenda (it is the main deliverable of the ETP, it prioritises the research and technological development in the medium and long term, it is coordinated by an industry advisory Council, the key elements for implementing of SRA are also defined at this stage) and
- implementation of SRA (during this phase the implementation of SRA with support of community research programmes).

On January 2002, the European Commission published its Communication on Life Sciences – a Strategy for Europe (European commission 2002). In this document the areas of life sciences and biotechnology are regarded as one of the frontier **science and technology areas that are** most promising for the coming decades. Life sciences and biotechnology are able to facilitate the development **of many technologies – like information and nano-technology** – and serve the benefits of both public and private sector. **European Technology Platform** is an instrument under development by the European Commission to face major economic, technological and societal challenges enabled by Research and Development. It is anticipated to contribute to achieving the Lisbon objectives, to develop the European Research Area and increase investment in R&D towards the 3% of GDP target (European Commission 2002).

One of the initiatives of the European Technology Platforms was " Innovative Medicine for Europe", under which the European Federation of Pharmaceutical Industries and Associations (EFPIA) has published in May 2004 **a vision paper for Creating biomedical R&D leadership for Europe to benefit patients and society** (EFPIA 2004).

This document outlines the four basic concepts on which the initiative is built:

- Prediction of Safety;
- Early indication of efficacy;
- Knowledge management;
- Education and training.

2.2. A vision for IMI and a Strategic Research Agenda

It was envisaged that we need a common European vision and a Strategic Research Agenda. The vision was formulated that we have to create biomedical R&D leadership for Europe to benefit patients and society. As Europe has a decreased investment in R&D, the European Commission is exploring ways to achieve the Lisbon goals. The European population is aging, the pharmaceutical R&D costs are increasing, and there is a pressure on prices. Applying new technologies to drug discovery requires a development and active participation of all stakeholders, such as Research based Pharmaceutical Industry, Physicians/healthcare Professionals, Academia, Small and Medium Sized Enterprises, Regulators, EU policy makers. Science and Technology advances present significant opportunities for better understanding of mechanisms of diseases and drug development. It promotes a more efficient drug discovery and development, faster production of better medicines that result in a more healthy EU population.

3. Strategic Research Agenda (SRA)

The European Federation of Pharmaceutical Industries and Associations' (EFPIA) Research Directors Group with the participation of the European Commission and the involvement and contribution of key actors – the European Medicines Agency (EMEA), national regulatory agencies, clinical and academic researchers from various institutions, SMEs and SME associations, patient organisations – has developed **The Strategic Research Agenda** (SRA 2005). A series of workshops have been held in the first half of 2005 with involvement and contribution of all stakeholders for defining the research that needs to be addressed in order to achieve the overall objectives. The components of the Strategic Research Agenda for Innovative Medicines are 1) identification of the bottlenecks of the R&D, 2) Analysis of current strength and weakness in Europe, 3) recommendations to address bottlenecks, 4) definition of the necessary research and technical priorities in the medium and long term, 5) estimation of resources and timelines and 6) the framework agreed by all the stakeholders to establish Public-Private-Partnership.

3. 1. Recommendations of SRA for IMI

The four components recommended at the Strategic Research Agenda are the same as in the vision paper: **1. Prediction of drug safety, 2. Early indication of efficacy 3. Knowledge management 4. Education and training** (SRA 2005, EFPIA 2004).

1. The main recommendations for the **Prediction of drug safety** are:
   - Creating and functioning a European Centre of Drug Safety in order to identify and coordinate research in this respect;

- Establishing a framework to develop biomarkers indicating the human relevance and regulatory utility;
- Developing a partnership with Regulators to find out innovative clinical trial analyses in order to assist acceptance of biomarkers and to promote data sharing and joint consideration of ethical issues.

2. Improving clinical research regarding efficacy and patient recruitment will be addressed with the following actions:

- using biomarkers as a means of improving prediction of efficacy;
- developing strategies towards the tailor-made medicines;
- improving patients' recruitment using biomarkers;
- improving consultation of patients and clinical groups;
- increasing the dialogue with regulatory authorities (SRA 2005, EFPIA 2004).

In this the research priorities are:
Cancer, Brain disorders, **Inflammation diseases, Diabetes mellitus.**

3. **Knowledge management** is important from the point of view of handling the enormous amount of data related in the process of biopharmaceutical R &D.

The Knowledge Management Group would like to introduce the following recommendations:

- develop for complex systems knowledge representation models and data exchange standards
- build a core reference database extracted from the literature
- design standards for databases and build an expert tool to allow the storage of local data in a secured environment.

4. The main recommendations for **Education and Training are:**

- Establish a European Medicines Research Academy for education and Training for professionals involved in biomedical R&D including regulatory officers;
- Draft existing activities within E&T including identification of European centres of excellence and develop programmes, implement these plans in the critical areas relevant to the biomedical R&D process;
- Evaluate options to foster mobility between academia and industry.

4. Budget/Financing

Each year for a period of 7 years, 400 million euros has been required to implement these recommendations. The detailed breakdown in million Euros for the four pillars is as follows:

- For Improved Prediction of Safety – 165.4 Euros,
- For Improved prediction of Efficacy – 247.7 Euros,
- For Improved Knowledge Management – 13.1 Euros and
- For Improved Education and Training – 8.2 Euros.

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The European Commission together with the biopharmaceutical industry contribute equally to the funding of these research projects through the **creation of a separate legal structure** (SRA 2005).

