1. Introduction

See Background Paper 1 (BP1_introduction.pdf)

1.1 Context

1.1.1 Introduction

This is the second report to be issued on *Priority Medicines for Europe and the World*. It is designed as an update to the original report, which was published in 2004. The original report was initiated during the second half of 2003, when the Government of the Netherlands established the Priority Medicines for Europe and the World Project with the World Health Organization (WHO). The aim was to establish a public-health-based medicines research and development (R&D) agenda and, where necessary, to help bridge the gap between public health needs and the development priorities of the pharmaceutical industry.

In response, the WHO prepared a R&D agenda and methodology based on public health needs and drew up a list of priority medicines to be proposed for research funding by the European Union (EU) as part of its Seventh Framework Programme (FP7) for 2007-2013. In addition to identifying priority medicines needed for EU citizens, the aim was to identify those research needs which are also relevant beyond Europe for countries in economic transition and for developing countries. This “commonality of interest” is an important bridging aspect between the health needs of Europe and the world.

The objective of the 2004 Priority Medicines Report, as described in the initial proposal, was:

> to prepare a public-health-based medicines development agenda, for support by the EU in the short- (2005-2006) and medium-term (2007-2010) future, and to develop a systematic methodology in this regard.

The 2004 Report was generally well received by most of the major stakeholders, including patients’ organizations, industry, governments and regulators. However, there was also some criticism. EURORDIS, the European alliance of rare disease patients’ organizations, had reservations about some aspects of the Report’s treatment

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Priority medicines may be defined as those medicines which are needed to meet the priority health care needs of the population (“essential medicines”) but which have not yet been developed. For the purposes of this Report, a “priority” medicine for a priority disease is by definition also an improvement on, a replacement for, or a better formulation than already-marketed products.
of rare diseases. The International Alliance of Patients’ Organizations (IAPO) in Europe, although generally supportive, would have preferred the Report’s content to be have been written in a way that would be more accessible to patients, whom they consider to be critical in moving biomedical innovation forward.

1.1.2 What has happened since the 2004 Priority Medicines report was published

The 2004 Report made several recommendations for future action, including suggestions for the development of new medicines for tuberculosis (TB) and neglected tropical diseases; a call for concerted efforts to deal with antimicrobial resistance (AMR) and a call for increased emphasis on public-private partnerships. Each of these recommendations was addressed in counterpart activities post-2004.

Top Institute Pharma

The pharmaceutical gaps identified in the first Priority Medicines Report now constitute the core research portfolio of the Netherlands-based Top Institute (TI) Pharma. TI Pharma’s mission is to establish, support and manage public-private collaborations between academia and the international and national pharmaceutical industry, in part to create cross-disciplinary research within the framework of the 2004 Report; to improve the efficiency of the entire medicines development process; and to educate and train biomedical scientists (http://www.tipharma.com/).

As of 2012, 60 research consortia had been formed, combining 31 universities, their affiliated medical centres and knowledge institutes and 48 industrial partners, including global pharmaceutical companies and small- and medium-sized enterprises (SMEs). Therapeutic areas, based on the findings of the 2004 Report, consist of immune diseases, cardiovascular diseases, infectious diseases and diseases of the brain.

Public-Private Partnerships: Innovative Medicines Initiative

The Innovative Medicines Initiative (IMI) was launched in 2008 as a large-scale public–private partnership between the European Union, represented by the Commission (EC) and the European Federation of Pharmaceutical Industries and Associations (EFPIA). With a total budget of €2 billion, the IMI aims to boost the development of new medicines across Europe through the use of public-private partnerships. The IMI constitutes a novel model for implementing the concept of “open innovation”. This has enabled large-scale pooling of industrial research assets by implementing new collaborative endeavours between large pharmaceutical companies and other key actors in health care, including academic institutions, SMEs, patients, and regulatory authorities. The Interim Report on the functioning of the IMI was uniformly positive. The authors formulated a series of recommendations for action and, significantly, stipulated which actor(s) should take responsibility for them.
Initiatives to combat antimicrobial resistance (AMR)

