

Promoting Access to Medical Technologies and Innovation

Intersections between public health, intellectual property and trade



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trade



**World Health
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Foreword by the Directors-General

Public health has been a priority for global action for many years. The right of everyone to the enjoyment of the highest attainable standard of physical and mental health is a universal human right, just as the burden of disease is shared by all humanity.

The constitution of the World Health Organization (WHO) underscores that achievements by any state in the promotion and protection of health are of value to all. In the age of globalization, progress made in public health in one country has an impact on the international community as a whole. Consequently, a compelling case can be made for effective international cooperation in public health, and such cooperation is an essential foundation for sustainable development.

Public health and medical technologies are an important focus of the international system, including in the system-wide work of the United Nations – most notably in the Millennium Development Goals (MDGs). The very founding objective of the WHO is the attainment by all peoples of the highest possible level of health. In addition, the World Intellectual Property Organization (WIPO) and the World Trade Organization (WTO) – in line with the mandates given to them by governments and their respective areas of expertise – have increasingly stepped up their efforts to support global endeavours to improve health outcomes.

International cooperation on public health takes many forms. Recent years have seen an intensified focus on the role of medical technologies – both the innovation processes that lead to new technologies and the ways in which these technologies are disseminated in health systems. Access to essential medicines as a dimension of the right to health has been a major concern for several decades. Now, however, the focus has broadened to consider how to promote the requisite innovation, how to address neglected health needs, and how to ensure equitable access to all vital medical technologies, including medicines, vaccines and medical devices. The evolving state of the global disease burden creates a constant demand for new and adapted technologies, so innovation and access are inevitably intertwined.

It is both a natural consequence of our mandated responsibilities and increasingly a practical necessity for the WHO, WIPO and WTO Secretariats to coordinate and cooperate ever more closely on issues such as patterns of innovation and access, legal and policy factors affecting the production and dissemination of medical technologies, and the interplay between public health, international trade rules and the intellectual property (IP) system. These are long-standing issues. Their relevance to a broad policy community was confirmed

by the Declaration on the TRIPS Agreement and Public Health (Doha Declaration), adopted on 14 November 2001 at the Fourth Ministerial Conference of the WTO. That Declaration was followed by a number of significant developments:

- The creation of new and innovative financing and procurement mechanisms, leading to significantly increased funding for medicines procurement and vaccine development.
- An evolving and more diverse pharmaceutical industry, and increasing innovative capacity in some developing countries.
- Innovative approaches to medical research and development (R&D) and its financing – particularly for neglected diseases – with an emphasis on public-private initiatives to develop required medical technologies.
- Renewed attention to the cost-effectiveness of national health systems.
- Growing global awareness of the impact of non-communicable diseases (NCDs) on health and socio-economic development, especially in developing countries.
- Increasing recognition of the need to move towards universal health coverage.
- Insights into the intersections between public health, the IP system, trade and competition rules, and measures to promote innovation and access to medical technologies.
- Better, more comprehensive and more accessible data on prices, access, patents and trade, enhancing the empirical base for informed priority setting and policy decisions.
- Greater policy coherence and practical cooperation on the intersection of health policy, trade and IP issues within the broader perspectives established by the human rights dimension of health and the UN MDGs.

Today there is now a richer, more diverse and more inclusive body of empirical data and practical experience available to guide technical cooperation. The technical cooperation offered by the three organizations has been characterized by active dialogue, coordination and partnership, leading to more effective and tailored capacity-building activities, all based on a better informed factual background. One of the objectives of this cooperation has been to create as much policy coherence as possible between the three organizations.

This study is an example of this strengthened trilateral cooperation, capturing a broad range of experience in

dealing with the interplay between IP, trade rules and the dynamics of access to, and innovation in, medical technologies. It draws together the three Secretariats' respective areas of expertise in relation to the overall framework concerning access to, and innovation in, the field of medical technologies, and it provides a platform for sharing practical experience and data, supporting and providing information to ongoing technical cooperation and policy discussions. The study is guided by the approach to cooperation on public health that has been catalysed by the Doha Declaration, by the WIPO Development Agenda, and by the WHO Global Strategy and Plan of Action on Public Health, Innovation and Intellectual Property.

We have been encouraged by the momentum, in recent years, towards a more informed, inclusive and nuanced policy debate on public health issues, buttressed by the

shared outlook defined by a common resolve to work towards universal access to essential medical technologies and to strengthen and diversify innovation systems.

The issues are complex and multifaceted, and call for diverse and tailored solutions: the following pages will not yield simple answers to the difficult questions confronting policy-makers. Yet we do expect that this study will provide a sound platform for future policy debate and analysis, and will serve those who seek answers to challenging questions. The publication of this study also represents a milestone in the efforts of the three agencies to deliver on their overlapping mandates in a coherent and cooperative manner; and we pledge continuing commitment on the part of the three agencies to continue to work, together with other international partners, towards the shared objective of universal coverage and better health outcomes for all.



Margaret Chan, Director-General, WHO



Francis Gurry, Director General, WIPO



Pascal Lamy, Director-General, WTO

Executive Summary

Why this study?

Public health is inherently a global challenge and thus assumes high priority for international cooperation. The World Health Organization (WHO) is the directing and coordinating authority for health, but the interaction between health issues and other policy domains – human rights, development policy, intellectual property (IP) and international trade – creates a strong rationale for cooperation and coordination between the WHO and other international organizations such as the World Intellectual Property Organization (WIPO) and the World Trade Organization (WTO). This study has emerged from an ongoing programme of trilateral cooperation between these agencies. It responds to an increasing demand, particularly in developing countries, for strengthened capacity for informed policy-making in areas of intersection between health, trade and IP, focusing on access to and innovation of medicines and other medical technologies. The need for cooperation and coherence at the international level has intensified over the past decade, as successive multilateral decisions have confirmed (see box).

The study is set in an evolving health policy context: notably, from an initial focus, a decade ago, on access to medicines for infectious epidemics, debate has broadened to consider innovation policy and a wider range of diseases and medical technologies. Policy-makers increasingly need to understand the complex interplay between different disciplines, at a time when stronger analytical tools and improved data open up new possibilities for this work. An integrated approach can reinforce a dynamic, positive interplay between the measures that promote innovation and those that ensure access to vital medical technologies. While addressing the broader issue of innovation and access to the whole range of medical technologies, the study focuses mainly on the area of medicines for which most practical experience and data are available.

Navigating the study

The study has been prepared as a capacity-building resource for policy-makers. The study is structured so as to enable users to grasp the policy essentials, and then to look more deeply into areas of particular interest. It therefore lays out a general panorama of the policy landscape (see Chapter II), so that all interrelated elements can be seen in context. It then provides more detailed accounts of issues specifically connected with innovation (see Chapter III) and access (see Chapter IV). The contents mirror the evolution of multilateral policy debate over the past decade, recognizing that innovation and access are inevitably intertwined – access without innovation would

Steps towards coherence	
2000	United Nations General Comment on the Right to Health
2001	WTO Doha Declaration on the TRIPS Agreement and Public Health
2002	WHO–WTO joint study <i>WTO Agreements and Public Health</i>
2003/5	WTO creates new TRIPS flexibility for access to medicines in countries lacking manufacturing capacity
2006	WHO Commission report on <i>Public health, innovation and intellectual property rights</i>
2007	WIPO Development Agenda
2008	WHO Global Strategy and Plan of Action on Public Health, Innovation and Intellectual Property
2009	WHO–WIPO–WTO trilateral cooperation commences

mean a declining capacity to meet an evolving global disease burden; and innovators need to consider how new technologies can reach those most in need.

- **CHAPTER I** presents the general background to health policy relating to medical technologies, sets out the distinct roles and mandates of the three cooperating agencies, and outlines the global disease burden that defines the essential challenge for health policy. In view of the significant contribution to health policy of a range of diverse actors, Annex I describes a selection of entities active in current policy processes.
- **CHAPTER II** outlines the essential elements of the international framework – health policy, IP and trade policy – laying an integrated basis for the following more detailed analysis of the innovation and access dimensions. It outlines the key insights of economics for medical technology innovation and access, in view of the growing use of economic concepts to inform health policy discussions. A final section reviews the policy issues associated with traditional medical knowledge, in view of its significance for national health systems and as an input to medical research.
- **CHAPTER III** provides a more detailed overview of policy issues concerning the innovation dimension of medical technologies. The historical pattern of medical research and development (R&D) provides a backdrop for analysing current trends in the R&D landscape. The

chapter looks at the innovation challenge presented by neglected diseases and related alternative and complementary instruments to promote research and development. It outlines the role of IP rights in the innovation cycle. A final section looks at influenza vaccines as a distinct example of innovation management and product development to address a specific global health need.

- **CHAPTER IV** deals with key aspects of the access dimension, describing the context for access to medical technologies and the current access framework for essential medicines. It then sets out the key determinants of access related to health systems, IP and trade. It reviews in particular pricing policies, taxes and mark-ups, and procurement mechanisms, as well as regulatory aspects and initiatives to transfer technology and boost local production, patent quality and review procedures, compulsory and voluntary licences, trade agreements, tariffs and competition policy.

As access and innovation issues are increasingly considered across a broader perspective, a more diverse set of stakeholders, values, experience, expertise and empirical data now shapes and informs policy debates, through:

- greater diversity of policy voices, creating opportunities for cross-fertilization between traditionally distinct policy domains (see Annex I)
- enhanced possibilities for harvesting the practical lessons of a far wider range of innovation and access initiatives
- improved global inclusiveness, quality and availability of empirical data on a range of interconnected factors, including the global health burden, access and pricing of medicines, regulatory and trade policy settings, and national IP systems.

The cross-cutting character of these policy domains means that some themes are introduced in Chapter II, in the course of sketching out the general policy framework, and are later elaborated in either Chapter III and/or Chapter IV which look in more detail at how these elements have bearing on innovation and access respectively. For example, the general elements and principles of IP policy are set out in Chapter II, while Chapter III elaborates aspects of IP policy, law and practice that bear particularly on innovation of medical technologies, and Chapter IV considers how specific aspects of IP impact on access to technologies. Similarly, the broad rationale for regulation of medical technologies is set out in Chapter II, and Chapters III and IV deal with the implications of product regulation

respectively for the innovation process and for access to medical technologies. Regarding trade policy, Chapter II sets out the main elements and Chapter IV considers the impact of trade and trade policy settings on access to medicines and other medical technologies.

The global disease burden is a moving target, requiring dynamic responses ...

Currently, most people in high-income countries live beyond the age of 70 and die of chronic diseases; these are also leading causes of death in middle-income countries, along with tuberculosis, HIV/AIDS and road traffic accidents; but in low-income countries, people predominantly die of infectious diseases and more than a third of all deaths are among persons aged under 15. Large declines in mortality from principal communicable, maternal, perinatal and nutritional causes are projected for 2030. But ageing of populations in low- and middle-income countries (LMICs) will result in more deaths due to non-communicable diseases leading to a double burden of disease. While preventive measures with respect to lifestyle, physical inactivity, tobacco use and harmful use of alcohol, nutrition and environmental factors are key, the innovation system has to adjust to these changes in the global disease burden. The focus on access to medicines – which in the past has been on communicable diseases such as HIV/AIDS and malaria – has broadened. Access to treatments for non-communicable disease, including expensive cancer treatments in middle-income countries, will be the challenge of the future and the focus of the access debate (see Chapter I, Section C).

Access to medicines and the right to health

Access to essential medicines and health services is an element of the fulfillment of the right of everyone to the enjoyment of the highest attainable standard of health. Furthering access to medicines is also part of the Millennium Development Goals (see Chapter II, Section A.1-3). The WHO framework for access to medicines recognizes that lack of access to medical technologies is rarely due to a single isolated factor and thus includes rational selection and use of medicines; affordable prices; sustainable financing; and reliable health and supply systems with quality as an underpinning element (see Chapter IV, Section A.1). Rational selection of the needed medication requires a country to identify which medicines are most important to address the national burden of disease. This selection can be guided by the WHO Model Lists of Essential Medicines. Political commitment to adequate and sustainable funding is a basic condition for effective and sustainable access (see Chapter IV,

Section A.1). Affordable prices are a critical determinant of access to medicines, especially in countries where public health sector is weak and where those with most limited means are often required to secure medicines at market prices. Generic competition is a key factor in driving prices down; yet even low priced generic medicines are often still unaffordable for large parts of the population in many LMICs and availability of essential medicines in the public sector is still insufficient (see Chapter IV, Section A). The overarching condition for providing access to needed medical technologies and health services is a functioning national healthcare system (See Chapter II, Section A.5, and Chapter IV, Section B).

Access for HIV/AIDS treatments has been a major focus for policy-makers in recent years. Low prices for generic antiretroviral treatments have helped governments and donor programmes progress towards the goal of having 15 million people on treatment by 2015 (see Chapter IV, Section A.2). Other critical areas are access to and innovation of paediatric formulations and medical devices (see Chapter IV, Sections A.2 and A.3). The changing burden of disease also leads to a greater focus on access and IP issues in relation to non-communicable diseases (see Chapter IV, Section A.2). National immunization programmes are a highly effective public health tool for the prevention of illness and the spread of infectious diseases. Distinct market conditions and know-how requirements create a different landscape for the development and dissemination of vaccines (see Chapter III, Section B.4, and Chapter IV, Section A.2, see also Chapter III, Section E).

Governments explore further measures to contain costs and increase access

Governments employ many different means to cut prices for medical technologies, including direct price controls, reference pricing, and reimbursement limits; and they increasingly use health technology assessments to control costs (see Chapter IV, Section B.1). On top of import tariffs (see Chapter IV, Section D), various taxes (see Chapter IV, Section B.3) and mark-ups along the supply chain (see Chapter IV, Section B.4) also boost consumer prices and constrain access. Removing tariffs and taxes and regulating supply chain distribution mark-ups can lower prices, where passed on to consumers. Yet, price regulation equally needs to ensure sustainable margins for commercial suppliers.

Differential pricing applied by companies can be a complementary tool to increase access, by linking prices to the differing capacity to pay according to income levels within distinct markets (see Chapter IV, Section B.2). Another strategy for enhanced access to medicines stresses developing local production capacity and

leveraging technology transfer, which raises issues of access to medicines, economic and commercial factors, and industrial policy (see Chapter IV, Section B.6).

With regard to access to patented products, countries also make use of the flexibilities available under the WTO Agreement on Trade-Related Aspects of Intellectual Property Rights (TRIPS Agreement).

Regulation of technologies is vital in itself, but can impact innovation and access

Regulation of medical technologies addresses essential health policy objectives: products must be safe, efficacious and of adequate quality. Yet, regulation also shapes the landscape for access and innovation: higher safety standards require the generation of more data and thus increases the cost of innovation. Unjustified regulatory barriers and lengthy marketing authorization processes delay access to needed medical technologies (see Chapter II, Section A.6). Most clinical trials are carried out by or on behalf of the companies developing the tested products. The registration of these trials is a scientific and ethical responsibility and therefore WHO runs the International Clinical Trials Registry Platform. From the perspective of public health policy, clinical trial results should be publicly available, so that researchers and other interested groups themselves can assess the efficacy and potential side effects of new products (see Chapter III, Section B.5). The emergence of biological medicines has raised challenges for established regulatory systems, notably how to regulate “biosimilar” follow-on products (see Chapter II, Section B.6) while still sufficiently incentivising originator companies.

Another challenge for regulatory systems is the steady increase of substandard and spurious/false-labelled/falsified/counterfeit (SFFC) medical products that are posing serious public health problems globally, and especially in regions where the regulatory and enforcement systems are weak. To effectively combat substandard and SFFC medicines a mix of measures is required. Enforcement of good manufacturing practice standards is required to eliminate substandard products while to fight SFFC products additional measures are needed, including border controls and criminal law along with collaboration between legislative bodies, enforcement agencies and courts at the national and international levels (see Chapter II, Section B.1, and Chapter IV, Section B.7).

Overall, regulators face the challenge to balance the benefit of the early release of new products with safety concerns and to define an acceptable level of risk. The need to simplify regulation while maintaining its stringency and cost-effectiveness requires more

coordination through regional and international regulatory mechanisms, so as to enable suppliers to service regional markets without undue regulatory complexity or cost (see Chapter II, Section A.6). Full international harmonization of regulatory standards remains an elusive goal. The WHO Prequalification Programme has greatly facilitated the access to quality medical products in developing countries (see Chapter IV, section B.7).

Innovation in medical technologies operates in a complex, fast evolving policy framework ...

Innovation in medical technologies requires a complex mix of private and public sector inputs; it differs from innovation in general due to the ethical dimension of medical research, a rigorous regulatory framework, liability questions, and the high cost and high risk of failure. Economic, commercial, technological and regulatory factors have precipitated rapid change in the current landscape for R&D, involving more diverse innovation models and a wider range of active players. Providing specific incentives to absorb the high cost and associated risks and liabilities is a central policy challenge; this has been the historic role of the patent system in particular as applied to pharmaceuticals. While estimates vary of the actual cost of medical research and product development, innovation is undoubtedly costly and time consuming. The risk and uncertainty of innovation increases R&D costs in this sector, as the cost of products that fail to clear regulatory hurdles to become commercialized products has to be added (see Chapter III, Section B.3). Rising expenditure for medical research has not been matched by a proportionate increase in new products entering the market, sparking a debate about research productivity and a quest for new models of innovation and for financing R&D. Many initiatives are exploring new strategies for product development, thus informing a rich debate about how to improve and diversify innovation structures to address unmet health needs. Current policy discussions have reviewed possibilities for open innovation structures, and a range of push and pull incentives, including schemes such as prize funds that would delink the price of products from the cost of R&D (see Chapter III, Section C.2).

... sparking new thinking on industry's role and structure, and on the public/private divide

This evolving innovation landscape is driving change in the pharmaceutical industry; driving factors include tighter government health budgets; non-profit entities engaged in

medical research and product development; the exposure to stricter product regulation and greater liability risks; new technologies enabling targeted treatment; and the greater share of global demand from emerging markets. The historic industry model of vertically integrated in-house R&D and exclusive marketing is opening up to more diverse and collaborative structures, with major industry players developing products by integrating technologies sourced elsewhere, either licensed in or acquired through mergers and integration of smaller firms. Research-based firms have also invested in generic production capacity. The role of public research and academic institutions, increasingly in developing countries, has also come under the spotlight as they seek to reconcile public interest responsibilities with the need for private sector partnerships to deliver new medical products (See Chapter III, Sections A and B, and Chapter II, Section C).

Neglected diseases: a policy challenge but a growing focus of practical initiatives

Market-based innovation models fail to address the disease burden specific to developing countries, the so-called neglected diseases. Since this research gap has been identified, the landscape of health research for these diseases has evolved. Product development partnerships (PDPs) have been a significant development over the past decade, drawing together not-for-profit entities and industry players, with major philanthropic funding, significantly increasing the number of products in development for neglected diseases, and identifying pathways regarding existing research gaps (see Chapter III, Section C.4). Pharmaceutical research based companies also engage increasingly in philanthropic research. Several companies have established dedicated research institutes to research on diseases disproportionately affecting developing countries or participated in cooperative projects to share assets and knowledge, such as WIPO Re:Search, which has been developed to make better use of IP protected assets and improve access (See Chapter III, Sections C.5-6). However, much more needs to be done by the international community in this area. The WHO Consultative Expert Working Group has recommended that negotiations begin on a globally binding treaty on R&D for neglected diseases. The recommendations of the Group were discussed by WHO member states in an intergovernmental meeting in November 2012 (see Chapter III, Section C.3).

The IP system at the centre of debate on innovation and access ...

Several elements of the IP system touch both on innovation and on access (see Chapter II, Section B.1).

The focus has been on the patent system and test data protection, but other relevant aspects of IP include the relationship between trademarks and international nonproprietary names (INN) and copyright questions regarding the package insert of medicines (see Chapter II, Section B.1). The patent system has been widely used for medical technologies especially by the pharmaceutical sector. Indeed, the pharmaceutical sector stands out in terms of its dependence on patents to capture returns to R&D, but its role in innovation and how to enhance its effectiveness are matters of continuing debate (see Chapter III, Section B). Patents, in principle, promote innovation by providing incentive to invest in R&D, a particular consideration for the private sector. Patents function to structure, define and build innovation partnerships. The impact of patents on access is complex and an area of particular focus: policy options mean that the mere existence of a patent need not be an absolute barrier to access, but equally the absence of an enforceable patent right does not guarantee effective access (see Chapter IV, Section C).

The TRIPS Agreement sets minimum standards for IP protection and enforcement. For example, patents must be available for any innovations in all fields of technology, provided they are new, involve an inventive step (or are non-obvious) and are capable of industrial application (or are useful). The role of intellectual property rights in the innovation cycle is addressed in Chapter III, Section D. Strict patentability criteria and strict patent examination supported by patenting examination guidelines contribute to prevent strategies employed to delay the entry of generic competition, such as “evergreening” (see Chapter III, Section D.3, and Chapter IV, Section C.1). Integral to the patent system is the requirement to make accessible such innovation through public disclosure, thus creating an extensive knowledge base. The resultant patent information serves as a tool for charting freedom to operate, potential technology partnerships, and procurement options, as well as giving policy-makers insights into patterns of innovation (see Chapter IV, Section B.5). Patent information is more accessible in general, but coverage of data concerning many developing countries remains a challenge. Recent trends show a growth in patent applications on medical technologies from a more diverse range of public and private entities, and from key emerging economies (see Chapter II, Section B.1).

The protection of clinical trial data also illustrates the complex relationship between the IP system and innovation and access. Protecting these data against unfair commercial use is important given the considerable efforts made to generate these data and thus bring new medicines to the market. On the other hand, certain forms of test data protection potentially delay the entry of generic medicines. The TRIPS Agreement requires

protection of test data, but does not specify the exact form it should take, and national authorities have taken diverse approaches (see Chapter II, Section B.1).

How patents are licensed can determine their impact on public health ...

Appropriate licensing of patents can help build partnerships and enable innovation through cooperation to bring new medical technologies to fruition. Private sector licensing strategies typically aim at commercial objectives, but public sector entities can use patents expressly to leverage public health outcomes. New models of socially responsible licensing protect IP while ensuring that new medical technologies are available and affordable for underserved communities. Public-private partnerships have resulted in creative licensing agreements that forgo profit maximization in favour of providing essential technologies to poorer countries at affordable prices. Voluntary licences also form part of corporate social responsibility programmes, especially for HIV/AIDS treatments. The Medicines Patent Pool has reinforced the trend towards voluntary licensing programmes that increase access to medicines by enabling new formulations and enhancing provision of cheaper generic medicines for developing countries (see Chapter IV, Section C.2).

... as do policy options and IP flexibilities

A wide range of policy options and flexibilities are built into the international IP regime that can be used to pursue public health objectives. These options are not self-actuating at the international level, though, and attention and action are needed at the domestic level as to how best to implement such flexibilities, so that the national IP regime responds to each country's individual needs and policy objectives. Key options include transition periods for LDCs (see Chapter II, Section B.1), differing IP exhaustion regimes, refining the criteria for grant of a patent, pre-grant and post-grant opposition procedures, as well as exceptions and limitations to patent rights once granted, including regulatory review exception (“Bolar” exception) to facilitate market entry of generics, compulsory licences and government use. Countries have used these instruments to improve access to medicines for both communicable and non-communicable diseases (see Chapter IV, Sections C.1-3). WTO members have agreed to amend the TRIPS Agreement to permit a wider use of compulsory licensing for access to medicines, clearing a potential legal barrier for countries that need to import medicines produced abroad under a compulsory licence, through

the grant of special compulsory licences for export under what is termed the “Paragraph 6 System” (see Chapter IV, Section C.2, and Annex II). While the legal scope for flexibilities is now clearer, thanks also to the Doha Declaration on Public Health, and some flexibilities are widely implemented (such as “Bolar” exceptions), policy debate continues on the use of measures such as compulsory licensing.

International trade is an essential avenue to access, but does not eliminate economic disparities

International trade is vital for access to medicines and other medical technologies, markedly so for smaller and less resourced countries. Trade stimulates competition, which in turn reduces prices and offers a wider range of suppliers, improving security and predictability of supply. Trade policy settings, such as tariffs on medicines, pharmaceutical ingredients and medical technologies, therefore directly affect their accessibility (see Chapter II, Sections B.3-5, and Chapter IV, Section D). Trade policy and the economics of global production systems, are also key factors in strategic plans to build domestic production capacity in medical products. Non-discriminatory domestic regulations founded on sound health policy principles are also important for a stable supply of quality health products. Access to foreign trade opportunities can create economies of scale to support the costs and uncertainties of medical research and product development processes.

Developed countries have dominated trade in health-related products but India and China have emerged as leading global exporters of pharmaceutical and chemical inputs, and some other developing countries have shown strong recent export growth. Countries’ imports of health related products differ dramatically according to level of development, illustrating substantial and widening gaps in access: over recent years, LDC imports have grown least, starting from a low base.

Import tariffs on health-related products can affect access: since they increase cost early in the value chain, their impact on price may be magnified. Developed countries have largely eliminated such tariffs, in line with a WTO deal on pharmaceutical trade. Other countries have reduced tariffs significantly, but the picture is still mixed: some developing countries structure tariffs to promote local production, while LDCs apply lower tariffs (see Chapter IV, Section D.1).

Competition policy promotes effective innovation and helps shape the conditions for access

Competition policy is relevant to all stages in the process of supplying medical technology to patients, from their development to their sale and delivery. The creation of sound competitive market structures through competition law and enforcement has thus an important role to play in enhancing both access to medical technology and fostering innovation in the pharmaceutical sector. It can serve as a corrective tool if and when IP rights hinder competition and thus constitute a potential barrier to innovation and access. Competition authorities in several jurisdictions have taken action to address anticompetitive practices in the pharmaceutical sector, including some patent settlements, certain licensing practices and pricing policies. Competition policy also has an important role to play in preventing collusion among suppliers of medical technology participating in procurement processes (see Chapter II, Section C.2, and Chapter IV, Section D.2).

