2. Background to the 2013 Priority Medicines Project

2.1 Introduction

Since well before the publication of the 2004 Priority Medicines Report, the goal of biomedical technology companies has been to conduct research and commercialize products in a stable, predictable operating environment that encourages and rewards innovation. However, various pressures currently being placed on pharmaceutical companies can have a negative impact on innovation. It appears that these pressures have been increasing since 2004. The financial investment required for pharmaceutical development has increased, threatening to make the development of new medicines increasingly unaffordable for companies, payers and patients.\(^1\)

2.2 Pharmaceutical innovation: current challenges

Although the data can be subject to different interpretations, some studies suggest that innovation in the pharmaceutical industry occurs in waves of activity, as evidenced by several successive "generations" of medical (and other) technologies over the past two hundred years\(^2,3,4\) (see Background Paper 2).

However, as of 2013 there had not yet been a corresponding increase in output in terms of new medicines being approved, as the rate of introduction of new molecular entities (NMEs) has remained about the same over the past 30 years.\(^5\) Meanwhile, attrition rates have risen sharply, especially in late-phase clinical trials.\(^6\)

Figure 2.2.1 (panel c) suggests that the rate of discovery of NMEs simply reflects the capacity of the pharmaceutical industry, although the data only go up to 2006. The output of industry NMEs tracks the expected value\(^6\) based on the established research and development model. The expected NME output and the number of companies are closely correlated in a nonlinear relationship that explains 95% of the changes in expected NME output simply by changes in the number of companies (Figure 2.2.1, panel d).
Figure 2.2.1: Dynamics of pharmaceutical innovation

Source: Munos B. Lessons from 60 years of pharmaceutical innovation. Reviews Drug Discovery 8, 2009, 959-968, doi: 10.1038/nrd2961

Panel c: Output of NMEs over time
Panel d: Correlation of the expected output of NMEs and the number of companies providing the NMEs.

However, more recent analysis shows that in 2011, the United States Federal Drug Administration (FDA) approved 30 NMEs, excluding new biologicals (see Background Paper 2). The 30 NMEs approved in 2011 represent the second highest total in the period 2002 to 2011, after the 32 NMEs approved in 2004 (see Figure 2.2.2). In 2012 the FDA approved 39 NMEs.

Figure 2.2.2: Time series of the output of NME applications (circles) and approvals (bars) for the U.S. Food and Drug Administration (FDA)

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2.3 The European pharmaceutical industry in context

Since 2004, and even before that date, the global pharmaceutical industry has seen a consolidation of companies and the creation of huge multinational corporations. This merging of companies across the Atlantic means that it is sometimes difficult to characterize a company as "European." North America is the world’s leading market for pharmaceutical products and most new products today are launched in the United States because of the size of its market and the absence of price controls.

Meanwhile, in 2011 Europe remained the second largest global market for pharmaceutical sales. The presence of a highly-skilled workforce and robust framework for the protection of intellectual property rights (IPRs) were key factors in the decision by industry to invest €27.5 billion in R&D in Europe in 2011.¹ The pharmaceutical industry is one of the few sectors to contribute positively to the EU’s trade balance. Its trade surplus of €48.3 billion in 2011 was the highest among the high-tech industries.¹

Annual global expenditure on medicines will reach nearly US$ 1.2 trillion by 2016 (EU5 countries, Japan, the United States, and emerging markets), up from over US$ 900 billion in 2011.⁸ In the developed markets, including Europe, Japan and the United States, spending is expected to decline to 57% of the global total – down from 76% in 2006. This is due to growth in emerging markets as well as the expiry of patents for a number of significant brand-name medicines, slower increases in spending on branded products, and increased cost-containment measures by payers.⁸

Of these sales, however, only 7% are driven by products launched within the last five years, indicating the continued reliance of industry on more established products. From a business viewpoint, the ever-increasing cost of medicines development is an incentive for companies to invest in products likely to provide the highest rate of return on R&D investment. This leads to a somewhat conservative business model (i.e. the development of medicines against proven targets) using approaches that have already been clinically and financially successful⁹ (see Background Paper 2).