The original Report identified AMR as a priority condition requiring coordinated efforts (see Chapter 6.1). The problem of AMR has been known for many years and has been recognized by the WHO, the EC and the European Parliament. The Swedish Government during their Presidency of the EU were very active on this issue and convened a major meeting. Through resolutions passed by the World Health Assembly (WHA), WHO Member States have highlighted not only the public health threat of resistant organisms, but also the harm caused by misuse of antimicrobials by patients, prescribers and medicine dispensers. Activities following publication of the 2004 Report are encapsulated in the following WHA Resolutions:

- WHA58.27 – Improving the containment of antimicrobial resistance, 25 May 2005 (see Appendix 1.1).
- WHA60.16 – Progress in the rational use of medicines, 23 May 2007 (see Appendix 1.2).
- WHA62.15 – Prevention and control of multidrug-resistant tuberculosis and extensively drug-resistant tuberculosis, 22 May 2009 (see Appendix 1.3).

Antimicrobial resistance is the subject of research funded under the FP7 and the IMI, and is also the subject of a Joint Programming Initiative (JPI), which aims to coordinate research activities among EU Member States. In early 2010 the JPI on Antimicrobial Resistance was proposed by Sweden and Italy. In late 2011, the EC issued a five-year “Action Plan against the rising threats from Antimicrobial Resistance”, an increasing problem which has been singled out by the EC as a major public health concern. In 2012 a resolution of the European Parliament on “Rising Threats of Antimicrobial Resistance” and the conclusions of the Council of European Union on the “Impact of antimicrobial resistance in the human health sector and in the veterinary sector – a “One Health” perspective” have underlined the importance which the EU attaches to this subject. One of these research priorities is implemented through the IMI 6th Call on AMR, which forms part of the ‘Action plan against the rising threats from Antimicrobial Resistance’ adopted by the EC.

1.1.3 Priority-setting experiences (2004 to 2012)

Today, even in the most developed countries, the demand for health care outweighs the level of resources allocated to finance health. Meanwhile, efforts by national policy makers to set priorities for their health care system, or for the introduction of new technologies, are often conducted on the basis of varying degrees of evidence about the safety, effectiveness and appropriateness of particular interventions. Because there are still no widely accepted models for legitimate and fair priority setting in health care, priority setting remains a real challenge for policy makers in health systems throughout the world. Many different approaches to priority setting have been developed and there has been considerable literature on this since the 2004 Report. This is reviewed briefly in Chapter 3 and in its associated Background Paper. In short, the majority of priority-setting exercises since 2004 have applied a broad definition of
health research as an activity that is not limited to generating new knowledge, but also has a wider vision of implementation in order to help reduce the current disease burden.

1.2 2013 Update to Priority Medicines for Europe and the World

The original Priority Medicines Report was presented on 18 November 2004 at The Hague in the Netherlands. Since then, new research agendas have been developed and the EU has expanded to encompass 27 Member States – with implications for a possible shift in priority diseases. In 2011, a Working Group of the European Commission reported that insufficient dissemination and implementation of the 2004 Report were weaknesses that should be carefully addressed during the 2013 Council Presidencies and recommended that an update of the 2004 Report be undertaken by the WHO (see Background Paper 1) for further information and analysis.

1.3 Burden of disease, the epidemiological transition and the commonality of interest

The Priority Medicines Project focuses on the unmet health needs of different populations. Within Europe, the EU27 all have rapidly ageing populations (see Background Paper 5). Elsewhere, in regions throughout the world, countries are undergoing their own epidemiologic and demographic transitions. As a result, health systems in many parts of the world are faced with ageing populations and an increase in chronic noncommunicable diseases (NCDs) associated with economic development and changes in lifestyle.

Various methods of measuring disease burden have been developed. In this report the concept of Disability Adjusted Life Years (DALYs) is used as an integrated single measure of mortality and disability due to a particular disease or condition. One DALY represents one lost year of healthy life and the burden of disease is a measurement of the gap between current health status and an ideal situation in which everyone lives into old age free of disease and disability (see Background Papers 4 and 5). Mortality is also used here as a measure of burden of disease as this is easy to understand. However, this measure is not able to reflect the burden of pain and suffering experienced by patients with chronic diseases such as osteoarthritis.