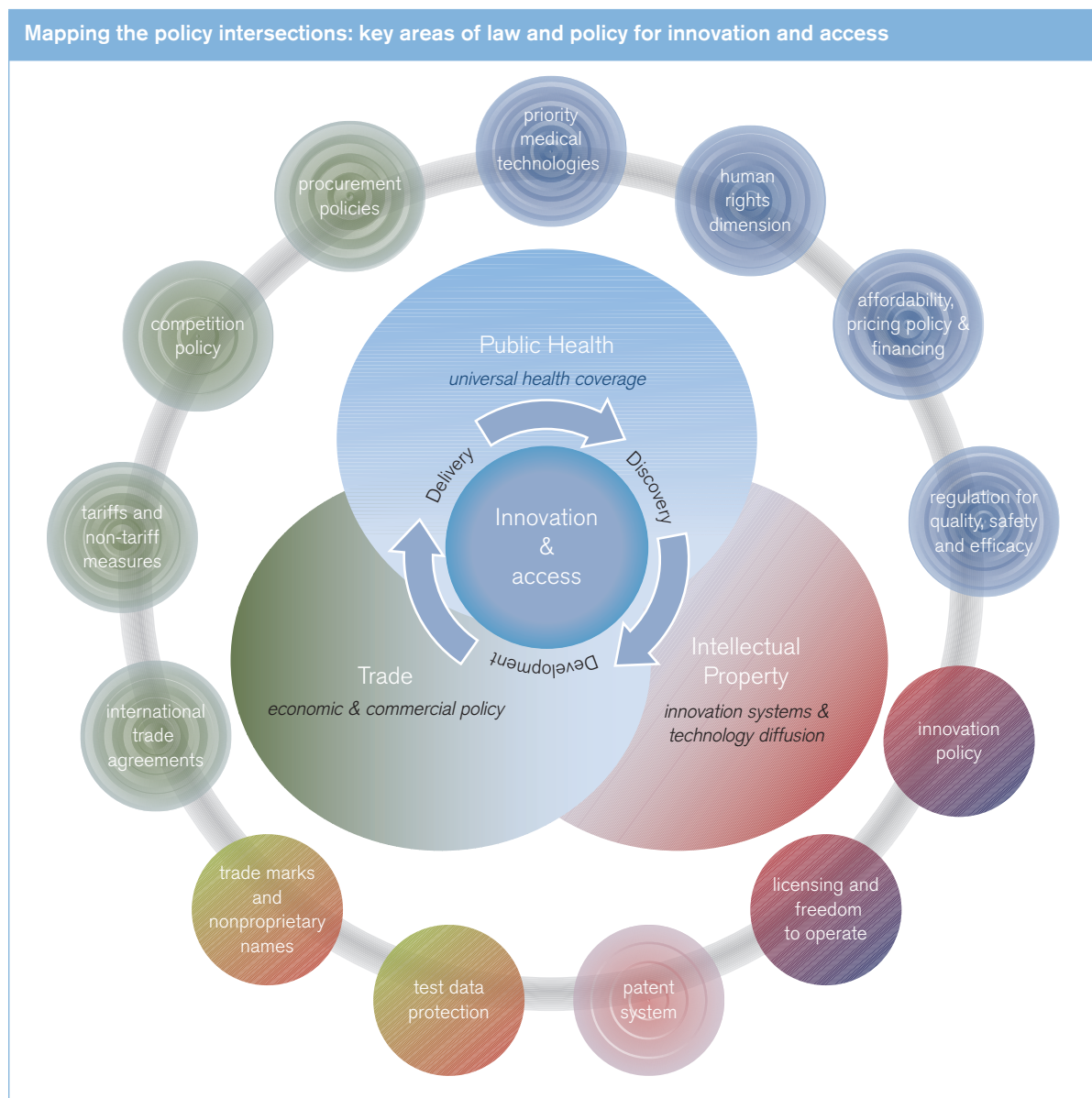
Access to medical technologies through more effective government procurement

Access to medical technologies in many countries largely results from government procurement, with pharmaceuticals made available through public funds or subsidies. Procurement systems aim to obtain medicines and other medical products of good quality, at the right time, in the required quantities, and at favourable costs. These principles are particularly important in the health sector given the large expenditures, health impact of value for money and quality issues, with some programmes reportedly paying considerably more than necessary for medicines (see Chapter IV, Section B.5). Procurement policies favouring open and competitive tendering become increasingly important in a fiscal climate when national budgets are under pressure, and philanthropic programmes confront funding constraints. Good governance in procurement is consistent with increasing access to medical technologies through lower prices and uninterrupted supply. The WTO’s plurilateral Government Procurement Agreement provides an international framework of rules to promote efficiency and good governance in public procurement, with particular application to procurement of medicines, promoting transparency, fair competition and improved value for public expenditure (see Chapter II, Section B.4).

Free trade agreements beyond the multilateral sphere have increasing relevance for access issues

The international policy and legal framework has been made more complex by the recent growth of trade and IP agreements, outside the established multilateral forums. Policy debate has focused on intellectual property and pharmaceutical regulation measures in these agreements, and their impact on access to medicines. For example, patent term extensions, data exclusivity and other measures such as patent linkage contained in certain free

trade agreements are designed to incentivize innovation, but also have the potential to affect access to medicines by delaying the market entry of generic products (see Chapter IV, Section C.5). These agreements also set standards in other policy areas with implications for access, notably standards established on government procurement and competition policy, as well as preferential tariffs on pharmaceuticals, inputs, and other health products (see Chapter II, Section B.5, and Chapter IV, Section C.5). The overall impact of this trend for the international system is yet to be systematically analysed, in particular the full implications of the entire range of such agreements for access to medical technologies.



I. Medical technologies: the fundamentals

Against the background of the global burden of disease and global health risks, this chapter outlines the fundamental imperative for collaboration between various stakeholders interested in medical technologies. It also demonstrates the need for a coordinated approach, taking into account health, intellectual property and trade variables, in order to ensure coherent decision-making in the area of public health at the international, regional and domestic levels.

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A. Public health and medical technologies: the imperative for international cooperation

Key points

- The WHO, WIPO and the WTO each have distinct, but complementary, mandates to work on issues relating to public health, innovation and intellectual property (IP), and trade.
- Although the main international developments mostly relate to medicines, this study also covers to a certain extent other medical technologies, such as vaccines and medical devices, including diagnostics, due to their importance for achieving public health outcomes.
- Public health and IP policy-makers are faced with the challenging task of identifying the right mix of policy options to best advance their national objectives. Governments are therefore seeking more coherent, comprehensive and accessible information for policy debate.
- The tenth anniversary of the adoption of the Doha Declaration provided a timely opportunity to harvest the experience gained in improving access to, and promoting, medical innovation.
- This study is designed to serve as a background reference for policy-makers in the widest sense – lawmakers, government officials, delegates to international organizations, non-governmental organizations (NGOs) and researchers.

Health is a fundamental and universal human right. The attainment by all peoples of the highest possible level of health is the foundational objective of the WHO. The Preamble of the WHO Constitution emphasizes that international cooperation is essential for the promotion of health:

“The health of all peoples is fundamental to the attainment of peace and security and is dependent upon the fullest co-operation of individuals and States.

The achievement of any State in the promotion and protection of health is of value to all.

Unequal development in different countries in the promotion of health and control of disease, especially communicable disease, is a common danger.”

This central objective of the WHO, the essential logic of international cooperation, and the responsibility to take practical action have compelling implications for the international community. Accordingly, public health outcomes are of importance to WIPO, which also focuses on the social and developmental dimensions of innovation and the transfer and dissemination of technology. WIPO policy discussions and technical cooperation activities, including a range of programmes conducted in partnership with the WHO and the WTO, have focused increasingly on public health matters.

WTO members have stressed the need for a positive link between public health and the global trading system. In the Declaration on the TRIPS Agreement and Public Health (Doha Declaration),¹ members “recognize the gravity of

the public health problems afflicting many developing and least-developed countries, especially those resulting from HIV/AIDS, tuberculosis, malaria and other epidemics”, and articulate “the need for the WTO Agreement on Trade-Related Aspects of Intellectual Property Rights (TRIPS Agreement) to be part of wider national and international action to address these problems”.

“... we will be exploring how best to harvest the potential of [the three organizations’] reserves of knowledge and information, to strengthen cooperation towards a goal all can surely share: put simply, that of getting needed medicines to the people who are in most need.”²

Pascal Lamy, *Director-General, WTO*

1. Policy coherence

The WHO, WIPO and the WTO each have distinct, but complementary, mandates to work on issues relating to public health, innovation and intellectual property (IP), and trade. The three organizations therefore share a responsibility to strengthen practical dialogue between themselves and other partners in order to fulfil their mandates more effectively, to ensure the efficient use of resources for technical cooperation and to avoid duplication of activities.

Coherence is vital in international action to address public health problems. Such coherence has never been

more important for the technical cooperation work of the three organizations than it is at the present time. The WHO brings vast expertise in all areas of public health, including medicine and vaccine policies, medical devices, regulatory questions, pricing and procurement, in addition to other factors affecting access to medicines. WIPO is uniquely positioned to help organizations work towards creating a truly global view and understanding of the IP system, including the flexibilities to implement the patent system at the national level, to provide information on patents, including information on the patent status of key medicines and vaccines in developing countries, and to lend its expertise on patent law and its interplay with public policy. The WTO works on several aspects of trade policy that have direct relevance to public health, including IP rules and flexibilities within the international legal system, as they affect both the access and innovation dimensions.

The Doha Declaration has served as a catalyst for developing coherence at the international level. In conjunction with its role of making public health issues a central focus of work carried out by the WTO on IP and international trade, the Doha Declaration has been taken up in a series of World Health Assembly (WHA) resolutions on ensuring accessibility to essential medicines and public health, innovation and IP. Notably, the Doha Declaration was a point of reference in the negotiations on the WHO Global Strategy and Plan of Action on Public Health, Innovation and Intellectual Property (GSPA-PHI). The WIPO Development Agenda³ deals extensively with flexibilities in international IP law, including the health-related flexibilities specifically identified in the Doha Declaration.

These mandates and competencies have been at the centre of policy debates. For example, the 2011 Political Declaration of the High-level Meeting of the General Assembly on the Prevention and Control of Non-communicable Diseases⁴ called for the WHO and other international organizations to work together in a coordinated manner to support national efforts to prevent and control non-communicable diseases (NCDs), and mitigate their impacts.

*"Discussions [of access to medicines] almost inevitably turn to questions of prices, patents, intellectual property protection, and competition."*⁵

Margaret Chan, *Director-General, WHO*

2. Scope of the study

Although the main international developments mostly relate to medicines, this study also covers to a certain extent other medical technologies, such as vaccines and medical devices, including diagnostics, due to their importance for achieving public health outcomes. While some of the

lessons learned about access and innovation with respect to medicines may also be useful with respect to these other medical technologies, there are also significant differences regarding the role of IP and innovation and access. Other important determinants for public health, such as human resources, health financing and health systems, do not fall within the scope of this study.

3. The need for this study

Governments have choices to make regarding the appropriate implementation of policy instruments in their domestic systems and practices. Even though international standards apply to most of the main policy instruments – in particular IP – there is "policy space" within and around those standards. Public health and IP policy-makers are faced with the challenging task of identifying the right mix of policy options to best advance their national objectives. Governments are therefore seeking more coherent, comprehensive and accessible information for policy debate. The aim of the technical cooperation activities of the WHO, WIPO and the WTO is to facilitate understanding of the full range of options and their operational context, rather than programmes that simply explain the legal framework. This study draws together the materials used in technical cooperation and it addresses emerging needs for information in an accessible, systematic format, in order to support ongoing collaborative efforts.

*"... [T]here is a vast area of practical cooperation, which is very important in the achievement of the balance between creation, on the one hand, and diffusion of the social benefit of creation, on the other hand."*⁶

Francis Gurry, *Director General, WIPO*

The Doha Declaration recognized that "intellectual property protection is important for the development of new medicines". However, it also recognized the concerns about IP effects on prices. The challenge for governments is to use the policy instruments at their disposal to address both aspects in a mutually reinforcing manner. Since the early 2000s, policy-makers have sought effective ways to strengthen the positive linkages between, on the one hand, the private sector's capacity to finance research and development (R&D) and, on the other hand, the public policy goals of selecting, supplying and using medicines in the most rational way.

*"Public health now finds itself caught in a cross-current of rising expectations and ambitions, set against rising demands and costs, at a time when funds are stagnant or shrinking. In such a situation, introducing greater efficiency is a far better option than cutting budgets and services."*⁷

Margaret Chan, *Director-General, WHO*

Rising health-care costs have led to increased national public health budgets and higher public expectations for health care. In difficult economic times, there is even more reason to evaluate the efficiency and fairness of their health services, including expenditure on medicine and medical technology. Effective delivery of health care also means adapting technologies to diverse local needs and priorities. Developing countries are facing an increased disease burden of NCDs. The increased availability of patents for medicines has implications which pose a further challenge in a wider range of countries, notably in key low-cost exporting countries that have traditionally specialized in generic medicine production. The evolving disease burden, the lack of medicines required for treating neglected diseases, and the challenges of drug resistance all require the development of new medicines, vaccines and effective dosage forms, as well as effective delivery mechanisms. Innovation needs to be encouraged – both in terms of inventing new medicines and also in terms of providing effective systems to bring new products through very complex product development stages, and to market and deliver them to patients. Policy-makers have recognized the need to look beyond conventional approaches to R&D in order to address the innovation gap – particularly in the area of neglected diseases.

“... [T]here is indeed great potential, still mostly untapped, for the use of empirical data to inform policy debate on health innovation and access to medicines. ... [A]ll of us who care deeply about health innovation and access to medicines would benefit from improved accessibility of these raw data, but also from the careful putting together of all the pieces of the empirical puzzle.”⁸

Pascal Lamy, *Director-General, WTO*

4. The timing of the study

The tenth anniversary of the adoption of the Doha Declaration provided a timely opportunity to harvest the experience gained in improving access to, and promoting, medical innovation. Today there is a greater understanding of legal and policy options, which has led to richer dialogue. There has been a change in the WTO rules on patents for medicines arising from paragraph 6 of the Doha Declaration, with the conscious goal of creating additional flexibility for countries with the least resources. Recent years have seen a proliferation of new initiatives – public, private and philanthropic – for innovation and product

development to address unmet health needs, together with new and adapted approaches to procurement. Today, much better data is available globally on areas such as pricing, scope of access to medicines and patent coverage.

This study follows on from the 2002 study entitled *WTO Agreements and Public Health: A Joint Study by the WHO and the WTO Secretariat*. This earlier study examined the linkages between trade and health policies in general to enable trade officials and health officials to better understand and monitor the effects of their work on each other's areas of responsibility. This new study updates the material on IP and other trade aspects as they relate to innovation of, and access to, medical technologies, the areas which have seen most change in the decade since then. The 2002 study remains a useful resource on many issues, such as health services, infectious disease control, food safety and tobacco.

“Health, trade and innovation are indispensable issues when tackling the problems that we are increasingly facing in a globalized world.”⁹

Francis Gurry, *Director General, WIPO*

5. Who should read this study?

This study is designed to serve as a background reference for policy-makers in the widest sense – lawmakers, government officials, delegates to international organizations, non-governmental organizations (NGOs) and researchers. It is also designed to serve as a resource for the three organizations' technical cooperation activities. It has been prepared to serve the needs of policy-makers who may already have a strong background in either trade or IP or the health aspects of improved access and medical innovation, and who seek a comprehensive presentation of the full range of issues, including institutions and legal concepts with which they are unfamiliar.

The study represents the first joint publication by the WHO, WIPO and the WTO, with the aim of providing a solid factual foundation for ongoing policy debates. Nothing in the study should be taken as a formal position or the interpretation of rights and obligations by any of the three organizations, or by any of their respective member states. Actual policy choices and interpretations of member states' rights and obligations remain exclusively a matter for governments.

B. The cooperating agencies: the WHO, WIPO and the WTO

Key points

- The WHO is the directing and coordinating authority for health within the UN system. It is responsible for providing leadership on global health matters, shaping the health research agenda, setting norms and standards, articulating evidence-based policy options, providing technical support to countries, and monitoring and assessing health trends.
- WIPO is the specialized agency of the United Nations dedicated to developing a balanced and accessible IP system which rewards creativity, stimulates innovation and contributes to economic development in the public interest.
- The core mission of the WTO is to open trade as well as to maintain and further develop the rules-based international trading system.
- Given that partnership is crucial for an effective international response to the ever-evolving challenges facing public health, the WHO, WIPO and WTO Secretariats have intensified interagency collaboration on matters related to public health, intellectual property and trade.

This section provides a brief overview of the specific roles, mandates and functions of the WHO, WIPO and the WTO, which cooperate within the general international framework on issues related to the interface between public health, intellectual property (IP) and trade concerning innovation in, and access to, medical technologies. Additional information on the work of a range of other international organizations, NGOs, industry bodies and other stakeholders can be found in Annex I.

1. World Health Organization

The WHO is the directing and coordinating authority for health within the UN system. It is responsible for providing leadership on global health matters, shaping the health research agenda, setting norms and standards, articulating evidence-based policy options, providing technical support to countries, and monitoring and assessing health trends.

Monitoring the impact of trade and intellectual property rights (IPRs) on public health is one of the strategic areas of the work of the WHO. Following the adoption of the WTO Agreement on Trade-Related Aspects of Intellectual Property Rights (TRIPS Agreement), the Forty-ninth World Health Assembly (WHA), in May 1996, adopted the first mandate of the WHO, to work on the interface between public health and IP.¹⁰ In subsequent years, often following long negotiations, many more resolutions were adopted, continually broadening and reinforcing the WHO mandate to work on issues related to public health, trade and IP.

In May 2003, WHO member states decided to establish the Commission on Intellectual Property Rights,

Innovation and Public Health (CIPIH), which was chaired by former Swiss Federal Councillor Ruth Dreifuss, to produce an analysis of the interface between IPRs, innovation and public health.¹¹ In April 2006, the CIPIH published its report (WHO, 2006b), which contained 60 recommendations aimed at fostering innovation and improving access to medicines. It concluded that:

“Intellectual property rights have an important role to play in stimulating innovation in health-care products in countries where financial and technological capacities exist, and in relation to products for which there are profitable markets. However, the fact that a patent can be obtained may contribute nothing or little to innovation if the market is too small or scientific and technological capability inadequate. Where most consumers of health products are poor, as are the great majority in developing countries, the monopoly costs associated with patents can limit the affordability of patented health-care products required by poor people in the absence of other measures to reduce prices or increase funding.”

Following CIPIH recommendations, WHO member states subsequently developed a global strategy and plan of action on public health, innovation and IP.¹²

Its adoption was the result of a debate that continued for many years and can be considered a major step forward in the process of achieving global consensus on practical action on public health, innovation and IP. For the WHO, the GSPA-PHI is a milestone, as it reaffirms and extends the mandate of the WHO to work at the interface of public health and IP. It also demonstrates that it is feasible to find a common ground, based on dialogue.

IP issues have also been addressed during other negotiation processes at the WHO, such as:

- the establishment of the Pandemic Influenza Preparedness (PIP) Framework for the Sharing of Influenza Viruses and Access to Vaccines and other Benefits
- the creation of an international mechanism to combat substandard and spurious/falsely-labelled/falsified/counterfeit medical products
- the WHO Global Health Sector Strategy on HIV/AIDS, 2011-2015
- the prevention and control of NCDs.

The WHO has produced a large body of material to provide evidence-based guidance to its member states in order to support them during the process of shaping their policies on public health and IP. The WHO has also jointly hosted with other relevant organizations numerous training and capacity-building activities in all WHO regions, and it continues to do so in close collaboration with WIPO and the WTO. Member states have also requested on a regular basis technical assistance on issues related to public health and IP.

2. World Intellectual Property Organization

WIPO is the specialized agency of the United Nations dedicated to developing a balanced and accessible IP system which rewards creativity, stimulates innovation and contributes to economic development in the public interest.

The core activities of WIPO include:

- administering multilateral treaties and supporting the evolution of the international legal IP frameworks
- providing global IP services to facilitate easier and more cost-effective international protection, and also to facilitate arbitration, mediation and other alternative dispute resolution services
- assisting in establishing national IP and innovation strategies, developing appropriate regulatory frameworks and building the infrastructure and human capacity needed to harness the potential of IP for economic development
- developing technical platforms to facilitate cooperation among IP offices
- developing free databases of patents, trademarks and industrial designs to facilitate access to knowledge
- building awareness, understanding and respect for IP
- working in partnership with the United Nations and other organizations to identify IP-based contributions to climate change, food security, public health and other global challenges.

The 2007 WIPO General Assembly established the WIPO Development Agenda¹³ to ensure that development considerations form an integral part of the work of WIPO. Development is considered a cross-cutting issue which impacts on sectors of the organization. The 45 Development Agenda recommendations guide the work of WIPO.

In addition to the promotion of technological innovation and technology dissemination as general objectives of the patent system, several areas of the work carried out by WIPO have particular relevance for public health.

In 2009, WIPO established the Global Challenges Program to address innovation and IP as they relate to global and interconnected issues, such as climate change, public health and food security. Innovation and access to the results of innovation are central issues in the area of IP. The challenge for public health policy-makers is to provide an environment for health innovation and to promote access to new medical technologies. The WIPO Global Challenges Program seeks to raise awareness and understanding of the interplay between innovation, technology transfer and the dissemination of technology, among others, as they relate to health innovation and access to medicines. WIPO works also with both private and public sector and has launched a new consortium, WIPO Re:Search, to enable the sharing of IP and expertise to promote the development of medicines to treat neglected diseases (see Chapter III, Section C.6).

WIPO seeks to ensure that the development of international patent law keeps pace with the rapidly evolving technological, economic and social environment. The continuing growth in the number of patent applications worldwide and the constant development of technologies present a challenge for the effective and efficient handling of patent applications, for the achievement of high quality in patents which are granted internationally, and for the role of patents in contributing to innovation and the dissemination of technology. WIPO not only advises its member states how to implement the requisite legal framework but also how to assess options and to develop coherent policy strategies. WIPO member states have been engaged in discussions with the Standing Committee on the Law of Patents (SCP) on issues related to patents and health since 2011.

In 1998, WIPO established the Traditional Knowledge Program. One of the objectives of this programme is to achieve the more effective use of IP principles and systems for the legal protection of traditional knowledge, including traditional medicine.

In line with its goal of fostering international policy dialogue on IP and public health, WIPO also engages substantively with other relevant stakeholders – UN and intergovernmental organizations, governments of member states, civil society and NGOs, as well as the private sector and academia.

3. World Trade Organization

The core mission of the WTO is to open trade as well as to maintain and further develop the rules-based international trading system. International trade and trade rules intersect with public health objectives in various areas and in many different ways. Most directly, integration into the world economy can enhance access to the most basic requirements for good health, such as the safe supply of food or access to health-related products and services. Indirectly, trade offers the opportunity for economies to grow and thus contributes to the alleviation of poverty and ill health.

The importance of public health has been recognized in the rules of the multilateral trading system since 1947. The General Agreement on Tariffs and Trade (GATT), adopted in 1947 and subsequently incorporated in the GATT 1994, contains an exception in Article XX(b) which explicitly recognizes the right of governments to enact trade-restricting measures whenever these are necessary to protect human life and health. The right to take measures for the protection of health is also included in other relevant WTO agreements, including the TRIPS Agreement.¹⁴

The implementation of the rights and obligations established under the WTO agreements, including those related to public health, is overseen by the competent WTO bodies. While most issues related to the implementation and compliance with those obligations are resolved through bilateral consultations, or within the competent WTO bodies, only very few disputes brought to the WTO have dealt with measures related to human health protection. In these particular cases, what was challenged was not the right to protect health, but the appropriateness of the measures chosen to achieve the objective of health protection.¹⁵ The WTO Dispute Settlement Body has consistently maintained that it is within the authority of each WTO member to set the public health objectives it seeks to achieve. Governments have thus retained the right to use available exceptions and flexibilities necessary to achieve their targeted levels of health protection.¹⁶

The search for a balance between the need to protect IPRs to provide incentives for R&D on the one hand and, on the other hand, to address concerns about the potential impact of such protection on the health sector – in particular its effect on prices – has been an important consideration in the WTO's work. A number of provisions in the TRIPS Agreement are directly relevant to public health. WTO members have the flexibility to interpret and implement these provisions in a manner supportive of their right to protect public health. The importance of creating a positive, mutually reinforcing link between the IP system and access to medicines was explicitly recognized in the Doha Declaration. Two years later, the Doha Declaration led to the adoption of a mechanism often referred to as the "Paragraph 6 System". This additional flexibility – in the form of a special compulsory licence for export

established under the 2003 waiver decision¹⁷ and the 2005 Protocol Amending the TRIPS Agreement¹⁸ – was designed to deal with the difficulties of WTO members lacking sufficient manufacturing capacities to make effective use of compulsory licensing.

These and other developments demonstrate that the WTO can serve as a useful and effective forum for discussions regarding the interface between IPRs and public health. Thus, the TRIPS Council's discussions have led to the adoption of the two important instruments referenced above. The Paragraph 6 System is also the first ever proposed amendment to the WTO Agreement in the form of the 2005 Protocol Amending the TRIPS Agreement. This provides evidence of the importance that WTO members attach to these questions.

Another core function of the WTO is the Dispute Settlement Mechanism, which has resulted in some important clarifications of the relevant rules under the TRIPS Agreement, including how they relate to public health.¹⁹ Furthermore, the WTO Secretariat aims to enhance the participation and informed decision-making of its members and observer governments through awareness-raising, capacity-building, and the provision of factual and technical information. To achieve this objective, the WTO regularly engages in technical assistance activities, which comprehensively cover the relationship between IPRs and public health.²⁰

4. Trilateral cooperation

The adoption of the Doha Declaration was a landmark occasion for issues that intersect public health, IP and trade. Since 2001, the principles enshrined in the Doha Declaration have shaped the framework for multilateral cooperation in this area, which included the provision of technical and policy support requested by members, joint publications and mutual participation in training programmes. Based on the adoption of the Development Agenda by the WIPO General Assembly in 2007 – specifically Recommendation 40 – WIPO was requested to intensify its cooperation on IP-related issues with relevant international organizations, and in particular with the WHO and the WTO, in order to strengthen the coordination required to achieve maximum efficiency when undertaking development programmes.²¹ The move towards reinforced coordination and dialogue was further supported by the process leading to, and the adoption of, the GSPA-PHI by the WHA in 2008. It explicitly requested the WHO Director-General "to coordinate with other relevant international intergovernmental organizations, including WIPO, WTO and UNCTAD, to effectively implement the global strategy and plan of action".²² In addition, in the case of more than 20 activities detailed in the plan of action,²³ the three organizations along with other international organizations are listed as the stakeholders responsible for the implementation of these activities.

Given that partnership is crucial for an effective international response to the ever-evolving challenges facing public health, the WHO, WIPO and WTO Secretariats have intensified interagency collaboration on matters related to public health, IP and trade.²⁴ Within their respective mandates and budgets, common activities are planned and carried out jointly to ensure that data, experiences and other information are exchanged, and also to ensure that the best use is made of the available resources. The three Secretariats' collaboration has primarily focused on supporting the implementation of the GSPA-PHI, but it is not limited to it. Other areas of cooperation have included addressing the IP-related issues raised during the preparatory work which led to the establishment of the WHO PIP Framework.

Of course, this collaboration does not exclude close cooperation with other international organizations, and the WHO, WIPO and the WTO have broadened the base of their collaborative and consultative networks dealing with public health issues. The WHO, for example, has stepped up its programme activities with other partners such as the United Nations Conference on Trade and Development (UNCTAD), in line with the GSPA-PHI.

At the Conference on Intellectual Property and Public Policy Issues, organized by WIPO in July 2009, the three Directors-General addressed the topic of strengthening multilateral cooperation on public health IP and trade.²⁵ In 2010, the WHO, WIPO and the WTO held a technical symposium on access to medicines, pricing and procurement practices.²⁶ It was followed by a second

symposium in 2011²⁷ on access to medicines, patent information and freedom to operate, highlighting the prospects for using patent information to assist more informed choices on access to medicines. This series of symposia is designed to improve the flow of practical information to guide and support technical cooperation in the future. Similarly, this trilateral study is a further milestone on the road towards stronger cooperation.