The level of investment in pharmaceutical R&D in Europe, Japan and the United States varies significantly, with the highest concentration of biopharmaceutical R&D expenditure in the United States. The latest 2011 data reported by EFPIA companies show pharmaceutical R&D expenditures leveling off in the United States and Europe (Figure 2.3.1). In 2011, a total of 49 innovative medicines were approved by the European Medicines Agency (EMA) for a range of different diseases (not including national authorizations). They include: 37 new medicines (not including medicines for rare (“orphan”) diseases), 11 new medicines for orphan diseases and one advanced-therapy medicine for the EU market.¹

¹ The EU5 countries are France, Germany, Italy, Spain and the United Kingdom.
The United States accounts for an estimated 38.1% of global pharmaceutical production, just ahead of Europe and well ahead of Japan (See Background Paper 2, Figure 2.4). Together, these three regions account for the bulk (approximately 82%) of global pharmaceutical production by value. In 2009, the Asian region was by far the fastest growing market, with an estimated growth of 15.9%, while the growth of the North American and European markets was estimated at 5.5% and 4.8% respectively in value (See Background Paper 2, Figure 2.5).

Today medicines regulators are progressively increasing the requirements for product authorization in an effort to promote safety and efficacy. At the same time, reimbursement authorities appear to be more and more interested in controlling pharmaceutical costs. The ability of the major pharmaceutical industries to innovate is under growing pressure from loss of revenue owing to patent expirations, increasingly cost-constrained health systems and more demanding regulatory requirements. As a result, it is becoming increasingly difficult to provide appropriate incentives for the development of products for important public health needs, such as medicines for rare diseases, individualized therapy, or diseases that occur mainly in low-income countries.
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2.4 EU Policy Space: Pammolli, G-10 Report

In addition to the general perception that the pharmaceutical R&D model has not been producing enough innovative molecules, in Europe in the late-1990s a specific perception emerged that the European pharmaceutical industry was losing ground to the United States. This was reinforced by the publication in 2000 of a report entitled Global Competitiveness in Pharmaceuticals: A European Perspective, the so-called Pammolli Report, named after one of its authors (see 2004 Report Appendix 2.1).\(^{11}\) The perception was further strengthened by the 2002 Report of the European Commission High Level Group on Innovation and Provision of Medicines (the “G-10 Medicines Group”). (See 2004 Report Appendix 2.2). Similar patterns of losing competitive advantage were also confirmed for the biotechnology industry in a 2007 report.\(^{12}\)

In 2011, a further analysis by Pammolli and colleagues confirmed that, although investment in pharmaceutical R&D has increased substantially over recent decades, there was still a lack of a corresponding increase in output in terms of the approval of new medicines, an indication of continuing challenges in therapeutic innovation.\(^{13}\) However, the authors also investigated potential variations in productivity with regard to the regional location of companies and found no evidence of any “productivity gap” between the United States and Europe.

2.5 The Framework Programmes

Since 1984, the European Commission (Directorate General (DG) Research and Innovation) has undertaken a series of multi-year Framework Programmes (FPs), funding programmes created in order to support and encourage research in the European Research Area (ERA). The specific objectives and actions vary between funding periods. The original Priority Medicines Report was designed to provide analysis for the FP6 (2002 to 2006: about €17.8 billion total budget of which €2.5 billion for the Thematic Area “Life Sciences, genomics and biotechnology for health”) and the planned FP7 (2007 to 2013).

2.5.1 The Seventh Framework Programme

The FP7 was adopted for the period 1 January 2007 to 31 December 2013.\(^{14}\) Figure 2.5.1 shows for 2007-2011 the actual FP7 expenditures in the referenced subject matter and the planned expenditure for 2012 to 2013.\(^{15}\) The total budget for health-related activities over the duration of FP7 is €6 billion.\(^{16}\)
2.6 Innovative Medicines Initiative (IMI)

Launched in 2008 with a total budget of €2 billion up to 2013, the Innovative Medicines Initiative (IMI)\(^\text{17}\) is an industry-European Union public-private partnership, involving the European Commission and the European Federation of Pharmaceutical Industries and Associations (EFPIA). Its aim is to facilitate the development of new medicines by supporting a more efficient discovery and development process.