We live in an interconnected world with increasingly shared health problems and a “commonality of interests”. The vast majority of chronic NCDs and conditions affecting populations in the EU27, such as cancers, cardiovascular disease, osteoarthritis and Alzheimer disease, are also occurring in the developing world or will be in the not-too-distant future. At the same time, large portions of the world’s poorest populations still have to contend with the onslaught of AIDS combined with other infectious diseases such as malaria, trypanosomiasis (sleeping sickness) and tuberculosis (TB) in what amounts to a double burden of disease, that is a burden of
both communicable and non-communicable disease. Perhaps even to a greater extent than in 2004, the health needs of Europe and much of the rest of the world are converging and the so-called commonality of interest identified in the 2004 Report continues to be relevant. A shift in priorities may now be needed, due to population changes such as ageing, or behavioural changes in smoking and dietary habits as well as alcohol consumption. Better understanding of these changes can be used to inform priority setting.

1.4 Priority medicines and pharmaceutical gaps: a public health perspective

Priority medicines are designed to fill pharmaceutical “gaps” (i.e. where treatments either do not exist or are inadequate, or where existing treatments are likely to become ineffective in the future, such as those for AMR). For a given disease or condition, priority medicines can be defined as:

1. Essential medicines which should be developed to treat conditions for which few or no effective treatments exist or where the available medicines are of limited efficacy or effectiveness. These are medicines that would fill pharmaceutical gaps and would be useful both in Europe and worldwide in countries where the targeted diseases occur.

2. Essential medicines that have not yet been developed but are needed for diseases and conditions that will become important public health concerns both in Europe and the rest of the world.

3. Medicines needed for special patient groups, including patients with rare ("orphan") and neglected tropical diseases, the elderly, children and women.

The 2013 Priority Medicines Project continues to identify pharmaceutical gaps and to identify areas for improved delivery mechanisms or better formulations of existing preventive and therapeutic medicines (e.g. formulations for children, fixed-dose combinations (FDCs) or heat-stable formulations).

Although the 2013 Report addresses some high-burden diseases that are largely preventable, such as lung cancer, chronic obstructive pulmonary disease (COPD), alcohol-related diseases, and type 2 diabetes, it should be underlined that, with rare exceptions, any new treatment is unlikely to be a “magic bullet” and that health promotion and disease prevention (not considered in the present Report) must remain very high priorities.

It is encouraging to note that since 2004 major pharmaceutical gaps identified in the original Priority Medicines Report have been addressed. The first of these is the continuing marketing approval of imatinib in more than 110 countries for the treatment of all phases of chronic myelogenous leukemia and also for the treatment of adult patients with KIT (CD117)-positive gastrointestinal stromal tumors (GIST), which cannot be surgically removed and/or have metastasized. Another example of a gap being addressed is the use of antibiotics to treat the disabling condition of Buruli ulcer,
which was being treated primarily with wide surgical excision. Recent studies have confirmed the efficacy of antibiotics in treatment \(^{17,18}\) (see also Chapter 6.9).

### 1.5 Conceptual framework

The 2004 Priority Medicines Report developed a conceptual framework for the Project, which continues to be relevant and is used in this updated report (see Chapter 3).

Figure 1.5.1 (see 2004 Report: Appendix 3.6) offers a public health perspective of the scale of unmet treatment needs or when existing therapies are inadequate. This model identifies that for some diseases effective treatments exist and are widely used (Area 1). For other diseases, effective treatments exist but obstacles to access are present (Area 2). These obstacles may be due to factors such as cost or weaknesses in the health system. The third category includes conditions for which some treatments exist but the delivery mechanism or formulation may be inappropriate for the target patient group (Area 3). The fourth category encompasses those conditions for which no effective treatment is available (Area 4). The Priority Medicines Project focuses on Areas 3 and 4 and not very much on Areas 1 and 2.

![Figure 1.5.1: Identifying pharmaceutical gaps (unmet therapeutic needs): a public health perspective](image)

Source: Adapted from the Report of the Ad Hoc Committee on Health Research Relating to Future Intervention Options, WHO, 1996
1.6 Structure of the 2013 Report

Work on this updated report was organized in several stages. The early stages (June-December 2012) involved a review of the original methodology and collection of new, post-2004 data on disease burden and mortality. This new information is, in part, based on the 2010 Global Burden of Disease Study (GBD 2010), with its series of major publications in late 2012. These early stages led to the production of a Preliminary List of diseases and conditions for more detailed studies.

Later stages (September 2012 to May 2013) involved the production of detailed Background documents (Chapter 6), used to develop a Final List of priority diseases and conditions and their pharmaceutical gaps (Chapter 9). Any gaps that had been closed since 2004 were noted. Further updates were related to cross-cutting themes in Chapter 7: relating to the elderly, women, children and stratified medicine and enablers and barriers to innovation in Chapter 8.