5. Other international key stakeholders

The period since 2001 has seen dramatic growth in the number and diversity of participants in international policy debates concerning innovation in, and access to medical technologies. Consideration of these issues necessarily entails a multidisciplinary and pluralistic approach. A distinctive feature of the debates has been the range of perspectives during discussions, coupled with the depth of expertise and practical experience that has been drawn from international and intergovernmental organizations, procurement and product development initiatives, and NGOs such as public health advocates and industry associations.

Annex I provides more detailed accounts of an illustrative – yet not fully representative – selection of some of these policy stakeholders provided by the organizations themselves. The study recognizes and values the work of many others, and no suggestion is made about the relative importance of any organization, whether mentioned or not.

C. The global burden of disease and global health risks

Key points

- Understanding the evolution of the global burden of disease (GBD) and the role of major health risks is important in order to develop effective strategies to improve global health and also in order to identify the range of medical technologies that are needed.
- Large declines in mortality between 2004 and 2030 are projected for all of the principal communicable, maternal, perinatal and nutritional causes of death, including HIV/AIDS, tuberculosis (TB) and malaria.
- The ageing of populations in low- and middle-income countries (LMICs) will result in a significant increase in total deaths due to non-communicable diseases (NCDs) over the next 25 years. Globally, NCDs are projected to account for over three quarters of all deaths by 2030.
- The leading global risks for mortality in the world are high blood pressure, tobacco use, high blood glucose, physical inactivity, and overweight and obesity. The leading global risks for burden of disease are underweight and unsafe sex, followed by alcohol use and unsafe water, sanitation and hygiene.
- A greater diversity of medical technologies will be needed in order to meet the challenges presented by the evolving GBD within a wider context of preventive measures focusing on lifestyle, nutrition and environmental factors.

The development of effective strategies to improve global health and react to changes in the global burden of disease (GBD) requires an understanding of the GBD and of GBD-related trends, coupled with an understanding of major health risks. These are introduced in this section.

1. Defining the need

International efforts to address public health issues need to be grounded in a clear empirical understanding of the GBD, and future efforts should be guided, as far as possible, by best estimates on the evolving disease landscape.

(a) Measuring the global burden of disease

The WHO studies on the GBD aim to summarize overall loss of health associated with diseases and injuries. GBD measurement methods were developed in order to generate comprehensive and internally consistent estimates of mortality and morbidity by age, sex and region. The key feature of this concept is a summary measure called the disability-adjusted life year (DALY). The DALY concept was introduced as a single measure to quantify the burden of disease, injuries and risk factors (Murray and Lopez, 1996). The DALY is based on years of life lost due to premature death, and years of life lived in less than full health (see Box 1.1).

(b) Current data on global average burden of disease

The average GBD across all regions in 2004 was 237 DALYs per 1,000 population, of which about 60 per cent were due to premature death and 40 per cent were due to nonfatal health outcomes (WHO, 2008). The contribution of premature death varied dramatically across regions, with years of life lost (YLL) rates seven times higher in Africa than in high-income countries. In contrast, the years lost due to disability (YLD) rates were less varied, with Africa having 80 per cent higher rates than high-income countries. South-East Asia and Africa together bore 54 per cent of the total GBD in 2004, although these regions account for only about 40 per cent of the world's population.

The high levels of burden of disease for the WHO regions of Africa, South-East Asia and the Eastern Mediterranean, compared with other regions, are predominantly due to Group I conditions (communicable diseases, and maternal, perinatal and nutritional conditions). Injury DALY rates are also higher than they are in other regions.

Almost half of the disease burden in LMICs is currently caused by NCDs. Ischaemic heart disease and stroke are the largest sources of this burden, especially in European LMICs, where cardiovascular diseases account for more than one quarter of the total disease burden. Injuries accounted for 17 per cent of the disease burden in adults aged 15-59 years in 2004.

Box 1.1. The disability-adjusted life year

The DALY extends the concept of potential years of life lost due to premature death to include equivalent years of “healthy” life lost by virtue of being in states of poor health or disability (Murray and Lopez, 1996). One DALY can be thought of as one lost year of “healthy” life, and the burden of disease can be thought of as a measurement of the gap between the current health status and an ideal situation where everyone lives into old age, free of disease and disability.

DALYs for a disease or injury cause are calculated as the sum of the years of life lost (YLL) due to premature mortality in the population and the years lost due to disability (YLD) for incident cases of the disease or injury. YLLs are calculated from the number of deaths at each age multiplied by a global standard life expectancy of the age at which death occurs. YLD for a particular cause in a particular time period are estimated as follows:

$$\text{YLD} = \text{number of incident cases in that period} \times \text{average duration of the disease} \times \text{weight factor}$$

The weight factor reflects the severity of the disease on a scale from 0 (perfect health) to 1 (death).²⁸

2. Trends and projections: major cause groups contributing to the total disease burden

The following trends and projections are the WHO estimations for the GBD from 2004 to 2030, using projection methods similar to those used in the original 1990 GBD study (Mathers and Loncar, 2006; WHO, 2008).

Global DALYs are projected to decrease by about 10 per cent in absolute numbers from 2004 to 2030. Since the population increase is projected to be 25 per cent over the same period, this represents a significant reduction in the global per capita burden. The DALY rate decreases at a faster rate than the overall death rate because of the shift in age at death to older ages associated with fewer YLLs. Even assuming that the age-specific burden for most non-fatal causes remains constant into the future, and thus that the overall burden for these conditions increases in line with the ageing of the population, there is still an overall projected decrease in the GBD per capita of 30 per cent for the period 2004 to 2030. This decrease is largely driven by projected levels of economic growth in the projection model. If economic growth is slower than recent World Bank projections, or if risk factor trends in LMICs are adverse, then the GBD will fall more slowly than projected.

The proportional contribution of the three major cause groups to the total disease burden is projected to change substantially. Group I (communicable, maternal, perinatal and nutritional conditions) causes are projected to account for 20 per cent of total DALYs lost in 2030, compared with just under 40 per cent in 2004. The NCD (Group II) burden is projected to increase to 66 per cent in 2030, and to represent a greater burden of disease than Group I conditions in all income groups, including low-income countries.

The three leading causes of DALYs in 2030 are projected to be unipolar depressive disorders, ischaemic heart disease and road traffic accidents.

Lower respiratory infections drop from leading cause in 2004 to sixth leading cause in 2030, and HIV/AIDS drops from fifth leading cause in 2004 to ninth leading cause in 2030. Lower respiratory infections, perinatal conditions, diarrhoeal diseases and TB are all projected to decline substantially in importance. On the other hand, ischaemic heart disease, cerebrovascular disease, diabetes mellitus, road traffic accidents, chronic obstructive pulmonary disease (COPD), hearing loss and refractive errors are all projected to move up three or more places in the rankings.

(a) Communicable diseases: trends

Between 2004 and 2030, large declines in mortality are projected for all of the principal communicable, maternal, perinatal and nutritional causes, including HIV/AIDS, TB and malaria (see Figure 1.1). HIV/AIDS deaths reached a global peak of 2.1 million in 2004, and the Joint United Nations Programme on HIV/AIDS (UNAIDS) estimated 1.7 million AIDS-related deaths in 2011 (UNAIDS, 2012). Deaths are projected to decline considerably over the next 20 years under a baseline scenario that assumes that coverage with antiretroviral (ARV) treatment continues to rise at current rates.

(b) Non-communicable diseases: trends

The ageing of populations in LMICs will result in significantly increasing total deaths due to most NCDs over the next 25 years. Global cancer deaths are projected to increase from 7.4 million in 2004 to 11.8 million in 2030, and global cardiovascular deaths from 17.1 million in 2004 to 23.4 million in 2030. Overall, non-communicable conditions are projected to account for just over three quarters of all deaths in 2030 (see Figure 1.2).

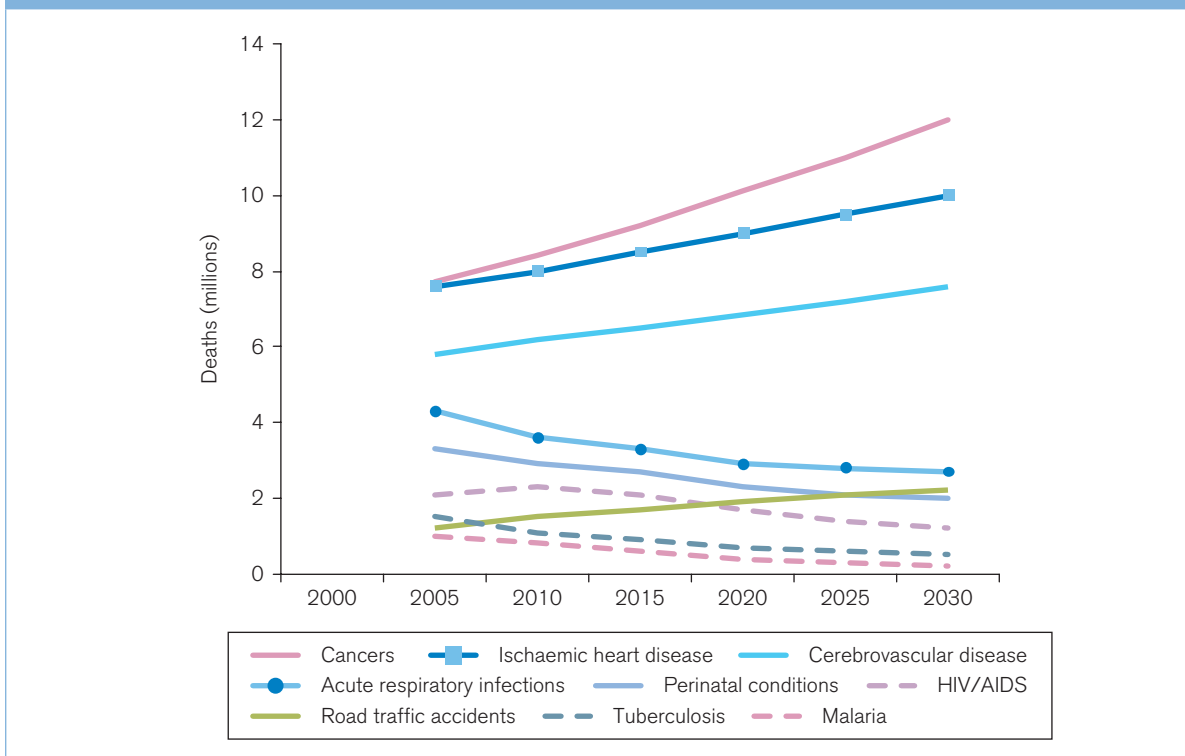
Based on these projections, people in all regions of the world will live longer and with lower levels of disability,

Figure 1.1. Projected changes in the ten leading causes of burden of diseases in 2004 and 2030

2004 Disease or injury	As % of total DALYs	Rank	Rank	As % of total DALYs	2030 Disease or injury
Lower respiratory infections	6.2	1	1	6.2	Unipolar depressive disorders
Diarrhoeal diseases	4.8	2	2	5.5	Ischaemic heart disease
Unipolar depressive disorders	4.3	3	3	4.9	Road traffic accidents
Ischaemic heart disease	4.1	4	4	4.3	Cerebrovascular disease
HIV/AIDS	3.8	5	5	3.8	Chronic obstructive pulmonary disease
Cerebrovascular disease	3.1	6	6	3.2	Lower respiratory infections
Prematurity and low birth weight	2.9	7	7	2.9	Hearing loss, adult onset
Birth asphyxia and birth trauma	2.7	8	8	2.7	Refractive errors
Road traffic accidents	2.7	9	9	2.5	HIV/AIDS
Neonatal infections and other	2.7	10	10	2.3	Diabetes mellitus
Chronic obstructive pulmonary disease	2	13	11	1.9	Neonatal infections and other
Refractive errors	1.8	14	12	1.9	Prematurity and low birth weight
Hearing loss, adult onset	1.8	15	15	1.9	Birth asphyxia and birth trauma
Diabetes mellitus	1.3	19	18	1.6	Diarrhoeal diseases

Source: WHO (2008).

Figure 1.2. Projected global deaths for selected causes, 2004-2030



Source: WHO (2008).

particularly from infectious, maternal, perinatal and nutritional conditions. Globally, there will be slower progress if there is no sustained and additional effort to achieve progress on the UN Millennium Development Goals (MDGs), or to address neglected tropical diseases (NTDs), tobacco smoking and other chronic disease risks, or if economic growth in low-income countries is lower than forecasted.

(c) Trends in total deaths and major causes of death

A total of 7.1 million children died in 2010, mainly in LMICs. More than one third of these deaths were attributable to undernutrition (Liu et al., 2012). The main causes of death in children under five were deaths arising during the neonatal period (40 per cent, e.g. preterm complications,

intrapartum-related complications, and neonatal sepsis or meningitis), diarrhoeal diseases (10 per cent), pneumonia (18 per cent) and malaria (7 per cent) (Liu et al., 2012; WHO, 2012c). Nearly half of these deaths occurred in sub-Saharan Africa (49 per cent) and in Southern Asia (39 per cent) (UNICEF, 2012).

During 2008, an estimated 57 million people died (WHO, 2011a). Cardiovascular diseases kill more people each year than any other disease. In 2008, 7.3 million people died of ischaemic heart disease and 6.2 million from stroke or another form of cerebrovascular disease (see Table 1.1). Tobacco use is a major cause of many fatal diseases, including cardiovascular disease, chronic obstructive pulmonary disease and lung cancer. In total, tobacco use is responsible for the deaths of almost one in ten adults worldwide.

There are some key differences between rich and poor countries with respect to causes of death:

- In high-income countries, more than two thirds of all people live beyond the age of 70 and predominantly die of chronic diseases: cardiovascular disease, chronic obstructive pulmonary disease, cancers, diabetes or dementia. Lower respiratory infection remains the only leading infectious cause of death.
- In middle-income countries, nearly half of all people live to the age of 70, and chronic diseases are the major killers, just as they are in high-income countries. Unlike in high-income countries, however, TB, HIV/AIDS and road traffic accidents also are leading causes of death.
- In low-income countries, fewer than one in five of all people reach the age of 70, and more than a third of all deaths are among children aged under 15 years. People predominantly die of infectious diseases: lower

respiratory infections, diarrhoeal diseases, HIV/AIDS, TB and malaria. Complications of pregnancy and childbirth together continue to be leading causes of death, claiming the lives of both infants and mothers.

3. Global health risks

The WHO has also attributed mortality and burden of disease to selected major risks. In this context, the WHO defines “health risk” as “a factor that raises the probability of adverse health outcomes” (WHO, 2009). The leading global risks for mortality in the world are high blood pressure (responsible for 13 per cent of deaths globally), tobacco use (9 per cent), high blood glucose (6 per cent), physical inactivity (6 per cent), and overweight and obesity (5 per cent) (WHO, 2009). These risks are responsible for raising the risk of chronic diseases such as heart disease, diabetes and cancers. They affect countries across all income groups: high, middle and low.

The leading global risks for burden of disease as measured in DALYs are underweight (6 per cent of global DALYs) and unsafe sex (5 per cent), followed by alcohol use (5 per cent) and unsafe water, sanitation and hygiene (4 per cent). Three of these risks particularly affect populations in low-income countries, especially in the regions of South-East Asia and sub-Saharan Africa. The fourth risk – alcohol use – shows a unique geographic and sex pattern, with its burden highest for men in Africa, in middle-income countries in the Americas and in some high-income countries.

The WHO identified the following risk factors:

- Five leading risk factors (childhood underweight, unsafe sex, alcohol use, unsafe water and sanitation, and high blood pressure) that are responsible for one

Table 1.1. The ten leading causes of death globally, 2008

World	Deaths in millions	Percentage of deaths
Ischaemic heart disease	7.25	12.8
Stroke and other cerebrovascular disease	6.15	10.8
Lower respiratory infections	3.46	6.1
Chronic obstructive pulmonary disease	3.28	5.8
Diarrhoeal diseases	2.46	4.3
HIV/AIDS	1.78	3.1
Trachea, bronchus, lung cancers	1.39	2.4
TB	1.34	2.4
Diabetes mellitus	1.26	2.2
Road traffic accidents	1.21	2.1

Source: WHO, Fact Sheet No. 310, 2011.

quarter of all deaths in the world and one fifth of all DALYs. Reducing exposure to these risk factors would increase global life expectancy by almost five years.

- Eight risk factors (alcohol use, tobacco use, high blood pressure, high body mass index, high cholesterol, high blood glucose, low fruit and vegetable intake, and physical inactivity) account for 61 per cent of cardiovascular deaths. Combined, these same risk factors account for over three quarters of ischaemic heart disease – the leading cause of death worldwide. Although these major risk factors are usually associated with high-income countries, over 84 per cent of the total GBD they cause occurs in LMICs. Reducing exposure to these eight risk factors would increase global life expectancy by almost five years.
- A number of environmental and behavioural risks, together with infectious causes – such as blood and liver flukes, human papillomavirus, hepatitis B and

C virus, herpesvirus and *Helicobacter pylori* – are responsible for 45 per cent of cancer deaths worldwide (WHO, 2009). For specific cancers, the proportion is higher: for example, tobacco smoking alone causes 71 per cent of lung cancer deaths worldwide. Tobacco accounted for 18 per cent of deaths in high-income countries.

Health risks are in transition: populations are ageing due to successes against infectious diseases. At the same time, patterns of physical activity as well as food, alcohol and tobacco consumption are changing. LMICs now face a double burden of increasing chronic, non-communicable conditions, as well as the communicable diseases which traditionally affect the poor. Understanding the role of these risk factors is important for developing clear and effective strategies for improving global health (WHO, 2009).

D. Factors shaping public health policy

Key points

- Achieving sustainable and more equitable public health outcomes depends on the dynamic interplay of national public health policy, including effective health systems and adequate financing of health systems, a sound regulatory environment, trade and competition settings, procurement policies, innovation strategies and the intellectual property (IP) system.
- The policy processes of the past decade have led to a better understanding of how these distinct policy components can and should work together to produce public health outcomes by seeking positive synergies between human rights, health, access, innovation and commercial dimensions.
- Innovation cannot take place in isolation from concerns about access, and access has to be seen in the broader context of the need for innovation and effective regulation.
- The greater availability and breadth of data in each of these policy domains offers a rich empirical basis for decision-making.
- An increasing number of national, regional and international policy processes, including the framing of trade agreements, involving a multiplicity of agencies, are tackling issues that impact on access to, and future innovations in, medical technologies.

1. Seeking effective outcomes within a complex policy environment

Building a sustainable global response to the demand both for innovations in medical technology and for effective and equitable access to needed technologies is a complex and constantly evolving challenge. While it is often expressed in abstract or political terms, the effort fundamentally concerns how to deliver improved health outcomes. Creating new medical technologies, assessing these technologies, providing for their effective distribution and ensuring that they are used rationally are, ultimately, practical processes. These processes range from the work of laboratory research scientists to the care provided by nurses in a field clinic.

The policy, economic and legal environment influences and can determine the actions, choices, priorities and allocation of resources that are applied at a practical level. This policy environment is complex: it comprises laws, regulations and policy instruments, at national, regional and international levels, that address diverse fields, including public health, international trade and the IP system. Effective progress and sustained impact on public health cannot be attained by working within the confines of one discrete set of policy measures or legal instruments. Lack of coherence, or the prospect of conflict, between law and policy in different fields can thwart progress and impede practical benefits. It follows that understanding the intersections between these different policy measures is key to ensuring that they work harmoniously for overall public health benefit.

2. Transforming policy intersections: from boundaries to synergies

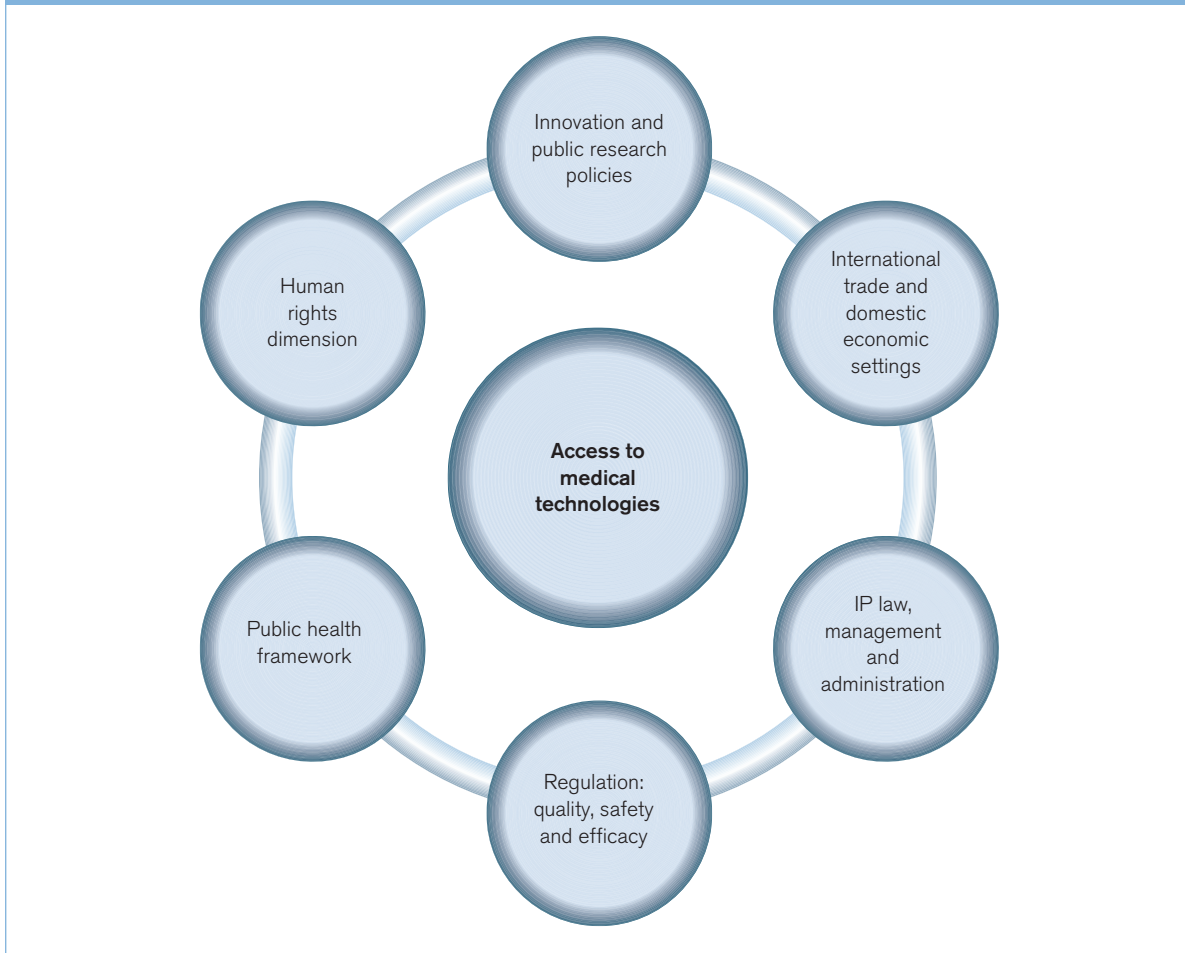
The emphasis on “intersections” – understanding the linkages and interplay between distinct areas of law and policy (see Figure 1.3) – is a consistent theme in recent debate on public health policy. This study identifies two levels of intersection:

- Points of interaction between the legal and policy principles in different domains, so that law and policy instruments can be interpreted and applied in practice to promote public health.
- The integration of sets of data drawn from diverse fields, so that policy-makers can work from an improved, integral base of information, combining data on public health, determinants of access to medical technologies, coverage of relevant IP rights, and trade settings.

The idea of synergy can illuminate how these intersections can be transformed from formal boundaries between different policy domains, to points of reinforcement and mutual benefit. Synergy refers to diverse elements working together to achieve results that could not be obtained by individual actions. Access to medicines is a compelling example of synergy in action. Indeed, the synergistic relationship between health, trade and IP is, perhaps, the core practical lesson to be learned from the decade-long debate about IP and access to medicines.

Trade and commercial perspectives are sometimes regarded as being essentially at odds with promoting

Figure 1.3. The distinct policy domains of public health



public health. Yet the commercial environment, promotion of competition and of private sector innovation, and the regulation of trade, are crucial determinants for access to medicines. International trade is vital for access to medical technologies, and no country can aim to be entirely self-sufficient, even though some aim at boosting local production. To the extent that access depends on affordability, economies of scale for industry and a more competitive marketplace yield opportunities for improved health outcomes. Openness to international trade generally promotes competition, and offers improved affordability and access. By enabling a wider range of suppliers to serve the population, it can also enhance security of supply. Trade policy settings, such as tariffs, quotas and other regulations, have a direct effect on prices and availability. Many governments have taken national legal and policy measures to enable or promote generic competition in the supply of medicines so as to help reduce prices. WTO rules have been interpreted in dispute settlement to provide for public health objectives, such as enhanced entry of generic medicines; and the Declaration on the TRIPS Agreement and Public Health (Doha Declaration) has affirmed that the Agreement can be interpreted from a public health perspective.

Trade policy and the economics of global production systems are also key factors in strategic plans to build domestic production capacity that aim for better access to medical products. Procurement policies favouring open and competitive tendering, coupled with the rational use of medicines, become all the more important in ensuring continued access in a fiscal climate where national budgets are under pressure and philanthropic programmes face funding constraints. Programmes for access to medicines also stand to benefit from better, more integrated use of data, including on current and projected disease burdens, on efficacy of medicines, on price and IP coverage of medicines, and on trade and regulatory measures.

Over the past decade, access to medicines has moved to the centre of a cross-cutting debate between different policy dimensions. Policy-makers have progressively developed the policy framework for access, including through the Doha Declaration, through World Health Assembly (WHA) resolutions, and through human rights instruments. More recently, policy discussions have turned also to the innovation dimension. Indeed, the intersection between innovation and access is fundamental, and forms the fulcrum of the present study.

Policy measures aimed at promoting access or innovation need to recognize that these two concepts are intrinsically intertwined. Merely to leverage enhanced access to the stock of existing, proven medicines is insufficient. The current pharmacopeia needs constant expansion to keep pace with the evolving disease burden. The disease burden continues to evolve, with policy-makers recently turning their attention, for instance, to the growing burden of non-communicable diseases (NCDs) in the developing world. New strains of viruses and the problem of resistance of bacteria against current medicines challenge the efficacy of existing treatments. And medical innovation has historically failed to address major diseases that are endemic in the developing world.

Shifting patterns of needs and requirements – due not least to the constant evolution of the disease burden – create an ever-changing set of demands both for new and adapted technologies. Accordingly, the interplay between access and innovation can be seen in an integrated way, as a positive feedback loop between the health burden and the innovative response: linking the identification of health needs; innovation in, and adaptation of, technologies to meet the needs identified; and the implementation, dissemination and distribution of safe and effective technologies of proven quality. Innovation may aim specifically at enhancing access: for example, where use of diagnostic technologies requires skilled clinical support or infrastructure – and this is simply not available for many patients – then leveraging access for communities in resource-poor settings may entail creating new versions of the technology that can be operated without such support or infrastructure.