Since 2008, the IMI has awarded grants totalling €580 million to the most promising research projects in areas including brain disorders, metabolic diseases, inflammatory diseases, cancer, infectious diseases and, most recently, antimicrobial resistance (AMR) (see Chapter 6.1). The IMI is currently engaged in an 8th Call for Proposals.

2.7 Horizon 2020

The most recent version of the FPs (2014 to 2020) is “Horizon 2020”, which at the time of publication is subject to negotiation between the Council of the European Union and
2. Background to the 2013 Priority Medicines Project

the European Parliament. This will combine all research and innovation funding currently provided through the FPs and other sources for a range of research areas not limited to biomedical topics.

2.8 U.S. Policy Space: the National Institutes of Health (NIH)

The National Institutes of Health (NIH) Common Fund was enacted into law by Congress through the 2006 NIH Reform Act to support cross-cutting, trans-NIH programmes that require participation by at least two NIH Institutes or Centers (ICs) or would otherwise benefit from strategic planning and coordination (see Background Paper 2, Appendix 2.5).

The requirements for the Common Fund encourage collaboration across the ICs while providing the NIH with flexibility to determine priorities for Common Fund support. To date, the Common Fund has been used to support a series of short-term, exceptionally high-impact, trans-NIH programmes known collectively as the NIH Roadmap for Medical Research (see Appendix 2.5). 18

Roadmap Programmes span all areas of health and disease research and IC boundaries. These are programmes that might not otherwise be supported by the NIH ICs, because of their scope or because they are inherently risky. Roadmap Programmes are expected to have exceptionally high potential to transform the manner in which biomedical research is conducted. They are also expected to be short-term (5–10 year) programmes. The annual Common Fund budget was US$ 498 million in 2008. To date, the Common Fund has been used exclusively to support the Roadmap Programme.

Initiatives funded through the Roadmap/Common Fund fit into one or more of these major themes and address specific roadblocks or gaps to:
- Foster high-risk/high-reward research
- Enable the development of transformative tools and methodologies
- Fill fundamental knowledge gaps
- Change academic culture to foster collaboration.


2.8.1 Criticism and defence of the NIH Roadmap Programme

The presentation of the 2006 NIH Roadmap, at a time of government cut-backs in general, led one critic to assert that the NIH should rely more on pharmaceutical companies to fund large clinical trials. The relatively more limited NIH funds could
then be reallocated to basic science grants (known as “R01 grants” in the United States).\textsuperscript{19,20,21}

In response, representatives of 50 leading academic medical centres focusing on clinical research argued that the pharmaceutical industry had to focus on profit-generating opportunities in order to meet its commitment to investors. Therefore, the pharmaceutical industry was not best qualified to deal with “… sustaining the issues specific to academic science.”\textsuperscript{22}

\section*{2.9 Regulatory strategic plans by the European Medicines Agency: EMA Road Maps}

In 2005, the European Medicines Agency (EMA) developed a new strategy for its work up to 2010.\textsuperscript{23} Since then, various initiatives have been undertaken and progress made with the implementation of the EMA 2010 Road Map (described in two Status Reports published in May 2006 and October 2007.\textsuperscript{24,25} In December 2010, the EMA published a further document (Road Map 2015) setting out a strategic vision for the operation of the Agency from 2011 to 2015\textsuperscript{26} (see Background Paper 2, Appendix 2.4). See also Implementing the European Medicines Agency’s Road map to 2015: The Agency’s contribution to Science, Medicines, Health EMA/MB/550544/2011.\textsuperscript{27}

The Road Map 2015 report identifies the following drivers for the future activities of the EMA:

- Need to ensure efficient operation of the Agency’s core business
- Addressing ongoing public health needs including demographic changes, emerging public health threats, AMR and rapid development of new technologies
- Evaluating new and emerging science which may address unmet medical needs
- Ensuring that the model for regulating medicines remains current and effective
- Protection of public safety
- Addressing the need for more openness and transparency and
- Addressing the impact of globalization.