5. IMI in the FP6

5. 1. FP6 – PredTox Project[1]

In **the FP6** there have been significant advances in four areas of technology carried out **in PredTox Project**. The main purpose of this project is to estimate the use of these **new technologies** in preclinical safety testing and to provide a functional database containing integrated information from the "omics" technologies with that from traditional toxicity endpoints for liver and kidney toxins.

These technologies include:

- In silico tools which aid the detection and prediction of specific toxicities;
- Toxico genomics, that detect changes in gene expression in cells in response to exposure to a toxic compound;
- Toxico proteomics, to detect abnormal patters of protein sin cells in response to exposure to a toxic compound;
- Metabonomics, to detect changes in endogenous cellular metabolism of a cell or organism.

Since the „omics" technologies result in the generation of huge volume of data it is necessary to carry out parallel research in bioinformatics/knowledge management and IT in order to identify key changes in the measured experimental parameters**.**

5. 2. Implementation of IMI

The Strategic research Agendas (SRA) for Innovative Medicines Initiative has been implemented through collaborative research in FP7 and also by means of **Joint Technological Initiatives (JTI).** The approach is through industry, which under the leadership of EFPIA and with the agreement of key stakeholders (Academia, Regulatory agencies, Patent organisations, Clinical researchers, Ethical experts, etc.) has identified the main obstacles that are in the way of development of new drugs.

The key features of JTI are arising from Technology Platforms, a critical mass of research and innovative effort to be created depending on scale and technical complexity, establishing public/private partnerships and mobilising public and private sources. An Executive Agency**, a Joint Undertaking** under the article 171. has been organised for implementing IMI Joint Technology Initiative (JTI) , which is neither a public nor a private entity. It is a non-governmental, non-profit organisation under the authority of the national applicable law.

[1] www.innomed-predtox.com

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IMI JTI will consist of a Board, Executive Office, Scientific Committee, Stakeholders Forum and Member States Group. In the operational phase the stakeholder Forum overlooks performance of the initiative and it provides input into the Scientific Committee.
The Joint undertaking will be adopted by the Council, acting on the proposal after consulting with the European Parliament and the Economic and Social Committee. Funds from EU to the IMI Joint Undertaking for research projects has been provided through FP7. Therefore FP7 adoption is crucial for IMI and its duration is planned till the end of FP7, i.e. 2013.

For the successful implementation of IMI, the governance of it must ensure a close cooperation between the EC and Industry and key stakeholders. It is also planned to involve the best European scientists from both public and private sector to ensure updates of the SRA and "quality control" of performed research.

Member States are not asked to directly contribute to IMI JTI budget, however contribution at a national level are essential for some activities and "Education and training".

5. 3. Benefits of IMI

Europe will benefit from IMI in the long run. There will be an increased economic value through establishing small and large enterprises in Europe. More jobs will be created in the EU, more education and training achieved in the biomedical area. By strengthening the European science base, the brain drain will be decreased and the scientific talent attracted to appropriate European countries. There will be an increased collaboration with all relevant stakeholders. A more effective healthcare will be created for the sake of healthier society and citizens of Europe. The following stakeholders and in the following way will benefit from IMI:

Patients and patient organisations will have an improved quality of life through more appropriate therapies; they will feel more influence on their own health.

Clinicians may benefit from the creation of a novel treatment mechanism; they may better influence the development of more appropriate therapies;

Health Departments will gain from improved integration of the developed new therapies into the unmet medical needs; more effective therapies will mean more efficient treatment and reduced costs for long term care

Pharmaceutical companies will benefit from the reduced risk and a more productive drug production; will get a more cost-effective R&D.

Treasuries will earn from increased GDP/capita, reduced cost of working days due to lost of disease, creation of new jobs;

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Academia (researchers) will benefit from better infrastructure, an information source, and a framework within which they can bid for work and establish cooperation; will get more funding for the research;

Research Councils and other funding bodies will enjoy a framework within which they will gain an overview of current research programmes, avoid duplication and gain cross disciplinary and cross institutional synergy;

General public will benefit from increased awareness of diseases, their symptoms and consequences.

6. Conclusions

European Governments and the Commission have recognised the importance of biomedical research and development and are taking steps for their improvement. Governments are trying to increase spending on health and education and including steps of long-term commitment to national science plans in this respect. The goals set in the Lisbon Agenda are also a step forward in this direction. A constant exchange of opinions between the European Ministers, representatives of pharmaceutical industry and other different sectors of healthcare industry are partially problem-solving. It has been recognised that Europe is lagging behind USA in pharmaceutical investment and healthcare. Together Europe may be able to compete with the USA and other competitors. The issue is not about the survival of the biomedical research and pharmaceutical industry, but whether it will prosper and be among the leaders. Innovative Medicine Initiative will contribute to a new approach to drug discovery and development in Europe. Its potential is to change the biopharmaceutical research and development process by a more systematic use of biomarkers and **by using highly innovative technologies.** The project contributes to a new approach in evaluating risk and its benefit to patients through intensive discussions with the regulatory authorities. This approach also favours cross-functional collaboration between pre-clinical and clinical scientists to promote translational medicine. The key deliverable of his initiative is reduced drug development time and production of a more targeted medicine to patients with fewer side-effects. The project also aims to change the **attitude and the way different stakeholders work together**. This will result in a better and easier interaction with the Regulatory Authorities. This will also lead to **establishing a new type of collaboration between industry, academia, clinicians and patients** and contribute to a real shift in culture in this area.

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