3. Building stronger links between local, national and global levels

Promoting medical innovation policy is a particular challenge, as it operates at the intersection of several policy domains. The essential challenge for innovation in the area of medical technologies can be expressed in simple terms:

- first, to secure the requisite resources (including know-how, research and product development capacity, clinical trial expertise, regulatory infrastructure, background and platform technologies and research tools, and the investment of public and private capital)
- second, to apply these innovation resources most effectively towards addressing unmet public health needs.

Yet, meeting this challenge entails working on complex intersections between different policy areas, applying a mix of incentives and market interventions, funding and other support for R&D, infrastructure development, and building a public research base and a skilled research

workforce. Equally, promoting innovation can entail better utilization of existing resources, leveraging access to existing technologies, drawing on drug development skills and R&D infrastructure, and drawing more effectively on indigenous research and innovation capacity, so as to expand the medical technology development pipeline. A host of international, regional and national legal and policy instruments influences innovative activity.

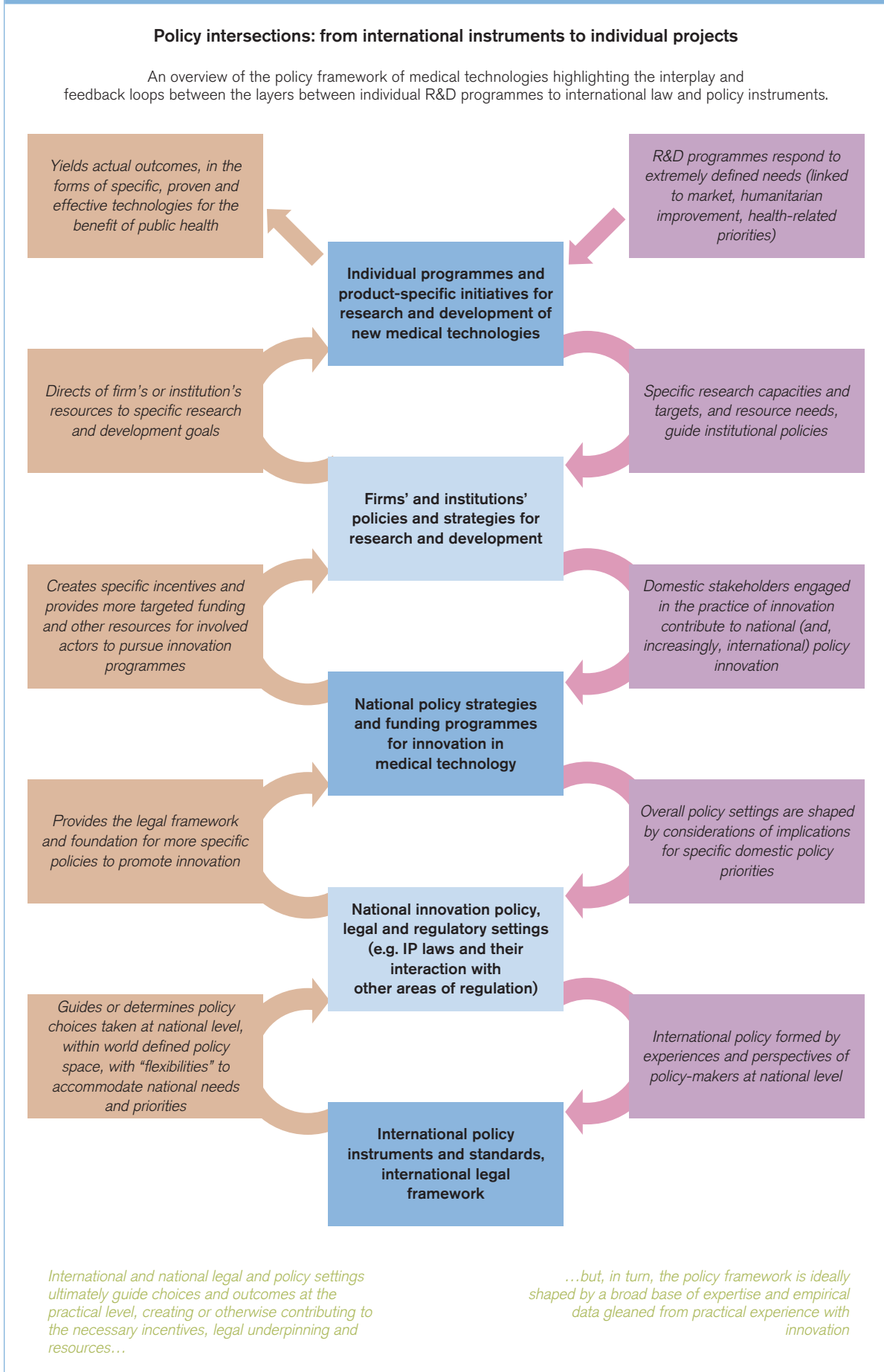
International legal instruments need to be understood through the prism of national experience with their implementation. Thus, a systematic understanding of the intersections between these different layers of policy and practice requires a more sophisticated understanding of how they interact and influence one another (see the central column in Figure 1.4) – so as to assess how international, national and institutional policies determine actual innovation outcomes, and how, in turn, practical experience influences the policy framework.

4. The empirical challenge: an accessible base for policy

Policy-makers dealing with the challenges of medical technology access and innovation are more numerous and more diverse than at any time previously, and contend with a host of policy, legal and administrative structures at national, regional and international levels. For example, national regulatory authorities who seek to safeguard the public against unsafe or ineffective medicines deal with clinical trial data that may be protected by IP laws, and work within a legal and policy framework shaped by multiple international and regional instruments. Patent offices, which face unprecedented workloads, must use the best possible sources of technological data when searching and examining prior art²⁹ to decide on whether or not to grant patents on claimed inventions. Procurement programmes have to contend with a host of rapidly evolving factors, while assessing evolving disease burdens, clinical needs, the selection of essential medical technologies, efficacy, prices and availability, and regulatory and IP aspects. Common to all these diverse challenges is the requirement for a stronger empirical base so that policy choices are more likely to address practical needs. Fortunately, the past decade has seen significant improvements in the quality and inclusiveness of data, as well as access to the necessary information technology tools required to convert raw data into accessible knowledge services for stakeholders.

Technology is unquestionably an essential component of public health (see Box 1.2): medicines, ranging from antibiotics to antiretrovirals (ARVs), have been central in ensuring dramatically improved public health outcomes; vaccines have all but eliminated the threat of certain diseases; and other technologies, such as medical imaging, have led to transformations in diagnosis and treatment. Such technologies cannot be taken for granted – they are the product of extensive R&D activities. Development of

Figure 1.4. Policy intersections between distinct levels



Box 1.2. Health and medical technologies: fundamental concepts

While the terms health technologies and medical technologies sometimes are used interchangeably, health technologies is the broader term, encompassing medical technologies. There are no watertight definitions of either term. The WHO defines health technology as application of organized knowledge and skills in the form of devices, medicines, vaccines, procedures and systems developed to solve a health problem and improve quality of lives.³⁰

Health technologies include, for example, assistive technologies, such as a white stick which may be used by a person who is blind, or a treadmill and exercise equipment which may be used as a health-promoting device. Medical technologies are associated with the concept of medical intervention. These interventions can be preventive (e.g. vaccine), diagnostic (e.g. in vitro diagnostic kit, stethoscope or thermometer), therapeutic (e.g. medicine, surgical instrument, surgical procedure and implant), rehabilitative (e.g. physiotherapy equipment, assistive device such as a crutch). Medical devices are a subgroup of medical technologies, including any instrument, apparatus, implement, machine, appliance, implant, in vitro reagent or calibrator, software, material or other similar or related article that does not achieve its primary intended action in or on the human body solely by pharmacological, immunological or metabolic means. Examples include syringes, defibrillators, in vitro tests or hip prostheses.

As technology evolves, more combination products materialize – mainly in the area of medicines in medical devices delivery sets. There are also more and more examples of combined medical technologies. The respiratory inhaler for the treatment of asthma is one example of a medicine delivered through a dosed aerosol device.

these technologies has been a complex, often risky and uncertain process, drawing on diverse inputs, originating from both public and private sectors, and often requiring scrupulous testing and regulatory oversight. Innovation in medicines is among the most uncertain and expensive forms of technology development, creating the need for distinct innovation structures, close regulatory and ethical

attention, appropriately high standards of safety and efficacy, and specific or targeted incentives.

Table 1.2 presents examples of health and medical technologies from the perspective of their purpose and material nature. Providing access to essential medical technology – the key focus of this study – is an essential

Table 1.2. Medical technologies: semantics, purpose and material nature

Health technologies: purpose or application (examples)
Prevention: Vaccines, contraceptive devices, immunization, hospital infection control programme, fluoridated water supply, iodized salt.
Screening: Pap smear, tuberculin test, mammography, serum cholesterol testing.
Diagnosis: Stethoscope, in vitro diagnosis, electrocardiogram, serological test for typhoid, x-ray.
Treatment: Antiviral therapy, haemodialysis, coronary artery bypass surgery, psychotherapy, medicines for pain, antibiotics.
Rehabilitation: Exercise programme for post-stroke patients, assistive device for severe speech impairment, incontinence aid, hearing aid.
Health/medical technologies: material nature
Medicines: Chemically synthesized substances intended for use in the medical diagnosis, treatment, or prevention of disease. Examples: acetylsalicylic acid, beta-blockers, antibiotics, antidepressants.
Biologics: Therapeutic substances derived from the human body or animals, and products of biotechnology. Examples: vaccines, blood products, cellular and gene therapies.
Medical devices: A medical device is any instrument, apparatus, implement, machine, appliance, implant, in vitro reagent or calibrator, software, material or other similar or related article that does not achieve its primary intended action in or on the human body solely by pharmacological, immunological or metabolic means. ³¹ Examples: syringes, defibrillators, HIV in vitro tests, surgical instruments, hip prostheses, linear accelerators.
Medical and surgical procedures: Psychotherapy, nutrition counselling, coronary angiography, gall bladder removal.
Support systems: Electronic patient record systems, telemedicine systems, medicine formularies, blood banks, clinical laboratories.
Organizational and managerial systems: Prospective payment using diagnosis-related groups, alternative health care delivery configurations, clinical pathways, total quality management programmes.

Source: National Information Center on Health Services Research and Health Care Technology (NICHSR), *HTA101: II. Fundamental Concepts*, available at www.nlm.nih.gov/nichsr/hta101/ta10104.html.

ingredient for an effective response, but it is far from being sufficient. At the national level, political commitment of governments is required in order to allocate the requisite financial resources to the health sector to develop strong health systems. Prevention is another key aspect. For example, major proportion of the burden of NCDs can be prevented by reducing the exposure of populations to tobacco use, unhealthy diets, physical inactivity and harmful use of alcohol. To this end, effective health prevention and promotion programmes are required to address the main risk factors. An improved medicine is potentially injurious if it is incorrectly prescribed or improperly administered. Advanced medical imagery technology is useless unless it is accompanied by skilled diagnosticians and the requisite infrastructure. Thus, effective access to medical technologies can be dependent on access to appropriate clinical infrastructure and medical services, whether clinical or technical.

As the disease burden shifts and evolves, there is a continuing need for new, adapted and more effective medicines. Access to necessary medical technologies is not, therefore, a static equation – an integral feature of appropriate access strategies must be a recognition of the value of targeted and appropriate innovation, both for major new breakthroughs and for adaptations to, and improvements in, existing technologies.

Innovation does not take place in isolation from concerns about equitable access to medicines and other medical technologies. Obviously, the social value of medical

innovation must be measured in part by the extent to which it is effectively and sustainably available to the people who need it. The widespread and equitable health impact of new technologies cannot be achieved without ensuring appropriate means of access to finished products. Thus, an overall policy on medical innovation needs to consider the access dimension as well – how, in practice, a new technology will be made available to those who need it, so that it does not remain an abstract theory and is not reserved for a narrow segment of society only. Building access considerations into innovation policy has numerous dimensions, ranging from the core aim of research and product development activities, to work on “appropriate” or adaptive forms of existing technologies suitable for resource-poor clinical environments, to consideration of freedom to operate strategies and mechanisms for integrating technologies in a finished product, so that it can be distributed widely and in the most effective form.

Access also has to be understood in a wider context. For example, regulation of medical products is an integral part of the access equation. “Access” is not simply the capacity to purchase – or to be supplied with – a basic commodity or consumer product. The availability of a technology generally must be backed by sound regulation that is both monitored and enforced, so as to provide reasonable guarantees that the technology is safe and effective. Equally, many medicines and technologies require a certain degree of clinical support and backup, including diagnosis, prescription and dispensation, and appropriate follow-up.

Endnotes

- 1 WTO document WT/MIN(01)/DEC/2.
- 2 Opening remarks, "Access to Medicines: Pricing and Procurement Practices", A Joint Technical Symposium by WHO, WIPO and WTO, Geneva, 16 July 2010.
- 3 WIPO, *The 45 Adopted Recommendations under the WIPO Development Agenda*.
- 4 UN document A/RES/66/2.
- 5 Opening remarks, "Access to Medicines: Pricing and Procurement Practices", A Joint Technical Symposium by WHO, WIPO and WTO, Geneva, 16 July 2010.
- 6 Ibid.
- 7 Opening remarks, "Access to Medicines: Patent Information and Freedom to Operate", A Joint Technical Symposium by WHO, WIPO and WTO, Geneva, 18 February 2011.
- 8 Ibid.
- 9 Ibid.
- 10 WHA, *Resolution: WHA49.14: Revised drug strategy*.
- 11 WHA, *Resolution: WHA56.27: Intellectual property rights, innovation and public health*.
- 12 WHA, *Resolution: WHA61.21: Global strategy and plan of action on public health, innovation and intellectual property; Resolution: WHA62.16: Global strategy and plan of action on public health, innovation and intellectual property*.
- 13 See www.wipo.int/ip-development/en/agenda/.
- 14 See also: Articles 8, 27.2 and 27.3(a) of the TRIPS Agreement; the Doha Declaration on the TRIPS Agreement and Public Health; Article 2.1 of the Agreement on the Application of Sanitary and Phytosanitary Measures; Article 2.2 of the Agreement on Technical Barriers to Trade; and Article XIV(b) of the General Agreement on Trade in Services.
- 15 The following WTO disputes have addressed, among others, health-related measures: *European Communities – Measures Concerning Meat and Meat Products (Hormones)* (DS26 and DS48); *European Communities – Measures Affecting Asbestos and Asbestos-Containing Products* (DS135); *European Communities – Measures Affecting the Approval and Marketing of Biotech Products* (DS291, DS292 and DS293); *Brazil – Measures Affecting Imports of Retreaded Tyres* (DS332); *United States – Continued Suspension of Obligations in the EC – Hormones Dispute* (DS320); and *Canada – Continued Suspension of Obligations in the EC – Hormones Dispute* (DS321).

- 16 A pro-public health interpretation of permissible exceptions to patent rights may be found in the panel report on *Canada – Patent Protection of Pharmaceutical Products* (DS114).
- 17 WTO documents WT/L/540 and WT/L/540/Corr.1.
- 18 WTO document WT/L/641.
- 19 See the panel report on *Canada – Patent Protection of Pharmaceutical Products* (DS114).
- 20 For more information on the WTO activities, see WTO document IP/C/W/577.
- 21 See www.wipo.int/ip-development/en/agenda/recommendations.html.
- 22 WHA, *Resolution: WHA61.21: Global strategy and plan of action on public health, innovation and intellectual property*, para. 4(5).
- 23 WHA, *Resolution: WHA61.21: Global strategy and plan of action on public health, innovation and intellectual property*; *Resolution: WHA62.16: Global strategy and plan of action on public health, innovation and intellectual property*.
- 24 See: www.who.int/phi/implementation/trilateral_cooperation/en/index.html; www.wipo.int/globalchallenges/en/health/trilateral_cooperation.html; and www.wto.org/english/tratop_e/trips_e/who_wipo_wto_e.htm.
- 25 WIPO, "WIPO Conference on Intellectual Property and Public Policies Wraps Up", PR/2009/594, 14 July 2009.
- 26 "Access to Medicines: Pricing and Procurement Practices", A Joint Technical Symposium by WHO, WIPO and WTO, Geneva, 16 July 2010.
- 27 "Access to Medicines: Patent Information and Freedom to Operate", A Joint Technical Symposium by WHO, WIPO and WTO, Geneva, 18 February 2011.
- 28 The weights used for the GBD 2004 are listed in Annex Table A6 of Mathers et al. (2006).
- 29 For more information on prior art, see Chapter II, Endnote 67.
- 30 WHA, *Resolution: WHA60.29: Health technologies*.
- 31 Based on definition adopted by the Global Harmonization Task Force (GHTF). See GHTF (2005) and this chapter, Section A.6.

II. The policy context for action on innovation and access

This chapter outlines the policy framework for public health, intellectual property (IP), international trade and competition, focusing on how they intersect, with particular emphasis on medical technologies. The policy framework described comprises the policy, economic and legal features of IP and innovation systems, regulation of medical products, competition policy and relevant trade policy measures, including import tariffs, rules on trade in services, government procurement, and regional and bilateral free trade agreements (FTAs). In addition, it outlines the human rights dimension of access to medicines and the interface between traditional medicine, IP and trade.

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A. Public health policy

Key points

- Ensuring access to essential medicines constitutes a core human right obligation of states.
- The UN Millennium Development Goals (MDGs) call, in particular, for enhanced global collaboration to ensure access to essential medicines.
- With the adoption of the WTO Agreement on Trade-Related Aspects of Intellectual Property Rights (TRIPS Agreement), the WHO began assessing the impact of trade agreements on public health, including by providing support on the implementation of TRIPS flexibilities in collaboration with other relevant international organizations.
- The GSPA-PHI aims to “encourage and support the application and management of intellectual property in a manner that maximizes health-related innovation, especially to meet the R&D needs of developing countries, protects public health and promotes access to medicines for all, as well as explore and implement, where appropriate, possible incentive schemes for R&D”.
- Effective regulation promotes public health by ensuring that products are of the required quality, safety and efficacy and also ensuring provision of the necessary information to enable the use of such products in a rational manner. Unjustifiably regulatory barriers can hinder access to needed medical technologies.
- Despite ongoing efforts, full international harmonization of regulatory standards remains an elusive goal at present.
- The emergence of newer biological medicines has challenged the established originator/generic distinction, raising questions of how to build national capacities to regulate biosimilar products based on appropriate guidelines from the WHO and leading regulators.

This chapter outlines the policy framework for public health, intellectual property (IP), international trade and competition, focusing on how they intersect with particular emphasis on medical technologies. The framework described comprises the policy, economic and legal features of IP and innovation systems, regulation of medical products, competition policy, and relevant trade policy measures, including import tariffs, rules on trade in services, government procurement, and regional and bilateral free trade agreements (FTAs). In addition, it outlines the human rights dimension of access to medicines.

As the epidemiological data presented in the previous chapter highlights, low- and middle-income countries (LMICs) are facing a double burden of infectious and non-communicable diseases. Internationally and nationally, the human rights framework, specifically the right of everyone to the enjoyment of the highest attainable standard of physical and mental health (in short the right to health), has provided an important mechanism to further the public health policy goals of ensuring and improving access to medicines for those who are most in need. Additionally, the MDGs provided a much needed international platform for action on key concerns ranging from alleviating poverty to improving access to medicines.

The policy context for innovation and access to medical technologies needs to consider the frameworks that currently exist at the intersection of public health, innovation and access. The following section focuses on

the right to health under international human rights law, the health-related MDGs, developments in the WHO on public health, access and innovation, national health policies, and regulation of medical technologies.

1. Health and human rights

The human rights dimension has provided an important legal and policy vantage point for consideration of public health and pharmaceutical issues. International human rights law defined under customary international law and international human rights treaties create binding obligations on member states. The WHO Constitution was the first international instrument to state that “the enjoyment of the highest attainable standard of health is one of the fundamental rights of every human being without distinction of race, religion, political belief, economic or social condition” (see Preamble). The right to health is a central element of the international human rights system. It is part of the Universal Declaration on Human Rights, adopted in 1948, the 1966 International Covenant on Economic, Social and Cultural Rights (ICESCR), as well as of regional human rights instruments and many national constitutions. By 2009, 135 countries had incorporated aspects of the right to health in their national constitutions (Perehudoff, 2008; Hogerzeil and Mirza, 2011). It also constitutes the basis for the overall objective of the WHO – laid out in Article 1 – which is “the attainment by all peoples of the highest possible level of health”. The Declaration of Alma-Ata, adopted in 1978,

provided a more global perspective on tackling the inequities in access to health care systems in general linking the social dimension of achieving the highest attainable level of health and access to essential medicines.

The scope and content of the right to the highest attainable standard of health under Article 12 of the ICESCR has been interpreted by the Committee on Economic, Social and Cultural Rights (CESCR) in General Comment No. 14.¹ The CESCR specifies that the parties' obligations under the ICESCR include "the provision of equal and timely access to basic preventive, curative, rehabilitative health services and health education; regular screening programmes; appropriate treatment of prevalent diseases, illnesses, injuries and disabilities, preferably at community level; the provision of essential drugs; and appropriate mental health treatment and care". General Comment No. 14 further explains that the four elements of availability, accessibility, acceptability and quality are essential to the enjoyment of the right to health by all. The CESCR lays down the general obligations of states, which are defined in the framework of "respect", "protect" and "fulfil":

- The obligation to respect includes, but is not limited to, requiring states to refrain from interfering with the enjoyment of the right to health.
- The obligation to protect, among other things, requires states to adopt measures to prevent other parties from interfering with the enjoyment of the right to health.
- The obligation to fulfil requires that sufficient recognition be given to the right to health through legislative implementation and adoption of positive measures and policies to enable individuals to enjoy the right to health.

Although obligations under the ICESCR are subject to progressive realization, the CESCR has set out minimum core obligations which ought to be implemented by countries without delay. These obligations include ensuring non-discriminatory access to essential medicines.² The

CESCR also expressed its view on the impact of intellectual property rights (IPRs) on prices of essential medicines in its Comment No. 17 on the right of everyone to benefit from the protection of the moral and material interests resulting from any scientific, literary or artistic production of which he or she is the author.³ The CESCR notes that this right cannot be isolated from other rights guaranteed in the ICESCR. Parties are therefore obliged to strike an adequate balance, whereby the private interests of authors should not be unduly favoured but adequately balanced with the interest of the public in enjoying broad access to their productions. The CESCR states that, ultimately, IP is a social product and has a social function and parties thus have a duty to prevent unreasonably high costs for access to essential medicines.

In the context of neglected diseases where innovation in medical technologies has not kept with the needs of developing countries, the right to health includes an obligation for states to promote R&D of new medical technologies.⁴

In April 2002, the United Nations Human Rights Council (HRC) established a mandate for a Special Rapporteur on the right of everyone to the enjoyment of the highest attainable standard of physical and mental health, in short the Special Rapporteur on the right to health. The Special Rapporteur has prepared independent reports, following consultations with many stakeholders, including the WHO. Some of these reports deal with access to essential medicines and the role of the pharmaceutical industry, as well as IP issues. In 2011, the HRC requested the Special Rapporteur to prepare a study by 2013 on the existing challenges with regard to access to medicines in the context of the right to health, ways to overcome these challenges and good practices.⁵ These intersections and their linkages to human rights have also been the focus of several reports and resolutions of the HRC and its predecessor, the UN Commission on Human Rights (see Table 2.1).

Table 2.1. Key UN reports and resolutions

Key Reports of the UN Special Rapporteur on the Right to Health	Key Resolutions of the HRC and Reports to the HRC and the former Commission on Human Rights
<ul style="list-style-type: none"> ■ Expert consultation on access to medicines as a fundamental component of the right to health: A/HRC/17/43 ■ Right to health, IP, TRIPS and FTAs: A/HRC/11/12 ■ Right to health including the Human Rights Guidelines for Pharmaceutical companies in relation to access to medicines: A/63/263 ■ Relationship between the right to health, access to medicines and the reduction of maternal mortality: A/61/338 ■ The right of everyone to the enjoyment of the highest attainable standard of physical and mental health: E/CN.4/2003/58 ■ Right to health indicators; good practices for the right to health; HIV/AIDS; neglected diseases; and an optional protocol to ICESCR: A/58/427 	<ul style="list-style-type: none"> ■ Resolution on the right of everyone to the enjoyment of the highest attainable standard of physical and mental health in the context of development and access to medicines: A/HRC/RES/17/14 ■ Resolution on the right of everyone to the enjoyment of the highest attainable standard of physical and mental health: A/HRC/RES/15/22 ■ Resolution on access to medicine in the context of the right of everyone to the enjoyment of the highest attainable standard of physical and mental health: A/HRC/RES/12/24 ■ Reports of the Secretary-General on access to medication in the context of pandemics such as HIV/AIDS, tuberculosis and malaria: A/HRC/7/30, E/CN.4/2006/39, E/CN.4/2005/38, E/CN.4/2003/48

Resolutions of the HRC call upon member states to promote access to medicines for all, including through the full use of the TRIPS Agreement and the flexibilities it provides. In promoting such access, member states are asked to bear in mind that protection of IP is important for the development of new medicines. They are also asked to bear in mind concerns about the effect that providing such IP protection has on prices.⁶ A 2011 resolution adopted by the HRC in the context of the HIV/AIDS epidemic also reaffirms the right of use, to the fullest extent, of the provisions of the TRIPS Agreement, the Doha Declaration and the WTO General Council Decision of 30 August 2003.⁷ In relation to access to medications for HIV, TB and malaria, the Commission on Human Rights has also stressed the need for member states to make full use of the flexibilities under the TRIPS Agreement in their national legislations.⁸

With respect to the HIV/AIDS epidemic, the UN General Assembly has passed several resolutions pertaining to protecting the human rights of people living with HIV and improving access to HIV treatment. The most recent political declaration made by the UN General Assembly included a commitment to remove obstacles that limit the capacity of LMICs to provide HIV/AIDS treatment, including through the use of the flexibilities contained in the TRIPS Agreement, as confirmed by the Doha Declaration, and to ensure that IPR provisions in trade agreements do not undermine the flexibilities (United Nations, 2011a).

2. Access to essential medicines: an indicator for the fulfilment of the right to health

The UN High Commissioner for Human Rights created sets of indicators for 12 aspects of human rights, including the right to housing and shelter, the right to education, the right to freedom of expression and the right to health. The indicators for the fulfilment of the right to health refer to five aspects which are often subject to inequity and discrimination:

- sexual and reproductive health
- child mortality and health care
- natural and occupational environment
- prevention, treatment and control of diseases
- access to health facilities and essential medicines.

Access to essential medicines is a vital component of fulfilling the right to health. A lack of equity in the supply of essential medicines, high prices, informal payments and out-of-pocket payments for the medication required exclude the poor and vulnerable, and do not facilitate the realization of the right to health. The segments of the population most in need of basic essential medicines are

mainly the poor, women, children, older people, internally displaced people, those with disabilities, minorities and prisoners. It is the obligation of governments, as part of their human rights commitments, to ensure that these vulnerable segments of the population have access to essential medicines. Different approaches exist to promote the fulfilment of governments' constitutional and international obligations with regard to the right to health including human rights impact assessments as well as rights-based litigation (Hogerzeil et al., 2006).