More specifically, to address current and anticipated public-health needs over the next five years, the EMA intends to focus on activities relating to addressing gaps in medicines development, responding to new and emerging science and putting in place the necessary preparedness mechanisms to respond to emerging health threats. In the context of this updated report, three main ‘gaps’ in drug development have been identified by the EMA; neglected and rare diseases, specific activities relating to ageing populations and the need to address the pipeline gap for new antibiotics. Each of these EMA priorities has a counterpart in the present report.

The focus of efforts to address the challenges of new and emerging science will include efforts to enhance liaison between approaches to drug and diagnostic development,
facilitation of biomarkers and the science supporting the development of more personalized medicines.

With regard to its responsiveness to public-health threats, the EMA intends to build on experience with influenza pandemic preparedness to assist the EC in the development of a strategy with European partners to ensure a coordinated European response. The EMA also intends to intensify work on a European and international perspective to minimize the risk of AMR arising from the use of both human and veterinary medicines within the framework of Community and international activities, including the Transatlantic Taskforce on AMR established based on the conclusions of the 2009 EU-US summit (see Chapter 6.1).

2.10 Regulatory strategic plans by the U.S. Federal Drug Administration (FDA): Critical Path

In March 2004, the United States. Food and Drug Administration (FDA), the American counterpart of the EMA, produced a document entitled “Innovation or Stagnation? Challenge and Opportunity on the Critical Path to New Medical Products” which argued that “… applied sciences needed for medical product development have not kept pace with the tremendous advances in the basic sciences.” In its 2006 Critical Path Report, the FDA presented its diagnosis of the scientific challenges as a medical product pipeline problem, which meant that innovative medicines were not reaching patients. The report then laid out a path forward, beginning with extensive outreach and consultation with public and private stakeholders.

The FDA has since developed a “Critical Path Opportunities List” including several aspects relevant to this Report: biomarker development; streamlining clinical trials; developing new antibiotics to combat emerging infections and bioterrorism; and the development of new therapies for children and adolescents. Most recently, the FDA produced a strategic plan, entitled “Strategic Priorities 2011–2015: Responding to the Public Health Challenges of the 21st Century” (see Background Paper 2, Appendix 2.6a).

2.11 Global initiatives

In March 2010 the European Commission issued a communication on “The EU Role in Global Health”. The communication states that the EU should apply the common values and principles of solidarity towards equitable and universal coverage of quality health services in all external and internal policies and actions. This would be achieved through democratic and inclusive governance, an emphasis on universal coverage and coherence between relevant EU policies related to global health. With regard to research, the communication stresses that research should benefit all people and that the EU Research Framework Programmes should continue to give priority to actions which address global health challenges.
On 26 May 2012, the WHO World Health Assembly (WHA) adopted a resolution calling for an inter-governmental meeting (held in November 2012) to examine in depth the proposals made in April in the report of the Consultative Expert Working Group on Research and Development: Financing and Coordination (see Background Paper 3) established in 2010 under Resolution WHA63.23. Such proposals included: open approaches to R&D; pooled funds; direct grants to companies in developing countries; prizes for milestones and end-products; and patent pools. One of the recommendations of the Working Group was to start multilateral negotiations for the possible adoption of a binding convention on health R&D.\textsuperscript{33}

In November 2012, a three-day closed door meeting resulted in agreement by WHO Member States to endorse a strategic work plan that includes proposals on the coordination, financing and monitoring of R&D expenditures.\textsuperscript{34}

### 2.12 Conclusions

Since 2004, the global and EU policy space has changed in a significant way. At the European level, FP7 and Horizon 2020 have created what is hopefully a broader, integrated vision of biomedicines policy and innovation going forward. Additionally, a growing involvement of regulatory agencies such as FDA and EMA is seen in this area through explicit priorities in their strategic agendas for the future. Also, at the global level co-ordination and discussions have evolved much since the previous Report.

### References


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