Throughout the Project, an international project Advisory Group, including European Economic Area Member States (Belgium, Italy, the Netherlands, Norway, Portugal and the United Kingdom), members of the pharmaceutical industry, academics, non-governmental organizations (NGOs), many patients’ groups, representatives of trade organizations, EC staff and WHO staff, met to review progress. In addition, meetings were held in Brussels with EC staff from the Directorates General (DG) for Research and Innovation, Enterprise and Industry and Health and Consumers.

Draft versions of the background documents were distributed for review and comment by external experts. An Interim Report was submitted to the EC on 28th March 2013 for review, comment and use in the priority-setting activities related to Horizon 2020 and the next IMI programme (see Background Paper 2).

1.7 Who is the target audience for this report?

It is essential that public health needs and incentives for biomedical innovation are aligned in order to spur the development of new medicines for high-burden diseases and conditions for which there are unmet therapeutic needs. This report is targeted to key decision makers with the expertise needed to bring about this alignment.

The primary audience includes: EU Member States, which are responsible for funding research and paying for medicines, the EU decision-makers, the Council of the European Union, the European Parliament and the European Commission (notably, but not exclusively, the DGs for Research and Innovation, Enterprise and Industry, Health and Consumer Protection and Development). Senior management and scientific directors of research in the European pharmaceutical industry are another crucial audience. Policy makers and politicians at national and regional levels may also find this report and the background papers useful for their decision making. Within WHO, headquarters departments such as Public Health and Innovation and disease control
departments, as well as regional and country offices may find useful information for their work. Meanwhile, researchers who are deciding on future directions for their research efforts may find the methods and conclusions useful for their decisions. In addition, patients’ groups and payers (social health insurance organizations and reimbursement authorities) have a common interest in identifying which research should be prioritized and encouraged.

1.8 Contents of the 2013 Report

This updated series of chapters has been produced in parallel with a series of updated background papers available on a CD-ROM and on the web. Some additional sections have been added to the background papers since 2004. The original 2004 Report remains available for reference on CD-ROM and on the web (http://archives.who.int/prioritymeds/report/index.htm).

Chapter 2 describes how innovation occurs in the pharmaceutical sector. It highlights continuing concerns about the decline in innovation and competitiveness in Europe, particularly in the context of the global and EU economic slowdown, a situation that did not exist in 2003 to 2004.

Chapter 3 briefly presents new information on approaches to setting priorities and outlines the approaches selected for use in this report.

Chapter 4 is an update on the methods used in the study. These were used to generate the preliminary results (Preliminary List) which are described in Chapter 5.

Chapter 6 includes 24 sections which outline the current situation with regard to the diseases or risk factors that comprise the Preliminary List and identifies possible pharmaceutical gaps from the available evidence. Where relevant, the sections also include information on diagnostics and vaccines. These 24 sections (each one a background document) are particularly important as they summarize the evidence base for the recommendations in Chapter 9 and provide a detailed source of reference material for both policy makers and others wishing to learn more about a particular condition or risk factor.

Chapter 7 deals with updates to cross-cutting themes. This chapter includes sections focusing on children, women and the elderly as population groups with particular health needs, together with sections on stratified medicine.

Chapter 8 takes a fresh look at issues related to promoting innovation. Specifically, one section addresses new ways of creating incentives for pharmaceutical innovation, and another looks at the development of public-private partnerships for new medicines. Two other sections discuss regulatory policies and pricing policies, while the two final sections deal with health information systems in the context of priority medicines and the role of patients in the pharmaceutical innovation process.
Chapter 9 provides the list of priority diseases and conditions for which pharmaceutical gaps exist and gives recommendations for different stakeholders, based on the updated information in this report. This chapter includes limited references, as comprehensive documentation is provided in the background documents.

1.9 Areas not addressed by this study

This study does not address in any detail health system issues such as access or quality of care. The importance of non-pharmaceutical prevention related to tobacco use, alcohol-related diseases and obesity are not dealt with. Nor does the report address gaps related to logistical or sociological barriers. The study makes limited reference to issues related to intellectual property, as this is the subject of much recent work and continuing debate (see Background Papers 1 and 2).

References