3. Universal access and the UN Millennium Development Goals

The MDGs are a set of eight international development goals to be achieved by 2015. All of them relate in some way to improving physical, mental and social well-being. The WHO *World Health Report 2010* focused on strategies for, and progress in, providing universal health coverage through member states' health financing systems as a means of promoting and protecting health, but without prohibitive costs (WHO, 2010h). In the area of medical technologies in particular, not only the price but also the ultimate availability, quality and appropriateness of resources are reflective of a long chain of policy decisions, market forces and other factors. Therefore, access to medical technology needs to be considered from the standpoint of a comprehensive framework of determinants that ultimately relate back to product innovation, IP protection, trade and distribution.

MDG 8 calls for enhanced global partnership for development issues (see Box 2.1). Target 8.E therefore focuses specifically on global collaboration for access to essential medicines, of which universal access is guaranteed as a right, stating: "In cooperation with pharmaceutical companies, provide access to affordable essential drugs in developing countries". Since the adoption of the MDGs, some countries have made substantial progress towards increasing access to essential medicines to fight HIV/AIDS, malaria and TB. In its 2012 report on the attainment of the MDGs, the United Nations noted that availability and affordability of essential medicines remain a challenge. Yet, new funding was pledged for the Global Fund to Fight AIDS, Tuberculosis and Malaria and the GAVI Alliance, which have demonstrated effectiveness. The report also noted that TRIPS flexibilities facilitating local manufacturing and importation of essential medicines appeared to be more broadly incorporated in national laws, but that the use of these flexibilities may be hampered by bilateral and regional free trade agreements (FTAs). Quality of medicines appeared threatened by counterfeit and substandard products, a problem compounded by the limited capacity of national regulatory agencies (United Nations, 2012). Overall access to essential medicines in developing countries is still insufficient.

Box 2.1. MDG Gap Task Force

The *MDG Gap Task Force Report 2012* was prepared with input from more than 20 UN agencies and the WTO. The MDG Gap Task Force was established by the UN Secretary-General to improve monitoring of MDG 8 by leveraging coordination.

The Report recommends taking the following actions to increase the accessibility and affordability of essential medicines:

- Donor commitments to support global initiatives for the treatment and prevention of acute and chronic diseases should be truly additional to Official Development Assistance.
- The international community should assist developing-country governments in increasing availability and use of medicines in the public sector and in providing these medicines at little or no cost to the poor through the public health system.
- The international community, including new partners from the South, should further strengthen cooperation for supporting local production of generic medicines in developing countries.
- The international community should further encourage the pharmaceutical industry to use voluntary licensing agreements and join patent pools.
- Developing countries should carefully assess possible adverse impacts on access to medicines when adopting TRIPS-plus provisions.
- The international community should continue to support efforts to strengthen developing-country regulatory capacity to oversee the quality of medicines.
- The international community should continue efforts to increase funding in research and development of new medicines, especially for neglected diseases.⁹

4. Public health, innovation and access in the WHO

The WHO policy framework for public health, innovation and access has been developed over many years and consists of a large number of WHO resolutions that reflect the growing consensus among member states regarding the distinct role of the WHO in this area.

(a) Resolutions dealing with public health, intellectual property and trade

Immediately after the TRIPS Agreement came into effect, member states in the WHO discussed its potential impact on public health and requested the WHO Director-General “to report on the impact of the work of the World Trade Organization (WTO) with respect to national drug policies and essential drugs and make recommendations for collaboration between WTO and WHO, as appropriate”.¹⁰ Since then, the interface of public health, IP and trade has been subject of many debates and resolutions that reflect a growing consensus over the years (see Box 2.2). The 52nd World Health Assembly (WHA) provided the WHO Secretariat with a mandate to work with WHO member states on the monitoring of the impact of the TRIPS Agreement and other trade agreements and to help member states develop adequate health policies to, if necessary, mitigate the negative impact of trade agreements.¹¹ The implementation of the resolution included the establishment of a WHO network for monitoring the implications of the TRIPS Agreement on public health.

The WHA recognized the importance of IPRs in fostering R&D in both innovative medicines and essential medicines, but also urged member states “to consider, whenever necessary, adapting national legislation in order to use to the full the flexibilities contained in the Agreement on Trade-Related Aspects of Intellectual Property Rights (TRIPS)”.¹² Many subsequent resolutions contain similar language. With regard to the area of HIV/AIDS, member states highlighted in the same year “the difficulties faced by developing countries in effective use of compulsory licensing in accordance with the Declaration on the TRIPS Agreement and Public Health (Doha Declaration)”.¹³

The WHA also mandated the WHO Secretariat, to support member states – at their request and in collaboration with the competent international organizations – in their efforts to frame coherent trade and health policies¹⁴ as well as to provide, on request and in collaboration with other competent international organizations, technical and policy support to countries on TRIPS flexibilities (see Box 2.2 for a list of the relevant WHA resolutions).¹⁵

Thus, while in the beginning, the resolutions focused on monitoring and assessing the impact of trade agreements, they became more specific over the years – specifically mentioning IP and TRIPS flexibilities. The mandate of WHO was extended to include, on request, technical and policy support on formulating coherent trade and health policies and the implementation of TRIPS flexibilities while, at the same time, making it clear that this should be done in collaboration with other relevant international organizations.

Box 2.2. Relevant World Health Assembly resolutions

1996	WHA49.14: Revised drug strategy
1999	WHA52.19: Revised drug strategy
2000	WHA53.14: HIV/AIDS: confronting the epidemic
2001	WHA54.10: Scaling up the response to HIV/AIDS
2001	WHA54.11: WHO medicines strategy
2002	WHA55.14: Ensuring accessibility of essential medicines
2003	WHA56.27: Intellectual property rights, innovation and public health
2003	WHA56.30: Global health sector strategy for HIV/AIDS
2004	WHA57.14: Scaling up treatment and care within a coordinated and comprehensive response to HIV/AIDS
2006	WHA59.24: Public health, innovation, essential health research and intellectual property rights: towards a global strategy and plan of action
2006	WHA59.26: International trade and health
2007	WHA60.30: Public health, innovation and intellectual property
2008	WHA61.21: Global strategy and plan of action on public health, innovation and intellectual property
2009	WHA62.16: Global strategy and plan of action on public health, innovation and intellectual property
2011	WHA64.5: Pandemic influenza preparedness: sharing of influenza viruses and access to vaccines and other benefits
2011	WHA64.14: Global health sector strategy on HIV/AIDS, 2011-2015
2012	WHA65.22: Follow up of the report of the Consultative Expert Working Group on Research and Development: Financing and Coordination

Based on this mandate, the WHO has provided guidance to its member states by publishing a wide range of material on: (i) how to make use of TRIPS flexibilities for improving public health, including improved access to HIV treatment (UNAIDS/WHO/UNDP, 2011); (ii) how to develop a public health perspective on the examination of pharmaceutical patents (ICTSD/UNCTAD/WHO, 2007); (iii) remuneration guidelines for the non-voluntary use of patents on medical technologies (WHO, 2005a); and (iv) how to implement the WTO General Council Decision on Paragraph 6 of the Doha Declaration (Correa, 2004).¹⁶

A major development in this regard was the establishment of the Commission on Intellectual Property Rights, Innovation and Public Health (CIPRH) and the subsequent adoption of the WHO Global Strategy and Plan of Action on Public Health, Innovation and Intellectual Property (GSPA-PHI).¹⁷

(b) The Commission on Intellectual Property Rights, Innovation and Public Health

In 2003, the CIPRH was established “to collect data and proposals from the different actors involved and produce

an analysis of intellectual property rights, innovation, and public health, including the question of appropriate funding and incentive mechanisms for the creation of new medicines and other products against diseases that disproportionately affect developing countries”.¹⁸ The CIPRH reviewed the interfaces and linkages between IPRs, innovation and public health, and examined in depth how to stimulate the creation of new medicines and other products for diseases that mainly affect developing countries.

In April 2006, the CIPRH published its final report that focused on the overarching question of how to promote innovation and improve access to medical technologies in developing countries through the different stages of the development of medicines – discovery, development and delivery. The report made 60 recommendations addressed to governments of developed and developing countries, the WHO, and other intergovernmental organizations and stakeholders. Recommendations covered the whole innovation cycle and included R&D policies, procurement and health delivery systems, the role of patents and protection of clinical test data, management of IP, TRIPS

flexibilities, competition policy, the regulation of quality, safety and efficacy of medicines as well as the impact of FTAs on access to medicines.

The report recommended that the WHO develop a global plan of action to secure sustainable funding for developing accessible products for diseases that affect developing countries, and also continue to monitor the public health impact of IPRs on the development of new products and access to medicines in developing countries. Based on the report, the WHA established an intergovernmental working group to draw up a global strategy and plan of action¹⁹ to provide a framework for securing an enhanced and sustainable basis for needs-driven, essential health R&D relevant for diseases that disproportionately affect developing countries.²⁰ This process led to the adoption of the GSPA-PHI in 2008.²¹

(c) The Global Strategy and Plan of Action on Public Health, Innovation and Intellectual Property

The adoption of the GSPA-PHI was a major step forward towards a global consensus on practical action on public health, innovation and IP (see Table 2.2). The overarching objectives of the GSPA-PHI are to promote new thinking on innovation and access to medicines, as well as, based on the recommendations of the CIPIH report, to provide a medium-term framework for securing an enhanced and sustainable basis for needs-driven, essential health R&D relevant to diseases which disproportionately affect developing countries, proposing clear objectives and priorities for R&D, and estimating funding needs in this area. The GSPA-PHI states that while IPRs are an important incentive for the development of new health care products, this incentive alone is not sufficient to trigger the development of the health products needed to fight diseases in a scenario where the potential paying

market is small or uncertain.²² The lack of financing for R&D into diseases disproportionately affecting developing countries was subsequently addressed by two subsequent WHO expert working groups.²³

Overall, member states agreed that the GSPA-PHI should “encourage and support the application and management of intellectual property in a manner that maximizes health-related innovation, especially to meet the research and development needs of developing countries, protects public health and promotes access to medicines for all, as well as explore and implement, where appropriate, possible incentive schemes for research and development” (see Table 2.2).²⁴

The GSPA-PHI also reaffirms and broadens the mandate of the WHO to work at the interface of public health and IP. The GSPA-PHI has been summarizing, updating and expanding the various mandates in the area of public health and IP which were given to the WHO through the resolutions adopted since the TRIPS Agreement came into effect. On the other hand, this mandate is linked to the clear aspiration of member states to ensure closer collaboration between relevant intergovernmental organizations and their respective work on public health and IP-related issues. Element 5 of the plan of action therefore requests governments and international organizations to “strengthen efforts to effectively coordinate work relating to intellectual property and public health among the secretariats and governing bodies of relevant regional and international organizations in order to facilitate dialogue and dissemination of information to countries”.²⁵ This provision, together with the text of the resolution itself which requests the WHO Director-General “to coordinate with other relevant international intergovernmental organizations, including WIPO, WTO and UNCTAD, to effectively implement the global strategy and plan of action”²⁶ also provides the basis for the trilateral cooperation established by the Secretariats of the WHO, WIPO and the WTO.²⁷

Table 2.2. The Global Strategy and Plan of Action on Public Health, Innovation and Intellectual Property

<p>The main components of GSPA-PHI are as follows:</p>
<p>Main aims:</p> <ul style="list-style-type: none"> ■ promote new thinking on innovation and access to medicines ■ promote and build capacity for innovation and R&D (for Type II and Type III diseases, and for the specific needs of developing countries in relation to Type I diseases) ■ improve access to medical technologies ■ mobilize resources for R&D
<p>The GSPA-PHI elements</p> <ul style="list-style-type: none"> ■ Element 1: Prioritizing R&D needs ■ Element 2: Promoting R&D ■ Element 3: Building and improving innovative capacity ■ Element 4: Transfer of technology ■ Element 5: Application and management of IP in order to contribute to innovation and promote public health ■ Element 6: Improving delivery and access ■ Element 7: Promoting sustainable financing mechanisms ■ Element 8: Establishing monitoring and reporting systems

(d) Other developments in the WHO

Other developments in the work of the WHO with bearing on access and innovation include:

- The Pandemic Influenza Preparedness (PIP) Framework for the Sharing of Influenza Viruses and Access to Vaccines and other Benefits, which addresses IP issues and was adopted by the WHA in May 2011.²⁸
- The new global health sector strategy on HIV/AIDS, 2011-2015, which guides the health sector's response to HIV and was endorsed by the WHA in May 2011.²⁹ Its goals are consistent with "Getting to Zero", the UNAIDS strategy for the same period.
- A new mechanism for international collaboration among WHO member states to prevent and control substandard and spurious/falsely-labelled/falsified/counterfeit (SFFC) medical products, established by the WHA in 2012.³⁰
- The Political Declaration on the Prevention and Control of Non-communicable Diseases, adopted after the First Global Ministerial Conference on Healthy Lifestyles and Noncommunicable Disease Control and the UN High-level Meeting on Prevention and Control of Non-communicable Diseases held in September 2011, as well as the follow-up process.³¹

5. National health policies and health systems

Countries develop national health policies and strategies for guiding health development, taking into account the international legal and policy framework. Conceptually, these policies and strategies are based on and draw their strength from a national vision for social development and relevant policies. For example, a country's social protection policy would influence that country's policy-making about providing universal health coverage for its people and establishing a social health insurance policy.

Health policy refers to decisions, plans and actions which are undertaken to achieve specific health care goals within a society. It may be in the form of a formal document backed up by institutionalized processes and reviewed periodically, or it may be dispersed among a number of different documents, including notices, plans, strategies, decisions and directives. Health laws, rules and technical guidelines are also considered to be components of health policy.

Various health subsectors often have their own policies, and these also form part of national health policy. For example, national medicine policy is usually a well-defined document about ensuring people access to safe and effective medicines. However, it draws its guidance and inspiration for this policy from overall national health policy.

In order to understand the scope and vision of a national health policy, it is important to accept the idea of a health system. The health system is a broad concept and it covers all organizations, people and actions where the primary intent is to promote, restore or maintain health (WHO, 2000a). Using this definition, the term health system covers all health subsectors – public, private, not-for-profit and international cooperation. It also covers all activities taking place in a country to promote health, prevent morbidity and provide curative and rehabilitative services. In addition, it covers relevant policy-making and planning, stewardship and intersectoral collaboration to tackle socio-economic determinants of health which are outside the general understanding and purview of the health sector and ministry of health.

The WHO approach to national health policy is explicitly enshrined in its Constitution, which came into force in 1948:

"Governments have a responsibility for the health of their peoples which can be fulfilled only by the provision of adequate health and social measures."

In 1978, the WHO member states also agreed on a primary health care approach towards health care systems which is captured in Article 6 of the Declaration of Alma-Ata.

"Primary health care is essential health care based on practical, scientifically sound and socially acceptable methods and technology made universally accessible to individuals and families in the community through their full participation and at a cost that the community and country can afford to maintain at every stage of their development in the spirit of self-reliance and self-determination. It forms an integral part both of the country's health system, of which it is the central function and main focus, and of the overall social and economic development of the community. It is the first level of contact of individuals, the family and community with the national health system bringing health care as close as possible to where people live and work, and constitutes the first element of a continuing health care process."

Both the WHO Constitution and the Declaration of Alma-Ata have inspired national health policies in many WHO member states. National health policy is aimed at organizing and strengthening the national health systems in such a way that they effectively help in achieving the objectives of the policy. The WHO has been working towards strengthening health systems to make them efficient, effective and responsive to the unmet and changing needs of populations. A conceptual framework for a health system has been developed and promoted by the WHO, and comprises six building blocks, intermediate goals and ultimate health outcomes.³²

6. Regulation of medical technologies

Regulation of medical technologies is intended to ensure the quality, safety and efficacy of medicines (including vaccines and other biological medicines), or, in the case of medical devices, the safety, effectiveness and performance of such devices (WHO, 2003a). Regulation also plays an important role in determining access to new products. Regulatory measures are established and enforced to ensure that products given to patients are safe, effective and are of acceptable quality. However, unjustified regulatory measures, coupled with lack of transparency in the regulatory process and slow procedures, can become an obstacle to access. Regulation can also have an effect on prices. Higher safety standards and other additional regulatory requirements may require manufacturers to generate more (clinical) data to prove the safety of products, or they may require manufacturers to further invest in production facilities and thus reach the necessary quality standards. As a consequence, higher regulatory standards can increase the level of investment needed and can contribute to higher prices for end products.

Regulatory systems also have a decisive impact on innovation. New and innovative medicines, vaccines and medical devices must comply with safety standards. Many innovative products do not make it to the market, as they fail to meet safety standards, or due to lack of product efficacy. Regulators have to balance the benefits of an early release of new treatments with safety concerns and the rights of patients in the context of acceptable levels of risk.

This section reviews the concept of regulation of medical technologies, with a specific focus on medicines.

(a) Why regulate medicines?

While people have been taking remedies of different origins to ease pain, discomfort and disease symptoms for millennia, ideas about how to ensure that medicines are of the requisite quality are relatively more recent. The era of modern medicines and medical technology regulation began after various breakthroughs in chemistry, physiology and pharmacology in the 19th century. Later, however, government response to various medical catastrophes effectively served to accelerate the development of regulation. Briefly, the US Federal Food, Drug, and Cosmetic Act, with its 1938 requirement for premarket notification for new drugs, was introduced following the deaths in the United States of more than 100 people as a result of ingesting diethylene glycol, which was used as a solvent in a sulfanilamide elixir, a raspberry-flavoured antibiotic syrup. The second major push for increased governmental oversight was the thalidomide disaster.

Thalidomide, a sedative, was also targeted at expectant mothers experiencing morning sickness. Between 1958 and 1960, thalidomide was introduced in 46 different countries worldwide, resulting in an estimated 10,000 babies being born with severe birth defects (Rägo and Santoso, 2008).

These disasters created a concerted push for more oversight precisely because medicines are not ordinary consumer products and because no medicine is completely safe. Consumers lack the knowledge to make informed choices about when to use a particular medicine, which medicines to use and how to use them. They do not have sufficient information to weigh potential benefits against the risk of side-effects. In most countries, therefore, professional advice from prescribers or dispensers is required. Even so, information asymmetry exists between manufacturers, prescribers, dispensers and consumers. In addition, vaccines, blood products such as immunoglobulins and anti-venom products, and medical devices are unlike other consumer goods in that they also seek to meet an important policy objective of improving public health. Medicines that are not effective or are of poor quality can lead to therapeutic failure, worsening of disease or resistance to the medicines. If such ineffective or poor quality products are widely distributed, patients lose confidence in the health care system. Furthermore, patients can actually be harmed by the use of such products. Consequently, products must conform to prescribed standards, and their quality should be controlled rigorously.

Governments have to ensure that the manufacture, distribution and use of medical products are regulated effectively to protect and promote public health (Rägo and Santoso, 2008). The objective of medicines regulation is to ensure that:

- products are of the required quality, safety and efficacy
- products are appropriately manufactured, stored, distributed and dispensed by licensed manufacturers, wholesalers and health professionals
- illegal manufacturing and trade are detected and adequately sanctioned
- health professionals and patients have the necessary information to enable them to use products (particularly medicines) in a rational manner
- promotion and advertising is fair, balanced and aimed at rational use
- access is not hindered by unjustified regulatory barriers (such as applying different standards for imported and locally manufactured products, lengthy processing time for registration and marketing authorization applications, and duplication of the work of other regulators without delivering added value)
- side-effects, pharmacovigilance and the use of the medicines are appropriately monitored.

The quality, safety and efficacy of new medicines is in large part determined through extensive pre-clinical and clinical research and trials, while, for a generic medicine, only therapeutic equivalence and interchangeability with originator products has to be proved by bioequivalence or other appropriate studies.

(b) Clinical trials

Clinical trials are research studies in which large groups of human participants are enrolled to evaluate the safety or effectiveness of new medicines or new medical devices by monitoring their effects in human subjects (both patients and healthy volunteers can be involved). However, the first use of new medicines by human beings is always carefully carried out on only a very limited number of trial subjects. It is also important to note that clinical trials have a vital role in evaluating the safety of interventions, as many safety parameters can be controlled by quality. Clinical trials may also be referred to as interventional trials. The researchers measure how the subjects' health changes when compared with no treatment (placebo) or standard treatment. Interventions may include medicines, cells therapies and other biological products, but they can also extend to surgical procedures, radiologic procedures, devices, other treatments, diagnostics or preventive methods (e.g. vaccines).

Most clinical research that involves the testing of new medicines progresses in an orderly series of steps called phases. This allows researchers to ask and answer questions in a way that results in reliable information about the product's safety and efficacy, and it also protects patients. Most clinical trials are classified into one of four phases:³³

- **Phase I trial:** the first studies in healthy volunteers evaluate the safety of the medicine, including the appropriate dosage and side-effects; how a new medicine should be given (by mouth, injected into the blood or the muscle); how often it should be given; and what dose is considered safe. A Phase I trial usually involves only a small number of healthy volunteers or patients (20-80).
- **Phase II trial:** a phase II trial continues to test the safety of the medicine and begins to evaluate how well the new medicine works (efficacy). Phase II studies usually focus on a particular condition or disease in a larger group of people (several hundred).
- **Phase III trial:** these trials investigate the efficacy of the medicine in large groups of human subjects (from several hundred to several thousand and more) by comparing the intervention against a "standard" or placebo, as appropriate. Phase III trials also serve to monitor adverse effects and to collect more information on safety.
- **Phase IV trial:** after a medicine is approved for market, the purpose of Phase IV trials is to evaluate further the side-effects, risks and benefits of a medicine over a

longer period of time and in a larger number of people than in Phase III clinical trials. Phase IV trials involve several thousand people.

(c) Research ethics

Clinical trials not only involve issues around safety of the tested products, they also touch on different ethical questions. Among the most important questions to be addressed by research ethics committees before allowing a clinical trial to proceed are:

- the benefit-risk ratio
- the protection of the dignity of potential participants, which includes the validity of the informed consent process (quality of information provided and absence of coercion of participants) and the protection of privacy (confidentiality of personal data)
- the equitable access to expected benefits of the research (new knowledge or new products)
- the special attention given to vulnerable groups and the absence of discrimination.

Many international and national bodies have developed guidance for the ethical conduct of research over a period of almost 40 years. In 1964, the World Medical Association (WMA) adopted the Declaration of Helsinki. It has been reviewed regularly in the interim, with the most recent version adopted in 2008. The *International Ethical Guidelines for Biomedical Research Involving Human Subjects*, published in 2002 by the Council for International Organizations of Medical Sciences (CIOMS, 2002), constitutes another globally recognized ethical guidance. One essential ethical condition for comparing two treatments for a disease with a randomized controlled trial (where participants are allocated at random to receive one of several clinical interventions) is that there must be a good reason for thinking that one treatment is actually better than the other.

Following a resolution of the WHA adopted in 2006,³⁴ an important tool designed to improve clinical trial transparency was developed by the WHO – the International Clinical Trial Platform, which provides public access to information about clinical trials which are under way around the world.³⁵

(d) Key stakeholders in the regulation of medicines and medical technologies

A functioning regulatory system is a prerequisite for ensuring the quality, safety and efficacy of products on the market. National governments are responsible for establishing national or regional regulatory authorities which have a clear mission, sound legal basis, realistic objectives, appropriate organizational structure, adequate number of qualified staff, sustainable financing, access to up-to-date evidence-based technical literature, equipment

and information, coupled with capacity to exert effective market control. These regulatory authorities must be accountable to both the government and the public and their decision-making processes should be transparent. Monitoring and evaluation mechanisms should be built into the regulatory system in order to assess attainment of established objectives. Most countries have a regulatory authority and formal requirements for providing marketing authorization for medicines. However, they tend to have fewer such provisions in place for other regulated medical technologies, such as medical devices.³⁶

The role of the WHO in strengthening drug regulation involves the issuance of recommended norms and standards through its expert committees, the assessment of regulatory systems and support of regulatory capacity-building at the national level, in addition to the prequalification of essential medicines (such as ARVs to treat HIV/AIDS or medicines to treat malaria and TB), vaccines and certain medical devices so as to facilitate the procurement of adequate quality products internationally.³⁷

(e) International convergence of regulatory procedures and harmonization efforts

Conveying the importance of convergence of regulatory procedures across countries is a challenge. National and sub-national registration authorities follow their own administrative rules and technical requirements, and they have established their own processes and procedures for medicines registration. Even within countries, there is often no clear indication at a national level of the length of time registration takes or the maximum period of time permitted for regulators to assess and register medicines. Furthermore, limited transparency may apply before or during the registration process. Different national-level interpretations and implementation of technical requirements for registration set out in international guidelines are often due to factors such as different governmental structures, cultural norms, levels of technical competence and availability of human resources, or they may be due to particular business environments. In addition, there is often a time lag between the publication of international/regional/subregional technical regulatory guidelines and their implementation by individual countries. Regional differences still exist in terms of how individual countries go about ensuring compliance with current international good manufacturing practices (GMPs), as well as numerous other regulatory requirements for ensuring quality, safety and efficacy of products. Such distinctions can influence costs and the speed with which a company obtains marketing approval.

Convergence of the different national systems, in conjunction with harmonization of technical requirements, can remove many of the transactional and human resource costs associated with multiple regulatory submissions in each country, including multiple testings. Thus such

convergence can result in saving scarce resources for countries as well as companies. Regulatory convergence and increasing trust in regulatory decisions made by other competent authorities should lead to: (i) more efficient resource use (e.g. international and regional sharing of scientific resources and “best practices”); (ii) better quality applications to register medicines from manufacturers; (iii) cost savings both at the company and government level; and, as a consequence, (iv) quicker access to quality essential medicines that are safe and efficacious.

One of the roles of the WHO in terms of improving regulation is to provide a platform for regulators to discuss common challenges and identify areas where further guidance for regulators needs to be developed. The WHO has convened the International Conference of Drug Regulatory Authorities (ICDRA) every two years since 1980 to build collaboration between regulators globally, to promote harmonization and exchange of information, to identify good practices and to seek common approaches to problems that medicines regulatory authorities face.³⁸ The ICDRA recommendations serve as a guide to the WHO and interested stakeholders in determining priority actions in national and international regulation of medicines, vaccines and other regulated medical products.

There are also a number of regional and interregional regulatory harmonization initiatives on the regulation of medicines and medical devices:

(i) *East African Community*

The East African Community (EAC) launched a project on the harmonization of medicines registration in all five EAC member states. The objective of the project is to improve public health by increasing rapid access to good quality medicines through the harmonization of technical requirements and procedures for medicines registration, so as to achieve shorter registration periods for priority medicines to treat communicable and non-communicable diseases. The project also seeks to increase collaboration between the authorities, thereby resulting in joint assessments and inspections, and leading to mutual recognition and the avoidance of duplication.

(ii) *European regulatory system and the European Medicines Agency*

The European Medicines Agency (EMA) is responsible for the scientific evaluation of applications to market certain categories of medicines in Europe for both human and veterinary medicines. It is based on EU-wide harmonization of certain areas of pharmaceutical legislation, including technical requirements for marketing authorization. Under a centralized procedure, companies submit a single marketing authorization application to the EMA. The EMA has the power to execute its functions and grant centralized marketing authorizations. Once granted, a centralized (or “Community”) marketing authorization is

valid in the European Economic Area (EU member states, Iceland, Liechtenstein and Norway).

The EMA centralized procedure applies only to certain categories of medicines, including all medicines for human and animal use derived from biotechnology and other high-tech processes, and also including medicines for the treatment of HIV/AIDS, cancer, diabetes, neurodegenerative diseases, auto-immune and other immune dysfunctions, and viral diseases. In addition to the above, there are many other medicines which do not fall within the scope of the EMA centralized procedure and thus are registered at the national level.

These harmonized regulatory requirements also enable companies to apply for simultaneous authorization of medicines in different EU member states (decentralized procedure). Furthermore, mutual-recognition procedures allow companies to apply for an authorization of a medicine to be recognized in other EU member states.

(iii) *Gulf Cooperation Council*

The Gulf Cooperation Council (GCC) drug registration was established in 1999. Members comprise the Kingdom of Bahrain, the State of Kuwait, Oman, Qatar, the Kingdom of Saudi Arabia and the United Arab Emirates. The GCC registers pharmaceutical companies, pharmaceutical products; inspects companies for GMP compliance; approves quality control laboratories; reviews technical and post-market surveillance reports; and is responsible for bioequivalence studies as a component of quality assurance procedures. Certain countries which have established regulatory systems rely on their own competencies for registration (Pateriya et al., 2011).

(iv) *Pan American Network for Drug Regulatory Harmonization*

The Pan American Network for Drug Regulatory Harmonization (PANDRH), a continental forum, was established to deal with medicines regulatory harmonization. It comprises representatives of all drug regulatory authorities in the Pan-American region. It set up the Pan American Forum of Drug Regulatory Agencies to discuss and explore solutions to common problems. National authorities participate in and lead this process. The main aim of PANDRH is to support harmonization processes through the analysis of specific aspects of such processes, and to adopt recommendations on priority subjects and harmonized regulatory guidelines.

(v) *Other regional initiatives*

Further regional initiatives on medicines regulation include:

- the Andean Quality System, which was established in 1995

- the Southern Common Market (MERCOSUR)
- efforts by the Association of Southeast Asian Nations (ASEAN) to create a harmonized medicines regulatory process
- the African Medicines Regulatory Harmonization (AMRH) initiative, of which the EAC project is the first subregional project.

There are also a number of interregional regulatory harmonization initiatives for technical requirements.

(vi) *International Conference on Harmonization of Technical Requirements for Registration of Pharmaceuticals for Human Use and related initiatives*

The International Conference on Harmonization of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH) was established in 1990 and brings together the regulatory authorities and pharmaceutical industries of Europe, Japan and the United States to discuss scientific and technical aspects of medicines registration, specifically focusing on new innovative medicines. The harmonization of technical requirements for the registration process can avoid unnecessary costs generated as a result of differences in national registration processes. Harmonization also helps to avoid the duplication of clinical trials, and speeds up the development and registration process for new medicines. Streamlining the regulatory assessment process can thus have a positive impact on both innovation and access by facilitating authorization and reducing duplication of efforts and related costs.

In response to increasing globalization in the development of medicines, the ICH also involves regulatory authorities from countries that are major producers of active pharmaceutical ingredients or clinical trial data. The ICH topics are divided into four category-assigned codes: Quality (Q) Guidelines; Safety (S) Guidelines; Efficacy (E) Guidelines; and Multidisciplinary (M) Guidelines. M Guidelines consist of cross-cutting topics which do not fit neatly into one of the other three categories. One such example is the Common Technical Document (CTD), covering the preparation of registration dossiers through a harmonized structure and content. This has been adopted by all partners in the ICH, as well as by Australia, Canada and Switzerland. Prior to the adoption of the CTD, each country had its own format for new drug applications. A company seeking to register a product for sale in more than one country was required to submit the application in the relevant country's format, which led to a considerable duplication of effort, with a corresponding waste of time, energy and money. The WHO is following the ICH CTD format in its prequalification programme, and it has provided numerous CTD training sessions for regulators and industries alike to promote the use of CTD for multisource (generic) medicines registration applications outside ICH regions.

(vii) *Global Harmonization Task Force: international harmonization in the regulation of medical devices*

The Global Harmonization Task Force (GHTF) is a response to the need for international harmonization in the regulation of medical devices. It was created in 1992 to achieve greater uniformity between national medical device regulatory systems. The GHTF was founded by Australia, Canada, the European Union, Japan and the United States as a voluntary group of representatives from national medical device regulatory authorities and the regulated industry. The aim of the GHTF is to further the convergence of regulatory practices related to medical devices. It also promotes technological innovation and facilitates trade in medical devices by contributing to more harmonized regulatory requirements. The GHTF publishes documents on regulatory practices, which provide a model for the regulation of medical devices and can be used by national regulatory authorities. The arguments in favour of the harmonization of regulatory standards for the safety, effectiveness, performance and quality of medical devices are substantially the same as those favouring the harmonization of regulatory standards for medicines. Different national standards for the regulation of medical devices lead to duplications, increased costs incurred by regulators as well as companies and, ultimately, the jeopardy of patient safety. Harmonized standards open up possibilities for countries, enabling them to rely on foreign authorizations of more advanced regulatory systems to approve medical devices. Countries with weaker regulatory systems can thus allocate scarce resources to other areas – thereby facilitating access to needed medical devices through shorter regulatory processes (WHO, 2003a).

(viii) *International Medical Device Regulators Forum*

Based on the work of the GHTF, the International Medical Device Regulators Forum (IMDRF) was established in 2011 to discuss future directions in medical device regulatory harmonization. The IMDRF comprises a group of medical device regulators, and currently includes representatives from Australia, Brazil, Canada, the European Union, Japan, the United States and the WHO. China, India and the Russian Federation have been invited to join. As a result, IMDRF membership is expected to become more internationalized than GHTF membership. The mission of the IMDRF is “to strategically accelerate international medical device regulatory convergence to promote an efficient and effective regulatory model for medical devices that is responsive to emerging challenges in the sector while protecting and maximizing public health and safety”. Regulatory convergence refers to the voluntary alignment of regulatory requirements and approaches across countries and regions.

(f) Future of regulation

It is a complex task to balance the benefits of the early release of new products with safety concerns and to find an acceptable level of risk. Regulators face the complicated challenge of using the best science available to balance the various different interests of the public in general, patients and producers of regulated medical technologies while ensuring that products are safe and efficacious. Optimizing the use of the scarce resources available to regulators will assume ever-increasing importance in the future. In this environment, new products will inevitably create new regulatory challenges.

Increasingly, complex new advanced therapy medicinal products include new medical products based on genes (gene therapy), cells (cell therapy) and tissues (tissue engineering). These advanced therapies may offer revolutionary treatments for a number of diseases or injuries, such as skin injuries in burn victims, Alzheimer's disease, cancer and muscular dystrophy. They offer huge potential for patients and industry. In addition, new technologies such as nanotechnology offer new horizons for treatment. For example, one particular application of nanotechnology in medicine that is currently being developed involves employing nanoparticles to deliver medicines, heat, light or other substances to specific types of cells (such as cancer cells). Particles are engineered so that they are attracted to diseased cells, thereby enabling direct treatment of these cells. This technique reduces damage to healthy cells in the body and allows for earlier detection of disease.

Nanoparticles that deliver chemotherapy medicines directly to cancer cells are currently in development, and testing on the targeted delivery of chemotherapy medicines is under way, with final approval for their use on cancer patients pending. New biological medicines, including follow-on (“biosimilar”) biological products, represent another challenging area (see Box 2.3). The future of medicines regulation and other regulated medical technologies is increasingly reliant on highly sophisticated scientific skills and the capacity of regulators, combined with a greater degree of collaboration and cooperation. In the future, regulators are more likely to function as a network, benefitting from each other's work as opposed to relying on individual duplicative efforts. The regulatory system, supported by relevant legislation, is an important component of a functioning modern health system and is essential in order to facilitate innovation and access to new safe and effective medicines.³⁹

Besides regulation, many other health policy aspects impact innovation of and access to medical technologies. The supply of medicines and medical technologies within health systems, as well as procurement, price regulation, and the funding of health systems are covered in Chapter IV, Sections B and C.

Box 2.3. Biosimilars

Biological products (also known as “biopharmaceutical products”, “biologicals” or “biologics”) represent one of the fastest-growing pharmaceutical industry sectors. Currently, the market is dominated by originator products, and prices for such products are often high. Biosimilars (sometimes called “generic biologics”, “follow-on biologics” or “subsequent-entry biologics”) are products of different manufacturers which are similar in terms of quality, safety and efficacy to the originator products (“reference products”). Unlike generic medicines, which are generally considered interchangeable with their reference products, biosimilars are generally not recognized as identical to their reference products due to complex structures and variations in manufacturing processes.

Pathways for the registration of biosimilars

Biosimilars generally cannot be easily and inexpensively authorized as generics because, unlike traditional small-molecule medicines, efficacy and safety cannot be assessed by relying on the in vitro test data and chemical structure of the originator product. Rather, they require more costly clinical trials. Regulatory systems need to define when such a product can be considered “similar” to, or “interchangeable” with, an originator/reference product, and specific regulations for different categories of biosimilar products have to be established.

While the characteristics of a small-molecule medicine are mainly defined by its chemical structure, making such medicines relatively easy to replicate, biopharmaceuticals consist of large and complex proteins which cannot be easily characterized by chemical or physical methods. Slight variations during the production process can significantly affect the unique properties of biopharmaceuticals, and thereby have an impact on the clinical safety and efficacy of the product. The manufacturing process of biosimilars should therefore ideally deviate only slightly (or not at all) from the process of the reference product. Achieving sufficiently similar production processes for biosimilars can be complicated by a lack of access to the information needed for manufacturing, as certain aspects of the process may be protected as trade secrets.

In recent years, some medicines regulatory authorities, such as the EMA⁴⁰ and Swissmedic,⁴¹ as well as the WHO,⁴² have issued guidelines with respect to the authorization of biosimilars. In the United States, the Biologics Price and Competition and Innovation Act of 2009 paved the way for the introduction of a specific pathway for the authorization of biosimilars. The legislation set out rules governing when applicants can rely on the clinical data of the reference product. In order to rely on such data, and thereby reduce redundancy by avoiding repetitive clinical trials, applicants generally must demonstrate that “there are no clinically meaningful differences between the biological product and the reference product in terms of the safety, purity, and potency of the product”.⁴³

While most developing countries have not yet established specific pathways for the registration of biosimilars, countries have registered a number of “alternative” biologicals (Saberwal, 2010). Such alternative biologicals are different from biosimilars approved through a specific pathway, as they have not undergone similar testing. Calls have been made for the development of specific guidelines and registration procedures for biosimilars. India has recently published *Guidelines for Similar Biologics*, which regulate the market authorization process for biosimilars in India specifying the data that has to be submitted in the authorization process (Government of India, 2012).

What will be the effect of biosimilars on prices?

Due to the complexity of biopharmaceutical products and the need for a comprehensive regulatory dossier, developing a biosimilar is much more costly than developing generic versions of traditional small-molecule medicines. It is difficult to predict to what extent competition will take place once patent protection for originator biologics has expired. This uncertainty is due to a number of factors, including the need for sophisticated technical know-how, high development costs, challenging storage and handling issues, laws which grant temporary exclusivity of testing data to the sponsor of the originator product, immunogenicity concerns, and possible additional regulatory requirements (such as post-market surveillance and pharmacovigilance) to ensure safety and efficacy (Roger and Goldsmith, 2008). Experience in the development of small-molecule generics has shown that substantial reductions in prices generally will not take place until such time as there are several manufacturers of the same product in the market. Therefore, it remains to be seen to what extent the prices of biosimilars will be lower than the prices of originator/reference products.

B. Intellectual property, trade and other policy dimensions

Key points

- The multilateral standards for each form of intellectual property (IP) are minimum standards, thus leaving considerable scope for policy-makers to decide on their implementation in a way that supports public health objectives.
- The patent system is designed to support innovation and, at the same time, offer a mechanism to ensure that such innovations are accessible to society.
- A product, its process of manufacture and its use can be covered by several patents. Patent information helps to determine the freedom to operate, and to what extent and with whom, licences need to be negotiated.
- The way in which test data are protected is relevant for innovation in, and access to, medicines. Countries have adopted different regimes of test data protection, ranging from data exclusivity to keeping the data secret, while allowing the competent authorities to rely on them.
- The trademark system serves to distinguish products and to inform the consumer. Trademarks are used to brand both original and generic products. To avoid confusion, trademarks for pharmaceutical products need to be distinct from the generic international nonproprietary names (INN) of the products.
- The WHO selects international nonproprietary names (INNs), i.e. single names of worldwide acceptability for each active pharmaceutical substance that is to be marketed as a pharmaceutical.
- The creation of sound, competitive market structures through competition law has an important role to play in enhancing access to medical technology and fostering innovation in the pharmaceutical sector. Unwarranted restrictions on competition, resulting from the abuse of intellectual property rights (IPRs), can be addressed on a case-by-case basis through competition law enforcement.
- All countries rely on imports, to varying degrees, to meet the health care needs of their populations. This reliance is particularly pronounced for the national health systems of smaller developing countries.
- Efficient, transparent and competitive procurement processes can contribute to improvements in the accessibility and affordability of medicines and thus towards more efficient and cost-effective health systems. The WTO Agreement on Government Procurement (GPA) seeks to promote transparency and fair competition to deliver improved value for money for governments which are parties to the GPA and also for agencies of these governments.
- Bilateral and regional agreements have shaped the framework for access and innovation in many countries. They are not limited to setting IPR standards, but also include rules on tariffs on pharmaceutical products, as well as rules that have been established regarding government procurement and competition law.

This section provides an overview of elements and legal and policy instruments relating to the IP and international trade system which are relevant to medical innovation and access to medical technologies at the international level.

1. Intellectual property systems

Those forms of IP that are most relevant to innovation in, and access to, medical technologies, as well as cross-cutting issues related to their enforcement are outlined in this section.

(a) Introduction to IP systems

IP systems operate by providing limited rights to exclude certain defined third-party use of protected material. Their protection is generally intended to strengthen market-based incentives for private-sector stakeholders to invest resources in product development and the marketing of new technologies. Such incentives are considered especially valuable for the development of medical technologies due to the considerable financial and technical resources required, coupled with the high risk of failure even at a late stage in product development and issues related to

product liability. Many medical technologies are expensive to develop but are relatively cheap to reproduce. In such instances, it would be unsustainable for companies to invest capital in product development and regulatory approval if their competitors were in a position to immediately introduce replica products.⁴⁴

Inasmuch as IP protection operates through a right to exclude others, it can inhibit forms of competition (such as market entry for generic medicines) and hinder further innovation (e.g. where no research exemption exists). IP policy, the laws that embody the policy, and the administration and enforcement of these laws, each aim to balance and accommodate a range of legitimate interests in a positive-sum way that promotes overall public welfare.

The balancing factors are diverse – in the case of patents, they comprise exclusions in patentable subject matter, exceptions and limitations on patent rights, limits on patent term and maintenance fees to encourage

under-utilized patents to lapse, in addition to instruments beyond the scope of patent law, such as competition policy. While the appropriate balance is ultimately set by national policy-makers and legislators, the international legal framework provides the context and general principles for national systems. The multilateral legal IP framework, which is the focus of this section, is defined in particular by the treaties administered by WIPO, and the TRIPS Agreement, which forms part of the WTO legal system and in turn incorporates the substantive provisions of several WIPO treaties, including the Paris Convention (see Box 2.4).

The TRIPS Agreement has considerable implications for the application of IP to medical technologies, notably through the implementation of new international standards requiring patents to be available for inventions in all areas of technology, including pharmaceutical products, and the requirement to protect clinical trial data against unfair commercial use. The negotiations on the TRIPS Agreement and its subsequent

Box 2.4. The Paris Convention

The Paris Convention for the Protection of Industrial Property (the Paris Convention) was concluded in 1883 and has been revised several times, most recently in 1967. Open to all states, it applies to industrial property in the widest sense, including patents, marks, industrial designs, utility models, trade names, geographical indications and the repression of unfair competition. It provides for national treatment, right of priority and common rules.

The principle of national treatment under the Paris Convention means that each contracting state must grant the same advantages to nationals of other contracting states as it grants to its own nationals with respect to the protection of industrial property. Nationals of non-contracting states are entitled to national treatment under certain conditions.

The right of priority means the following: on the basis of an earlier regular application filed in one of the contracting states, the applicant applies for protection of the same industrial property subject matter within a certain period of time (priority period) in any of the other contracting states. Then the later applications will not be affected by any event that may have taken place in the interval between the filing date of the first application (priority date) and the filing date of the later application, such as any publication of the invention claimed in a patent application or the sale of articles bearing the mark or incorporating an industrial design. The priority period under the Paris Convention lasts 12 months in the case of patents and utility models, and six months in the case of industrial designs and marks.

The common rules that must be followed by all contracting states include:

- Patents granted in different contracting states for the same invention are independent of each other.
- The grant of a patent may not be refused, and a patent may not be invalidated, just because the sale of the patented product, or of a product obtained by the patented process, is not allowed, restricted or is limited under national law.
- Contracting states may take legislative measures providing for the grant of compulsory licences, with certain limitations, to prevent the abuses which might result from the exclusive rights conferred.
- The registration of a mark in a contracting state is independent of its possible registration in any other country, including the country of origin. Consequently, the lapse or annulment of the registration of a mark in one contracting state will not affect the validity of registration in other contracting states.
- A contracting state must accept an application for a trademark which has been previously duly registered in another contracting state (the country of origin), but it is allowed to refuse that application when it does not comply with the requirements under the national law.
- Each contracting state must refuse registration and prohibit the use of marks which constitute a reproduction, imitation or translation, liable to create confusion, of a mark considered by the competent authority of that state to be well known in that state as being already the mark of a person entitled to the benefits of the Paris Convention and used for identical or similar goods.
- Each contracting state must provide for effective protection against unfair competition.

Table 2.3. TRIPS and public health: key milestones

1986	Punta del Este launches Uruguay Round negotiations with mandate on IP.
1994	Negotiations conclude and the TRIPS Agreement is adopted at the Marrakesh Ministerial Conference.
1995	TRIPS Agreement enters into force, and the WTO is established and is given legal and administrative responsibilities for TRIPS.
2000	Most TRIPS obligations come into effect for developing-country members, but not in relation to pharmaceutical product patents.
2000	WTO panel rules on TRIPS dispute concerning regulatory (Bolar) exceptions to facilitate entry of generic medicines.
2001	WHO–WTO Workshop on Differential Pricing and Financing of Essential Medicines (Høsbjør, Norway).
2001	Doha Declaration on the TRIPS Agreement and Public Health, including extension of transition period to 2016 for LDC members to implement patent and test data protection.
2003	WTO members adopt "Paragraph 6" mechanism enabling special compulsory licences for export of medicines, as additional TRIPS flexibility, initially in the form of a legal waiver, followed by the 2005 Protocol on a permanent amendment of the TRIPS Agreement.
2005	TRIPS obligations to protect patents for pharmaceutical products apply to developing-country WTO members (but not LDCs).
2005	TRIPS Council adopts extension until 2013 of transition period for LDCs to implement TRIPS as a whole.
2010	TRIPS Council's process of annual review of Paragraph 6 mechanism intensifies substantive discussion of its functioning and of broader aspects of access to medicines.

implementation have seen a continuing focus on IP and health issues (see Table 2.3) and, particularly, the nature and impact of obligations under the TRIPS Agreement on pharmaceutical patents and test data protection.

Article 7 of the TRIPS Agreement notably describes the objectives of protection and enforcement of IPRs in terms of a balance of rights and obligations. The objectives refer to "the promotion of technological innovation", to "the transfer and dissemination of technology", to the mutual advantage of both "producers and users of technological knowledge" and also to "social and economic welfare". The principles set out in Article 8 expressly state that WTO members may adopt measures necessary to protect public health and nutrition, provided that such measures are consistent with the provisions of the TRIPS Agreement. The Doha Declaration, a landmark declaration made by the WTO Ministerial Conference in 2001, reaffirmed these objectives and principles as guidance for the implementation of TRIPS provisions in line with public health policy. The Doha Declaration referred to a set of flexibilities, or legal options within the TRIPS framework, which are discussed further below, after a general review of IP issues.

The multilateral standards for each form of IP are generally minimum standards that often leave considerable scope for implementation. The TRIPS Agreement specifies that WTO members are free to determine the appropriate method of implementation of TRIPS standards within their own legal practice. When determining the range of options for implementation, policy-makers therefore consider international standards as well as practice in other countries and their own national needs and priorities. Countries may also implement more extensive protection if they wish, provided it is TRIPS-consistent. Such protection is sometimes referred to as "TRIPS-plus". These standards

have been established in the IP sections of an increasing number of bilateral and regional agreements.⁴⁵

The principle of non-discrimination forms a cornerstone of the international IP system. "National treatment" provides that countries must not discriminate against the nationals of foreign countries with regard to the protection of IP, other than as permitted by some fairly narrow exceptions. The principle was set out as early as 1883 in the original text of Article 2 of the Paris Convention, and subsequently largely applied in Article 3 of the TRIPS Agreement. "Most-favoured-nation (MFN) treatment" provides that countries must not discriminate between the nationals of different foreign countries with regard to the protection of IP. The application of MFN treatment is also subject to some exceptions. Long an obligation in international trade law, MFN was applied to IP for the first time through Article 4 of the TRIPS Agreement. Application of the principle means that if two countries agree to give each other's nationals a higher level of IP protection in a bilateral treaty, they must extend the same benefit to nationals of all other WTO members.⁴⁶

Apart from such general principles, each form of IP is subject to specific standards, reflecting their distinct policy purposes, different subject matter and economic effects. These differences are apparent in the scope of protected subject matter, the scope of rights, the duration of protection, and the nature of exceptions and other safeguards for third-party interests, as well as in how these rights are enforced.

(b) Patent law and policy

The past decade has seen considerable growth in the use of patents for medical technologies, in terms of the volume of patent filings, the geographical base of activity (with a

notable rise in patents from certain emerging economies), and the diversity of private and public entities seeking patents. This same period has also been marked by an intense debate on the role of the patent system regarding innovation in, and access to, medical products.

The dual effect of IP protection – promoting the development of new medicines and impacting on prices – was recognized in the Doha Declaration. Since then, debate has focused on the implications of patent rights for access to essential medicines. In addition, it has been discussed whether the patent system provides sufficient and appropriate incentives to ensure the development of new products in certain areas – for example, with respect to neglected diseases or certain countries. In practice, patents are also used as a medium for concluding many technology partnerships and R&D collaborations, with multiple licensing arrangements in order to deliver a new medical technology to the public.

(i) *The rationale of the patent system*

The rationale for having patents is to make investment in innovation attractive and to offer a mechanism which ensures that the knowledge contained in the patent application is accessible to society. Among others, the obligation of patent owners to publicly disclose their inventions enables society to know, and eventually use, the knowledge contained in patent documents. If an invention could be freely used by others at no additional cost, “free riders” would not bear the cost of development. This would reduce the expected returns of the original inventor and would result, in theory, in the under-provision of new inventions. A recent WIPO report explains that, it is for this reason that the patent system intends to correct the market failure that would result in the under-provision of innovative activities by providing innovators with limited exclusive rights to prevent others from exploiting their invention, thereby enabling the innovators to appropriate returns on their innovation activities.⁴⁷

However, the use of the exclusive right can itself contribute to a market distortion and can lead to a situation characterized by inefficiencies, high prices and the under-provision of goods. Empirical studies find evidence of both positive and negative effects of patents on innovation. Inconclusive evidence on the role of the patent system in encouraging R&D and technology transfer makes it difficult to draw any clear-cut conclusions about the effectiveness of the patent system for economic development.⁴⁸

A number of mechanisms exist in patent systems to prevent and correct undesired effects:

- Patent rights only last for a limited period of time.
- Exclusions from patentable subject matter and exceptions and limitations to patent rights are permitted in order to ensure harmony with broader public policy goals.

- Patent application, examination and grant procedures, as well as opposition, appeal, and other review procedures allow courts and other review bodies to correct erroneous decisions and give relief where necessary, in order to ensure that the patent system as a whole functions as a public interest policy tool.

(ii) *The international framework*

The substantive multilateral standards for patent protection are largely those set out in the Paris Convention (Stockholm Act of 1967) and the TRIPS Agreement of 1994. The Paris Convention did not regulate what is considered patentable and, until the TRIPS Agreement came into effect in 1995, there was considerable diversity in national law and practice in this respect. In 1988, at an early stage in the TRIPS negotiations, a WIPO report cited 49 countries that either did not grant patent protection for pharmaceutical products at all or only provided a limited form of such protection. Some of these countries also excluded pharmaceutical processes.⁴⁹ The duration of patents also varied considerably from country to country.

The TRIPS Agreement is the first multilateral treaty to stipulate the core criteria⁵⁰ for patentable subject matter. It provides that patents must be “available for any inventions, whether products or processes, in all fields of technology” (Article 27 of the TRIPS Agreement). The reference to “all fields of technology” means that patents must be available for pharmaceutical products (such as a new chemical compound with medicinal effect) and processes (such as a method of producing the medicine). It also provides that the available term of protection shall not end before the expiration of a period of 20 years counted from the date of filing the application. These requirements came into effect progressively, but now apply to all WTO members, except LDCs. The most significant change of relevance to the area of public health was the requirement that pharmaceutical products be patentable in developing countries from 2005.

Even with these international standards for patent protection, there is no such thing as a worldwide patent. Patents are granted under national law or on a regional basis. Article 4*bis* of the Paris Convention provides the independence of patents obtained for the same invention in different countries. This means that a patent granted in one country conveys no rights in any other country. A granted patent on a pharmaceutical technology in one country cannot be used to prevent generic competition in other countries where no patent is in force. An invention may be patented in one country and not in another.

There is, however, a global system for filing patent applications, known as the Patent Cooperation Treaty (PCT), administered by WIPO (see Box 2.5). A final decision on whether a patent should be granted is not taken internationally. Rather, it is taken separately by the national or regional authorities responsible for national

Box 2.5. The Patent Cooperation Treaty

The Patent Cooperation Treaty (PCT)⁵¹ makes it possible to seek legal protection for an invention simultaneously in all PCT contracting states by filing an international patent application. Such an application may be filed by anyone who is a national or resident of a PCT contracting state, either, in general, with the national patent office of the contracting state of which the applicant is a national or resident, with a competent regional patent office or with the International Bureau of WIPO in Geneva (the “receiving office”). The effect of the international application is the same as if national patent applications had been filed with the national patent office of each contracting state. The PCT regulates in detail the formal requirements with which any international application must comply, but it does not determine the substantive rules that a country applies in deciding whether or not ultimately to grant a patent.

The PCT provides an international phase within which the international application is subjected to an international search, resulting in an international search report (a listing of the citations of published documents that might affect the patentability of the invention) and a preliminary and non-binding written opinion on whether the invention appears to meet the patentability criteria in light of the search report. The international application, if not withdrawn, is published together with the international search report. In addition, an optional non-binding international preliminary examination is carried out on receipt of a request from the applicant. However, no patents are granted during the international phase under the PCT. If the applicant decides to continue with the international application, with a view to obtaining national or regional patent protection, the applicant needs to commence separately the national/regional procedure in each PCT contracting state in which the applicant wishes to obtain patent protection (the “national phase”). During this “national phase”, a country’s authorities can apply the substantive rules on eligibility for patents that are defined under national law, which may result in different outcomes from country to country.⁵²

patent jurisdictions. A number of regional agreements have also harmonized and simplified patent laws within different regions.⁵³

Despite this regional and international cooperation, national patent laws and practices differ, leading to potentially diverging outcomes. Where patent applications are filed for the same invention in different national or regional patent offices, they are processed separately according to the applicable national law or regional law, and such processing may have diverging outcomes. For example, when a PCT application relating to a certain pharmaceutical compound reaches the national phase in the PCT contracting states, different substantive patentability requirements may apply under the patent law of each country or region. Based on the application of these requirements in the national examination processes, the patent claims⁵⁴ may be amended in one country and remain unchanged in another. Consequently, the same PCT application may result in a patent grant in one country, a modification in another country and a patent refusal in a third country. Moreover, a patent could be invalidated by a court in one country but confirmed by a court in another country.

The majority of patents are applied for, and ultimately obtained in, a relatively small number of countries – typically, those countries where the patent holder intends to concentrate production or marketing efforts, or where there are significant competitors or production capacity. In countries where no patent application is filed, or where a patent application has been abandoned or refused, the claimed invention enters into the public domain following the publication of the patent documents, provided there is no other patent or other right covering the same technology.

(iii) Basic patent issues

Patents are territorial rights. In addition, patent protection is limited in time. Patent laws generally provide a protection term of at least 20 years. Patent owners, on the other hand, may abandon a patent earlier if, for example, the commercialization of the invention does not generate the expected return on investment and fails to cover the costs of maintaining the patent. Patents may also be invalidated based on grounds established by the national law.

Five criteria are common to all patent laws: (i) the application must relate to patentable subject matter; (ii) the claimed subject matter must be new; (iii) it must involve an inventive step (or be non-obvious); (iv) it must be industrially applicable (or useful) (Article 27 of the TRIPS Agreement); and, (v) as determined by Article 29 of the TRIPS Agreement, the invention must be properly disclosed. These requirements apply cumulatively. Failure to satisfy any one criterion leads to rejection of a patent application.

Even though the same essential patentability criteria are found in the vast majority of countries, there is no agreed international understanding about the definition and interpretation of these criteria. This creates some policy space regarding their establishment under the applicable national law. Accordingly, patent offices and courts interpret and apply national patentability requirements on a case-by-case basis within the applicable legal framework. Many patent offices provide patent examination guidelines for consistent and coherent application of patent law, often basing this guidance on cases previously decided by the responsible courts.⁵⁵

Inventorship, ownership and entitlement to apply

Every invention begins with an inventor or inventors. While international IP law is silent on who should be considered the inventor – leaving this question to be determined by national laws – the general practice is that those who contribute to the conception of at least one of the claims in the patent grant are joint inventors, irrespective of the proportion that they contributed.

Inventorship does not necessarily imply ownership. Inventions by employees made during the course of their employment, depending on the rules of the national law, may belong to the employer, with or without a specific agreement. Contracts of employment or a consultancy may provide that inventions made outside the course of employment also belong to the employer or the party who engaged the consultant. Inventors frequently assign their economic rights to an invention to the bodies that provide funding for their research.

Policies on ownership of patents on research undertaken within public institutions such as universities can have a significant effect on how medical technologies are developed. In the absence of clear guidelines, uncertainty can ensue.

Patentable subject matter

Patents are only available for patentable subject matter, generally defined as “invention” in patent law. In the absence of an internationally agreed definition of patentable subject matter, national laws define the requirement either positively or through a negative list of excluded subject matter – or both. Exclusions from patentable subject matter may be general – such as mere discoveries, scientific principles or abstract ideas. Patentable subject matter that does not fall into such categories can be excluded on other grounds. This would include, for example, inventions that would be considered against morality if commercially exploited (see Box 2.6), or certain methods for medical treatment of humans or animals (Article 27.3(a) of the

Box 2.6. Societal and moral values in the patent system

What is considered contrary to morality depends on the fundamental values of a society in a given context. Article 27.2 of the TRIPS Agreement provides a flexible framework for moral assessments to be made which leaves room for societal and ethical values to be taken into account. For example, Article 53 of the European Patent Convention (EPC) stipulates that European patents shall not be granted on inventions whose publication or exploitation would be contrary to *ordre public* or morality (paragraph (a)), and shall not be granted for methods for treatment of the human or animal body by surgery or therapy, and diagnostic methods practised on the human or animal body (paragraph (c)).⁵⁶ The use of human embryos in research has sparked particular ethical concerns that touch on patent law and its interpretation.

A landmark ruling on human stem cell cultures was issued by the Enlarged Board of Appeal of the European Patent Office (EPO) in 2008 in a case involving the Wisconsin Alumni Research Foundation (WARF case).⁵⁷ The Enlarged Board of Appeal ruled that the EPC forbids the patenting of claims directed to products which could only be prepared by a method which necessarily involved the destruction of the human embryos from which the said products were derived, even if the said method was not part of the claims. This ruling did not, however, address inventions based on cell lines produced in the laboratory.

In 2011, the Court of Justice of the European Union, *Oliver Brüstle v. Greenpeace e.V.*,⁵⁸ clarified the application of the EU Directive 98/44/EC on the legal protection of biotechnological inventions.⁵⁹ While not touching upon questions of a medical or ethical nature, the court ruled that the concept of “human embryo” must be understood in a wide sense. Accordingly, any human ovum capable of commencing the process of development of a human being, whether fertilized or not yet fertilized, must be regarded as a “human embryo” under Article 6(2)(c) of the Directive. The court ruled that patents on inventions using human embryos were prohibited under the Directive. The prohibition also included the use of such patents for scientific research.

Microorganisms and gene patenting

The TRIPS Agreement expressly provides for optional exclusions of plants and animals and essential biological processes for their reproduction. However, this exclusion does not extend to microorganisms and other processes for the reproduction of plants or animals, which must be patentable. There has been no definitive determination of the scope of this provision, although the WTO TRIPS Council has reviewed it since 1999,⁶⁰ and has heard reports of the diverse ways in which countries have exercised this option. This provision is relevant to access to medical technologies because it overlaps with the question of biotechnological health-related inventions, such as genetic diagnostics, genetically modified organisms used in medical research or other aspects of gene patenting. Some patent systems explicitly exclude parts of plants and animals, such as cells, cell lines, genes and genomes; others consider them a particular type of chemical substance, if isolated and purified from their natural environment, and thus patentable subject matter. A number of countries have expressly elected to exclude patents on any unaltered genetic materials.⁶¹

TRIPS Agreement). A number of countries have opted to exclude from patent grant (or not permit the enforcement of) inventions concerning methods of medical treatment (or, with similar effect, to limit the enforcement of such patents). Some national laws also articulate very specific exclusions, such as for first and second medical uses, or expressly allow for the patenting of such uses.⁶²

Novelty

The criterion of novelty is intended to ensure that patents are only granted to technologies that are not already available to the public. In many jurisdictions, this criterion is understood to mean that a claimed invention must not already have been disclosed to the public, anywhere in the world, before the filing or priority date of the patent application) – for example, through publication, or as a result of having been publicly made, carried out, orally presented, or used, before filing a patent application. National laws define which kind and form of documentation, if any, constitutes prior public disclosure relevant to an assessment of novelty.

For example, consider a case where a patent application claims a new type of cast used to immobilize a patient's arm. At the time of filing the patent application, this invention was known only to the employees of the company filing the application. These employees were bound by their employment contracts not to disclose their knowledge to the public. However, if, before the patent filing took place, the cast was tested on patients without confidentiality arrangements already agreed and in place, the claimed invention may no longer be considered novel, since access to the relevant knowledge may not have been sufficiently restricted and therefore it may be considered to have been disclosed to the public.

Inventive step/non-obviousness

Patent law, in general, defines only the basic concept of what constitutes an inventive step and leaves interpretation to patent offices and supervising courts. Practice has developed different methodologies to determine the existence of an inventive step based on a number of indicators checked by a patent examiner. This criterion is understood in many jurisdictions to mean that the invention must represent a sufficient technical advance in relation to the state of the art – a technical advance from what has been used or described before in the relevant area – that could not be obvious to a person working in the technical area related to the invention with “ordinary skill” or average knowledge (“person skilled in the art”). For example, the inventive step (or non-obviousness) may be demonstrated by an “unexpected” or “surprising” effect that would not have been evident, at the time of invention, to the average person familiar with that area of technology. What is obvious, or not obvious, may change over time. For example, considerable effort was needed to isolate a gene at the end of the 20th century. Today, however, this is considered more routine.⁶³

Industrial applicability/utility

Industrial applicability (or utility) means that the invention can be made or used in any industry, including agriculture, or that it has a specific, credible and substantial utility. In general, the application of this requirement does not pose practical problems. However, in the area of biotechnology, it needs some consideration, given concerns that patent applications claiming gene-related inventions would block the use of the claimed gene sequence for uses that were not yet known by the applicant and, therefore, would not justify the grant of a patent in respect of the function which the applicant was not even aware of.⁶⁴

Disclosure

Sufficient disclosure of an invention is required in order to grant a patent. Article 29 of the TRIPS Agreement sets out the rule that an applicant for a patent shall disclose the invention in a manner sufficiently clear and complete for the invention to be carried out by a person skilled in the art. In some countries, the applicant may also be required to indicate the best mode for carrying out the invention known to the inventor at the filing date. In some countries, the applicant may also have to disclose details of patents applied for or granted in other jurisdictions.

Some critics of the patent system have argued that disclosure of a patented invention is often not sufficient to “work” the patent. One of the fundamental questions raised with respect to the disclosure requirement is to what extent a patentee must disclose his invention within the patent system in order to contribute to the promotion of innovation and to the transfer and dissemination of technology to the mutual advantage of producers and users of technological knowledge. While an invention must be described in the patent in such a manner that a person skilled in the art can carry out the invention without undue experiment or trials, in order to produce the invention to an economically profitable extent, the technical information contained in a patent often needs to be supplemented with further information assumed to be available already to a specialist reader of the patent. The disclosure requirement is designed for the specific legal and technical purposes of the patent system. Technical information disseminated through the patent system cannot replace other sources of information, for example text books and scientific journals.⁶⁵

In some cases, a patent might be inadvertently granted even if the requirement concerning the sufficiency of disclosure under the applicable national/regional law has not been complied with. If so, the patent may be defective. Most patent laws provide procedures for the revocation or invalidation of patents where the statutory patentability requirements are not met. Therefore, it would be a risky strategy for a patentee to intentionally not fully disclose an invention in a manner inconsistent with the disclosure requirement under the applicable national/regional law.⁶⁶

(iv) Patent procedures

Whether a claimed invention in a patent application meets all patentability criteria is usually established by the patent office that receives the application. In some countries, a prior art⁶⁷ search and substantive examination are carried out by the national/regional patent office. If the office establishes that all applicable requirements have been met, it grants a patent. Such substantive examination leads to a higher degree of legal certainty regarding the validity of granted patents – higher than the degree of certainty provided by a system that simply registers patent applications without carrying out substantive examination.

However, where search and examination are of low quality, this can have an adverse effect because it may raise false expectations in respect of the patent's validity. Where patent offices do not have the necessary resources to maintain up-to-date prior art documentation and employ examiners with the requisite expertise – or where they do not have a sufficient number of applications to justify having qualified examiners across all technical areas – a substantive examination system may not be the most suitable approach. Alternative options include: grant of patents without substantive examination; the registration of patents granted following substantive examination elsewhere; the use of other offices search and examination results; and cooperation between different patent offices.⁶⁸ For example, the Patent Cooperation Treaty (PCT) provides for non-binding international search and international preliminary examination, carried out by a number of patent offices which are specifically appointed for that purpose by the PCT Union Assembly. These search and examination reports can be used by national patent offices to decide on a patent grant.

Some developed and developing countries currently employ “registration systems” (as opposed to “examination systems”) which do not provide for substantive examination and thus do not assess whether a claimed invention fulfils the patentability requirements. Some argue that it is sensible to defer substantive examination until a patent is actually litigated. The validity of such an argument may depend on the cost, duration and amount of patent litigation on the one hand, and the cost of setting up and maintaining an examination system on the other hand. In countries with less well-functioning judicial systems, correction of erroneously granted patents may be challenging.

Where patent laws provide for full examination of patent applications, patent offices examine them with regard to the formal and substantive patentability criteria. Applicants must often narrow the scope of the claims during this process in order to avoid rejection of their applications. The applicant may also have to remove claims which the patent examiner considers do not meet the patentability criteria. This may be because they are already known and therefore are not novel, or because they may be obvious and therefore are not inventive. Often, the scope of rights

in a granted patent may end up significantly less than what is originally claimed in the application.⁶⁹

(v) Review procedures

In practice, patent grants may be erroneous. To address any such deficiencies, patent systems provide review procedures (before an administrative body, such as an appeal board, or before a court). In some countries, third parties may oppose the patent grant before an administrative body within a limited period of time. Such procedures complement the office procedures for patent grant and enable the public to contribute to patent quality. Some countries provide pre-grant opposition proceedings, some provide post-grant opposition proceedings and some provide both.⁷⁰

(vi) Rights conferred by a patent

Once granted, patents confer the right to the patentee to exclude others from making, using, offering for sale, selling in, or importing the patented invention into, the country where the patent rights are granted (Article 28 of the TRIPS Agreement). The scope of protection conferred by the patent is defined by the patent claims. The claims must be drafted in a clear and concise manner and must be fully supported by the disclosure of the invention.

In practice, patents are used not only to exclude competitors but also to allow a third party to make, use, offer for sale, sell or import the patented invention through licensing.

Patent owners can license, sell or transfer ownership of their patents. A licence is a contract in which the patent holder allows another party to use the IP, either in return for a payment of royalties (or some other consideration) or free of charge, for a certain field of use, in a certain territory (which may be for the life of the patent). Licences are frequently used to allow other companies with specialized research or development expertise to access the diverse bundle of patented technologies required to produce a complex pharmaceutical under mutually agreed terms.⁷¹

Patents and marketing approval are separate issues. The grant of a patent on a new medicine in a country does not give the right holder the right to sell the medicine in that country without the approval of the regulatory authority. It is irrelevant for the regulatory approval whether or not a patent is granted. Some countries, however, require applicants for regulatory approval to submit information on whether and which patents are granted, and they do not allow their regulatory authorities to grant marketing approval when a relevant patent subsists (“marketing approval/patent linkage”).⁷²

(vii) Exceptions and limitations

Exceptions and limitations to patent rights are tools used to address diverging interests. Such tools are common to all IP systems. Exceptions and limitations may, for

example, restrict certain uses of the patented invention in the enforcement of patent rights. Articles 5 and 5ter of the Paris Convention contain certain rules on compulsory licences and certain limitations on exclusive rights in the context of safeguarding the public interest. Articles 30 and 31 of the TRIPS Agreement provide for exceptions and limitations to the rights, and these provisions set out the conditions under which they may be applied.⁷³

One very common exception is the research exception, which allows others to use the patented invention for research purposes during the life of the patent.⁷⁴ Another common exception is the regulatory review exception, which allows generic competitors to make limited use of a patented invention before the patent expires to obtain marketing approval of a competitor product. This exception, also known as the “Bolar” exception, is discussed in Chapter IV, Section C.3(a)(i).

National laws may also authorize the grant of “compulsory licences” under certain conditions to third parties for their own use, or for use by or on behalf of governments, without the authorization of the right holder. Under a compulsory licence or government use authorization, a court or the responsible authority grants specific permission to a person other than the patent owner to produce, import, sell or use the patent-protected product, or use the patent-protected process, to address specific requirements. Patent owners are entitled to receive remuneration. The TRIPS Agreement sets out certain requirements regarding the way in which compulsory licences and government use authorizations should be issued, in order to define some practical limits and thus safeguard some of the patent holder’s interests. Notably, each case must be considered on its individual merits (Article 31(a)); prior efforts to negotiate a voluntary licence are required except in circumstances of extreme urgency or in cases of public non-commercial use (Article 31(b)); and the licence must be limited to predominantly supplying the domestic market (Article 31(f)). There are limitations regarding scope and duration (Article 31(c)), and termination (Article 31(g)). The right to use the patent must not be exclusive (Article 31(d)); neither may it be assignable to any third party (Article 31(e)). The patent holder has a right to apply for a judicial or administrative review that could lead to termination of the use or licence (Article 31(g)) and a right to receive adequate remuneration (Article 31(h)).

The requirement to negotiate a voluntary license within a reasonable period of time may be waived in situations of national emergency, in other circumstances of extreme urgency, or in cases of public non-commercial use (Article 31(b)). In cases where the use of the patent is authorized without the consent of the patent holder to remedy anti-competitive practices after a judicial or administrative process, WTO members are not obliged to apply these conditions. In such cases, the licence need not be predominantly for the supply of the domestic market (thus allowing exports of unlimited quantities) and the amount of remuneration can be different (i.e. it could be a lesser

amount or even none at all). Some countries have used compulsory licences and government use to manufacture or import pharmaceutical products from generic producers at lower prices to increase access before patents on the products expire.⁷⁵

The limitation of compulsory licences and government use to predominantly supply the domestic market, found in Article 31(f) of the TRIPS Agreement, was revised following the Doha Declaration to allow production exclusively for exports under a compulsory licence in limited circumstances (see Chapter IV, Section C.3(a)(ii)).

(viii) Patent information

The patent system requires disclosure of inventions to the public and makes published patents (and patent applications in many countries) an important source of technical and legal information. Patent information is a basis for IP and business strategies and decisions, and input into R&D processes. As such, the patent system constitutes a comprehensive and systematic record of technical knowledge (Bregonje, 2005).⁷⁶

WIPO standards, recommendations and guidelines help industrial property offices establish and administer their patent information and publication systems.⁷⁷ WIPO standards have led to a fairly uniform structure of patent documents all over the world. They address the transmission, exchange, sharing and dissemination of patent information between industrial property offices, and they facilitate access to technical information contained in patent documents and retrieval.⁷⁸ This has made patent information search easier and more user-friendly.

Nevertheless, the form of patent publication varies considerably from country to country. Under Article 12 of the Paris Convention, patent offices must regularly publish the names of the proprietors of granted patents with a brief designation of the patented inventions in an official periodical journal. In practice, patent applications are generally published for public access 18 months after their filing dates (priority dates). Similarly, publication of PCT international applications at 18 months from the priority date is generally required by Article 21 of the PCT. Some countries publish only granted patents and not patent applications. The publication may be limited to a short notice about the patent grant. In such a case, access to the technical information and assessment of the scope and legal status of a patent is much more difficult, and only a file inspection at the patent office will yield detailed information about the claimed invention. Countries may also opt to publish additional useful information, such as search and examination reports, corrections, amendments, translations and legal status information.

A patent family means a number of different patent documents that are related to each other through one or more common priority documents or are technically

equivalent. Subsequent applications in other countries usually claim the priority of a first application. Members of patent families may therefore be related to each other by such priority claims. Since subsequent filings can claim several priorities of different earlier applications, a variety of different family concepts exist.⁷⁹ Databases may use different definitions of what makes up a patent family. For this reason, search results based on patent families may be different for different databases.

Publication and digitization of patent information have made knowledge more easily accessible and searchable. Nevertheless, the retrieval, analysis and exploitation of patent information are very complex matters and require specialized skills. Performing effective patent searches may also pose challenges in relation to the availability of data in databases (WIPO, 2010).

(ix) Patent status and legal status information

Patent status and legal status information help to determine the freedom to operate in respect of a project and to which extent and with whom licences have to be negotiated. The term “patent status” is used in this study to refer to all patents related to a specific product, while the term “legal status” refers to various legal and administrative events that occur during the life cycle of a single patent.⁸⁰

All patent registers record the most important legal events, such as patent grant and ownership. Reliable and authoritative information on legal status can only be obtained from these primary sources. Secondary sources may also provide information, often involving a delay, but they may lack some of the data contained in primary sources.⁸¹

Assessing the patent status of medical products generally requires specific expertise. A product (including products made of combinations of components, e.g. in the case of fixed-dose combinations), its manufacturing process and its use can be covered by several patents protecting various technological aspects. The manufacturers and sellers of a product are not obliged to disclose all pertinent patents. In addition, it is challenging to verify the legal status of all patent family members.

For medicines commercialized in the United States, some information can be obtained from the US Food and Drug Administration (FDA) *Orange Book*,⁸² which lists FDA-approved medicines and related product and method of use patent information. Process patents and patents claiming packaging, metabolites and intermediates are not covered by the *Orange Book*, and information on these patents is not submitted to the FDA.⁸³ Health Canada maintains a similar patent register containing an alphabetical listing of medicinal ingredients and their associated patents, patent expiry dates and other related information.⁸⁴ The Medicines Patent Pool has made legal status information for antiretroviral (ARV) medicine patent publicly available in a database (see Box 2.7).

(x) Filing trends under the Patent Cooperation Treaty system

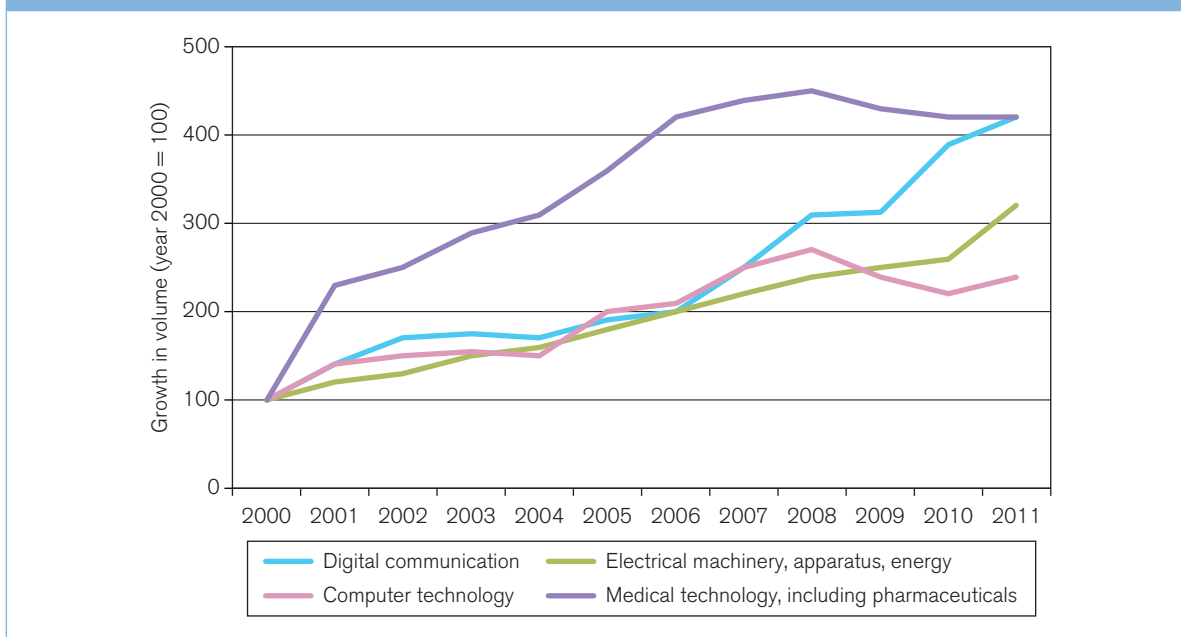
According to WIPO (2012), the greatest number of PCT applications filed between 1978 and 2011 related to the area of medical technology. However, this accounted for only a relatively small proportion of all applications (6.6 per cent in 2011). It should be noted that the term medical technologies, as used in WIPO (2012), is different from the term used throughout this study. This study also includes data relating to pharmaceuticals (4.7 per cent of all PCT filings in 2011). The PCT filing numbers for both medical technologies and pharmaceuticals accounted for 11.3 per cent of all filings in 2011 and, in this consolidated form, medical technologies and pharmaceuticals represent the field of technology with the highest number of PCT filings between 1978 and 2011 (see Figure 2.1).

In the area of medical technologies, the total number of PCT applications filed annually remained in a band between 4,496 and 10,481 each year from 2000 to 2010. In the area of pharmaceuticals, the total number of PCT applications filed annually remained in a band between 3,789 and 7,863 each year from 2000 to 2010. With respect to medical technologies (as understood in the context of this study, i.e. including pharmaceuticals), the total number of PCT applications filed annually remained in a band between 8,785 and 18,344 each year from 2000 to 2010 (see Figure 2.2). The total numbers

Box 2.7. The Medicines Patent Pool's Patent Status Database for Selected HIV Medicines

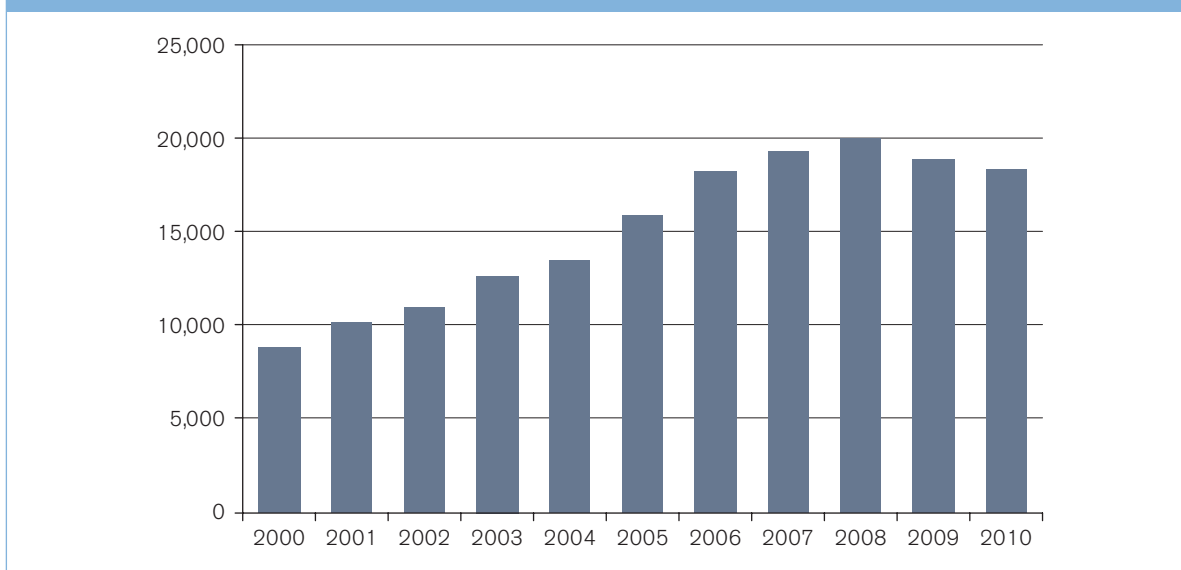
The Medicines Patent Pool has established a patent database containing information on the patent status of selected antiretrovirals (ARVs) in certain low- and middle-income countries (LMICs). The legal status data was obtained from, and cross-checked with, a variety of sources, including national and regional patent offices, which made this information available through WIPO. Although the information was obtained from primary sources, the database provides just a snapshot of a particular point in time, and it includes only some of the patents relating to each ARV. The information includes the expected expiry date of the patents, based on a 20-year term from the filing date of the patent application. However, it is possible that some patents may have expired or lapsed, or may have been withdrawn, rejected, revised, revoked or opposed, following the inclusion of information about these patents in the database. This shows that it is important to confirm the status of information with the competent patent authority should precise information be needed at a later point in time.⁸⁵

Figure 2.1. Growth of the top four technology fields, 2000-2011



Source: WIPO Statistics Database.

Figure 2.2. PCT applications in the field of medical technology, including pharmaceuticals, 2000-2010



Source: WIPO Statistics Database.

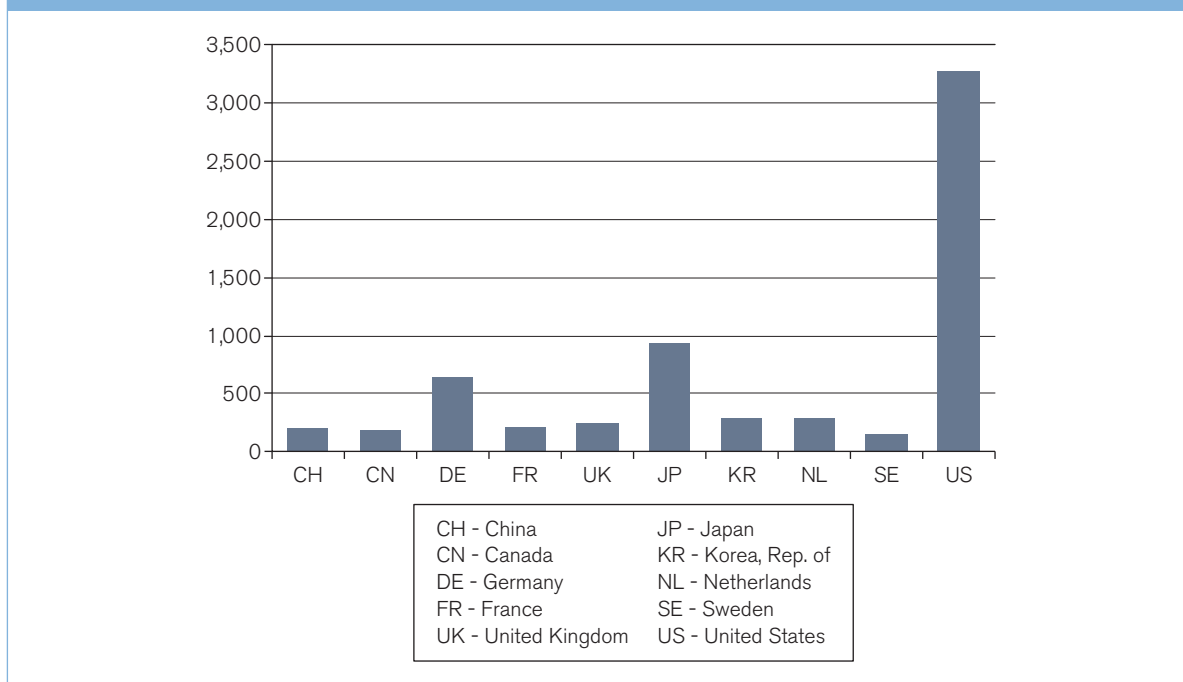
increased each year until 2008, and then declined in the two following years. Among the top ten countries of origin are the United States, Japan, the Republic of Korea and a number of Western European countries (see Figure 2.3).

(c) Clinical trials and protection of test data

As seen in Chapter II, Section A.6, in order to obtain marketing authorization for any new pharmaceutical product, submission of test data to regulatory agencies

is generally required in countries that undertake an independent evaluation of the quality, safety and efficacy of medicines. Test data are generated by the applicant company (not the public authorities) through pharmacological and toxicological tests and clinical trials. Test data protection impacts on what the regulatory agency can do with confidential data in the originator's application dossier. It is closely related to the regulation of medicines. At the same time, it is also part of the IP system, since it represents a form of protection against unfair

Figure 2.3. Main countries of origin of PCT applications in the field of medical technology, including pharmaceuticals, 2011



Source: WIPO Statistics Database.

competition. The underlying reason for the protection is that considerable effort, both in terms of time and money, is often required to produce the data, especially with increasingly stricter regulatory requirements. In producing the data, originator companies therefore have a strong interest in protecting their investment. Conversely, competing public interests may be trying to ensure early access to generic products. Test data protection is thus one of the more controversial topics in the debate about public health and IP.

(i) *International legal standards*

Article 10bis of the Paris Convention (which requires effective protection against unfair competition in general) and, in particular, the WTO TRIPS Agreement contain multilateral standards on this subject.

The TRIPS Agreement requires WTO members to prevent the unauthorized disclosure and unfair commercial use of confidential information submitted to a regulatory authority, subject to certain conditions. Test data must be protected against:

- **Disclosure:** this is a straightforward obligation not to disclose the data submitted for regulatory approval purposes. Regulatory agencies may, however, disclose the data when this is necessary to protect the public or where steps are taken to ensure that there is no unfair commercial use of the data concerned (see Chapter III, Box 3.6).

- **Unfair commercial use:** the TRIPS Agreement does not provide a definition of the term “unfair commercial use”, nor does it deal with the way in which such protection may be achieved. Therefore, opinions, as well as national practices, differ on what exactly is required. Some argue that the most effective way of ensuring such protection is to give a reasonable period of data exclusivity to the originator companies. Under a data exclusivity regime, the respective regulatory authorities would be prevented for a certain number of years from relying on the data submitted in the application for the originator product, in order to approve later generic versions of the product, possibly on the basis of bio-equivalence data showing that it is similar or essentially similar to the originator product. Others reject the view that TRIPS requires such exclusivity, arguing that other forms of protection against unfair commercial use are permissible. During the Uruguay Round negotiations, the option of making data exclusivity an explicit obligation under the TRIPS Agreement was discussed, but negotiators instead adopted the general wording of the current Article 39.3.

There is no WTO jurisprudence or authoritative WTO guidance on either of these issues (although the matter was raised, but not resolved, in consultations between the United States and Argentina under the WTO Dispute Settlement Mechanism; the mutually agreed solution merely noted that the Parties had expressed their points of view and agreed that differences in interpretation are to be solved under the DSU rules (see WTO documents

WT/DS171/3 and WT/DS196/4)). Nor had they been resolved in the TRIPS Council in the lead-up to the Doha Ministerial Conference in 2001, although some views on the interpretation of Article 39.3 of the TRIPS Agreement were put forward by members. What can be stated at this point, however, is that: (i) the flexibilities and pro-public health interpretation in the Doha Declaration cover the TRIPS Agreement as a whole and therefore apply to test data protection under Article 39.3; (ii) there is no explicit TRIPS requirement to provide data exclusivity, but some form of protection against unfair commercial use is required; and (iii) the fact that two forms of protection are to be provided under Article 39.3 of the TRIPS Agreement highlights that protection against unfair commercial use must involve more than merely not disclosing the data.

That being said, there are certain qualifying conditions that apply to the protection of test data:

- **The data is undisclosed:** Article 39.3 only requires the protection of undisclosed data, not previously published information. If the data has been disclosed, for example, in a scientific journal, patent document or elsewhere, no further protection needs to be granted.
- **The submission of test data is required by countries:** any country that does not require the submission of test data or other data to conduct its own regulatory review of a pharmaceutical product has no obligation under the TRIPS Agreement to provide any test data protection with respect to that product either. The obligation to protect data stems only from the existence of a regulatory requirement to submit those data as a condition of receiving marketing approval.
- **The products for which marketing approval is sought use new chemical entities:** the test data at issue in the TRIPS Agreement only concerns applications for marketing approval of products that utilize “new chemical entities”. This term is not further defined in the TRIPS Agreement and the WTO has not issued any determination of its scope.
- **The generation of the data involves considerable efforts:** the TRIPS Agreement does not specify the nature of such efforts, that is, whether they must be technical or economic. Neither does it prescribe that the applicant is required to prove that such efforts have been made.

LDC WTO members are, in any event, not obliged to protect test data with respect to pharmaceutical products due to an extended transition period, which currently runs until 1 January 2016.

(ii) *Distinction between protection of patents and of test data*

Patents and test data are two distinct categories of IP. The TRIPS Agreement deals with test data protection as a form of protection against unfair competition in the section

on protection of undisclosed information and not in the section on patents. While a patent protects the invention – for example a new molecule – irrespective of the effort and investment involved, test data protection covers a different subject matter, specifically the information submitted for regulatory approval (sometimes called the “regulatory dossier”). A patent could therefore be held by one party and the regulatory dossier held by another (e.g. a local licensee under the patent). Both forms of protection can run in parallel for the patented medicines that do make it to market. However, patent protection will typically have begun a number of years earlier. This is because patent applications are filed as soon as an invention is made, whereas clinical trials are undertaken only at a later stage in the product development cycle. By the time clinical trials begin, a patent may still be pending or may have been granted. Since test data protection and patent protection are distinct, protecting test data can deliver certain benefits to the company generating the data. Such benefits would apply, for example, where a product is either not under patent protection, where it has only a short remaining period of patent protection or where the validity of the patent is challenged during opposition procedures. In such situations, an exclusivity period may delay the early entry of generics into the market because producers of generics are obliged to wait until the exclusivity period expires.

(iii) *National implementation*

The disagreement on how to provide for test data protection under the TRIPS Agreement referred to above is also reflected in the way in which this obligation has been incorporated into national law. In line with their political priorities, countries have adopted different approaches to protection against unfair commercial use. In many cases, the approach chosen has also been guided by provisions which countries have subscribed to in free trade agreements (FTAs)⁸⁶ or, in a few cases, by legally binding commitments providing expressly for data exclusivity in WTO accession protocols (i.e. China and Ukraine). These countries have thus agreed to enter into more detailed obligations than are required under the TRIPS Agreement.

Most developed countries, and some developing countries, provide for a regime of data exclusivity. Other countries, such as India and many other developing countries, prohibit their respective regulatory authorities from allowing third parties to access and use information submitted to them, in accordance with laws on confidentiality and unfair competition. However, they do not prohibit regulatory authorities from relying on test data submitted in an application for a previously approved originator product in order to review and approve an application for second and subsequent market entrants. Furthermore, they do not grant a period of exclusivity.

Among the other options discussed for test data protection are compensation or cost-sharing models, under which reliance on the originator data would be

permitted, provided that the generic supplier participates in the costs of generating the data. The United States, for example, provides both data exclusivity and a mandatory data compensation system of this kind in relation to data submitted in applications for regulatory approval of pesticides (but not pharmaceuticals). The European Free Trade Association (EFTA)–Korea FTA (Article 3, Annex XIII) also admits a compensation scheme as an alternative to data exclusivity.

Countries which grant exclusivity rights generally provide for a fixed period of between five and ten years, with the possibility of an extension in some cases. The fixed period usually runs from the date of marketing approval of the originator product in the same country where the test data protection is sought. Some WTO members, such as the European Union and the United States, allow an additional period of exclusivity for new indications and formulations.

Exceptions and limitations to data exclusivity are applied in some countries. US law shortens the period to four years where the applicant for a second product certifies that the patent is invalid or that the second product does not infringe the patent (subject to a possible stay during infringement proceedings). Canada does not provide data exclusivity if the originator product is not being marketed in its territory. Nor do Chile or Colombia if the originator product is not marketed in their respective territories within 12 months of the grant of local marketing approval. Chile does not provide data exclusivity if the application for local marketing approval is filed more than 12 months after registration or marketing approval was first granted in a foreign country.

Other exceptions may cover the protection of the public interest, such as in situations of health emergencies or for exports under compulsory licence under the Paragraph 6 System.⁸⁷ If it takes the form of data exclusivity, test data protection has the potential to impede the implementation of compulsory licensing of patents, including the situation in which a country requires regulatory review of products destined for export under the Paragraph 6 System.⁸⁸ Canada and the European Union decided to waive data protection for products produced under compulsory licence solely for export under the Paragraph 6 System. Chile does not provide data exclusivity if the product is the subject of any kind of compulsory licence.

(iv) *Innovation and access dimensions of test data protection*

The way in which test data are protected is particularly relevant in the context of enabling new product innovations and also in the context of facilitating access to existing medical technologies. The form of protection at the country level will therefore influence the development or introduction of new products and will also determine how early generic competition with an originator product can begin.

New medicines must undergo several phases of clinical trials in order to demonstrate their safety and efficacy for the purposes of regulatory approval. These regulatory requirements are an integral part of the development process of new medical products, setting medical innovation apart from other technological areas. Currently, the generation of quality, safety and efficacy data through clinical trials, is still – despite various proposals and debate on this subject – largely funded by companies seeking to introduce a new medical technology to the market.

Even though clinical trials serve legitimate health objectives, the costs involved create significant barriers to market entry for new pharmaceuticals. As product patents on chemical compounds are usually filed relatively early in the R&D process, the length of time involved in carrying out clinical trials, coupled with the regulatory approval process, reduce *de facto* the period of market exclusivity enjoyed by a patented product, thus reducing the scope to recover the R&D costs of that product, as well as the R&D costs of other unsuccessful products.

The research-based pharmaceutical industry therefore argues that test data protection, especially in the form of data exclusivity, provides an important incentive for that industry to invest in the development of new products and related clinical trials. In addition, innovator companies evidently value the relative certainty of data exclusivity when compared with the increased uncertainty that applies in relation to the validity or scope of a patent which, in turn, increases uncertainty with respect to the ability to temporarily exclude competitors. One such example would be the development of a paediatric version of an existing medicine, which in certain jurisdictions would be denied a patent, due to lack of novelty. In such a situation, the protection of the clinical test data would be the only incentive to invest in the development of this formulation. A similar situation could arise in relation to clinical trials to test the safety and efficacy of known traditional medicines that are not patentable, due to lack of novelty.

On the other hand, public health advocates highlight that with regard to developing countries the additional incentive for carrying out research and clinical trials is considered marginal whereas the negative impact on prices, and thus on access to medical technologies, is considerable. Similarly, the report released by the Consultative Expert Working Group on Research and Development: Financing and Coordination (CEWG) in April 2012 found that “there was no evidence that data exclusivity materially contributes to innovation related to Type II and Type III diseases and the specific R&D needs of developing countries in relation to Type I diseases, and therefore we concluded that its removal where it existed would not adversely affect innovation incentives for these diseases and also would contribute to reduced prices of affected medicines” (WHO, 2012a).

One of the main issues with regard to access to medicines is how to deal with applications for market authorization for identical generic products. Under a data exclusivity regime, the market entry of generic medicines may be delayed, as later applicants have to wait for the expiration of the exclusivity period. While the generic producer could, in principle, redo the clinical trials or agree with the originator company on the use of the original data, this does not seem to happen in practice. Among the reasons for this are the cost and time implications associated with the requirement to produce such data. On the other hand, applications for later market entrants for the same medicine can avoid reproducing this original data if they are allowed to rely on the data provided in relation to the originator application to show that their products have an equivalent effect (bioequivalence). This allows generic competitor products to be placed on the market sooner, either in situations where there is no patent protection or after expiry of the patent, and, by enabling a competing medicine to enter the market, creates an alternative for consumers as well as generally reduces prices. From a public health perspective, this is seen as positive because it avoids the unethical duplication of clinical trials and enables the swift entry of generics into the market. However, from the perspective of the first applicant, this may be considered unfair because the second and subsequent market entrants will not have been obliged to invest in costly clinical trials (including failed trials) and thus could compete directly with a major cost advantage.

The issue of test data protection is a good example of the essential dilemma for IP protection. In order to provide an incentive for the development of new products, market exclusivity is created deliberately in some countries to facilitate a certain return on investment, although this may delay generic entry.

(v) *Biosimilars: protection of pharmacological, toxicological and clinical test data*

One emerging issue, which has implications both for innovation systems and access to the new generation of “biological” medicines, is the potential protection of the pharmacological, toxicological and clinical test data submitted to a regulatory agency to support the approval of original reference products. Established models of protection for small-molecule pharmaceuticals are not necessarily suitable for the more complex, and less easily reproduced, biological medicines (see Box 2.3 on the role of biosimilars). In the European Union and Switzerland, among other countries, data exclusivity associated with the protection of pharmacological, toxicological and clinical test data applies to both small-molecule medicines and biotherapeutics. While Directive 2004/27/EC,⁸⁹ provides for the submission of supplementary data for biological medicinal products, which are different from generic medicinal products, it does not establish specific rules for the data exclusivity of such products. The rules for authorization of generic medicines therefore apply.

In contrast, the US Congress adopted specific legislation with the Biologics Price Competition and Innovation Act of 2009. The FDA may not approve an application for a biosimilar “until the date that is 12 years after the date on which the reference product was first licensed”. This duration of exclusivity for biologics differs from that of small-molecule or orphan drugs, which under US law lasts for only five or seven years, respectively.

(d) Trademarks

(i) *The trademark system*

Trademarks allow manufacturers and traders to distinguish their goods from those of competitors. They help consumers make informed choices and they aim to prevent consumer deception. The registration of trademarks is subject to certain requirements that are reasonably standardized throughout the world and appear in practically all trademark laws. Trademarks must be distinctive, or at least capable of becoming distinctive, of the owner’s goods or services, and they must not be misleading. Trademarks must not infringe rights acquired by third parties and they must not consist exclusively of signs or indications which may serve, in trade, to designate the kind, quality, quantity, intended purpose, value, place of origin, of the goods, or the time of production, or have become customary in the current language or established practices. Generic terms that use ordinary words to define the category or type of good are not distinctive and should remain available for all competitors to use free of trademark rights.

There is a crucial distinction between the generic name of a product – for example ampicillin – which must be available to identify any product, and the proprietary trademarks used by individual companies to distinguish the product they are responsible for manufacturing and distributing. These are sometimes termed “brand names”. The WHO maintains a system of such generic names, called international nonproprietary names (INNs), which are universally recognized as unique names that identify particular pharmaceutical substances or active pharmaceutical ingredients. Trademarks are linked to a product and are used by both research-based and generic companies to create trust and build a relationship between the company, the prescribing practitioner and the patient, potentially allowing the trademark owners to charge higher prices. The distinction, commonly used, between the “brand name” pharmaceutical manufacturer and the generic pharmaceutical manufacturer can be misleading because both originator and generic companies use trademarks to market and distinguish their products.

Trademarks are protected under the laws of each country or region, and not globally. All countries that are party to the Paris Convention have a trademark registry. Trademark applications must be filed separately in each country or region where registration is sought, or with WIPO, using

Box 2.8. The Madrid System for the International Registration of Marks

The Madrid System is governed by the Madrid Agreement Concerning the International Registration of Marks (concluded in 1891) and the Protocol Relating to the Madrid Agreement Concerning the International Registration of Marks (concluded in 1989). The Madrid System offers a simple, flexible and user-friendly option for trademark holders to obtain and maintain trademark protection in export markets. By filing one international application, in one language (English, French or Spanish), with payment of fees in one currency (Swiss francs), a trademark holder may obtain protection in more than 80 countries, including the European Union, provided that the holder has a “basic mark”, meaning a trademark application or registration with “the Office of origin”. The International Bureau of WIPO carries out a formality examination. Any matter of substance, such as whether the mark qualifies for protection or whether it is in conflict with an earlier mark, is left to each designated contracting party to determine, in accordance with their national trademark legislation. If the trademark office of a designated contracting party does not refuse protection within a specified period, the protection of the mark is the same as if it had been registered by the office concerned.

The Madrid System also greatly simplifies the management of the mark, as it regards one international registration with one renewal date to follow up, and it may afford trademark protection in many designated contracting parties. It is subsequently possible to extend the trademark protection to additional contracting parties. It is also possible to renew the international registration and record changes to the international registration. Such changes might include a change in name or address or a change in ownership. These can be made using one centralized procedure.

The International Bureau records the mark in the International Register, publishes the international registration in the *WIPO Gazette of International Marks* and notifies each designated contracting party accordingly.

the Madrid System for the International Registration of Marks (see Box 2.8).⁹⁰ It is not unusual for a trademark to be protected in some countries but not in others.

The owner of a trademark has an exclusive right to prevent using signs that are identical or similar to their trademark on certain types of related goods or services where such use would result in a likelihood of confusion. The trademark owner, and typically any licensees, may enforce their rights against infringement. Trademarks are not restricted to a maximum term of protection but can be renewed indefinitely, provided they remain in use and maintain their distinctive character. Rights to a trademark can be lost through cancellation, or removed from the registry, if the trademark is not renewed or the due renewal fees not paid. A mark can lose its distinctive character and can become a generic term. This may happen if either the trademark owner or the public, tolerated by the trademark owner, uses a trademark as, or instead of, a product designation or a term in common usage. International minimum standards for protection of trademarks are set out in the Paris Convention and the TRIPS Agreement.

(ii) *Trademarks and international nonproprietary names*

In contrast with trademarks, which are proprietary private rights, INNs are generic names for active pharmaceutical ingredients. Each INN is a unique name that is globally recognized in almost all WHO member states and is not subject to exclusive rights. The WHO has a constitutional mandate to “develop, establish and promote international standards with respect to biological, pharmaceutical and similar products”. The WHO Secretariat and the WHO

INN Expert Group collaborate closely with national nomenclature committees, drug regulatory authorities, pharmacopoeias and the pharmaceutical industry to select a single name of worldwide acceptability for each active substance that is to be marketed as a pharmaceutical.

The existence of an international nomenclature for pharmaceutical substances, in the form of an INN, is important for the clear identification, safe prescription and dispensing of medicines to patients, and for communication and exchange of information among health professionals and scientists worldwide. As unique names, INNs have to be distinctive in sound and spelling, and should not be liable to confusion with other names in common use. In order to make INNs universally available, they are formally placed by the WHO in the public domain, hence their designation as “nonproprietary”. An INN can be used by any producer or distributor for their product provided that the INN is used accurately. For example, “ibuprofen” is an INN and can be used by any producer or distributor for the designation of this product.

Another important feature of the INN system is that the names of chemically and pharmacologically related substances demonstrate their relationship by using a common “stem” as a part of the INN. The use of common stems ensures that a medical practitioner, pharmacist or anyone dealing with pharmaceutical products can recognize that the substance belongs to a group of substances having similar pharmacological activity. For example, all the monoclonal antibodies are given the suffix/stem “-mab”, while all adrenoceptor antagonists use the suffix/stem “-olol”.

Ensuring that trademarks are clearly distinguished from INNs is important for the accurate identification of products, and thus for the safety of patients. It is also important to keep INNs in the public domain and to avoid granting private property rights for them. Trademarks must not be derived from INNs and, in particular, they must not include their common stems. The selection of additional names within a series will be seriously hindered by the use of a common stem in a brand name. For the same reasons, INNs should not contain existing trademarks. The INN Expert Group convened by the WHO thus generally rejects a proposed INN that contains a known trademark and there is a procedure for dealing with objections by interested parties. Such objections may be based on a similarity between a proposed INN name and a trademark. On the other hand, trademarks that include an established INN stem infringe the INN system. The WHO has requested member states to prevent the granting of trademarks or other exclusive proprietary rights to any INN and INN stem. It circulates every newly published list of proposed or recommended INNs to all WHO member states. Lists of proposed and recommended INNs are also available on the WHO website.⁹¹

Following a decision of the WIPO Standing Committee on the Law of Trademarks, Industrial Designs and Geographical Indications (SCT), and in collaboration with the INN Programme, WIPO officially notifies the national and regional trademark offices of its member states about the publication of each new list of proposed and recommended INNs. A WIPO survey of trademark offices showed that 72 per cent of surveyed offices examine trademark applications for possible conflict with INNs.⁹²

Distinguishing between the INN and the proprietary trademark is important in order to assist the process of selecting specific medicines during a procurement process. This is because procuring a product under its INN name opens the process to all manufacturers of the same product designated by the INN. Many countries require distinct labelling with the INN, printed separately from either generic or originator company names, brands or trademarks. While the TRIPS Agreement states that the use of a trademark in the course of trade shall not be encumbered by special requirements, it allows justified limitations (Article 20 of the TRIPS Agreement). Inaccurate or misleading labelling can also be considered a form of unfair competition. It is covered by Article 10*bis* of the Paris Convention, as well as by consumer protection laws and similar provisions in many countries, and is designed to safeguard against deceptive or misleading labelling.

(iii) *Regulatory approval of proprietary names*

The names under which new medicines are to be sold in the market (i.e. trademark/brand names) are also reviewed by regulatory authorities and require approval as part of the marketing authorization of a new medicine. Medicine name similarity and medication errors in the

1990s led the US Food and Drug Administration (FDA) and the European Medicines Agency (EMA) to introduce assessments of proprietary nomenclature in the interest of public health and safety.⁹³ Examination of these names in the context of regulatory approval has become more formalized over the past decade, with the establishment of dedicated bodies in the FDA and the EMA,⁹⁴ which reject 30 per cent to 40 per cent of brand names submitted for approval.⁹⁵

The criteria for proprietary name evaluation applied by the pharmaceutical regulatory authorities are intended to counter confusion and potential medication errors in the specific context of pharmaceutical distribution and prescription practices. The evaluation thus overlaps to some extent with criteria that are also examined in the context of a trademark application. It aims to exclude names that contain or imply claims regarding drug efficacy and safety which are false, misleading or unsupported by data. In addition, in order to take account of the risks presented by the specific context of pharmaceutical prescription, the regulatory evaluation eliminates names that are verbally or graphologically similar to other drug names or to abbreviations typically used in handwritten prescriptions, such as dosage schedules and forms, or routes of administration.

The requirement for approval of the proprietary name of a new medicine as part of the overall pharmaceutical regulatory authorization is an important factor in ensuring the safety of a new medicine in the specific context of pharmaceutical distribution and prescription. As the marketing of the medicine is approved by the authorities under a specific name (i.e. it cannot be marketed under another name), the challenge for the pharmaceutical companies is to develop a medicine name that will not only meet the approval of the regulatory authorities but can also be protected as a trademark in the main markets where the medicine will be sold. In order to meet this double objective, and to ensure a successful outcome, companies usually develop a number of possible names for the new medicine and register all of them as trademarks in their main markets, before submitting them as alternatives to the regulatory authorities. This practice partly explains the proliferation of trademark applications in the pharmaceuticals area, which accounted for 4.7 per cent of all trademark applications in 2010 (WIPO, 2011a). Such volumes of applications can lead to a situation where there are many unused trademark registrations in existence.

(e) Copyright and pharmaceutical products

Copyright relates to every original creation in the literary or artistic domains, irrespective of the type of work, (as provided by the Berne Convention for the Protection of Literary and Artistic Works, and incorporated into the TRIPS Agreement), but it does not extend to ideas, procedures, methods of operation or mathematical concepts as such.

For pharmaceutical products, a key issue in relation to copyright is whether protection covers the package inserts or information leaflets that accompany pharmaceutical products. Generic producers are free to use the information provided in an insert, since copyright does not extend to the information as such, just the way it is expressed. However, given that copyright generally extends to making copies of original works on a commercial scale, courts have sometimes found that generic pharmaceutical producers cannot reproduce for their own products direct copies of the original expressions contained in package inserts of the first producer of the product. This was the finding in 2002 in South Africa concerning a package insert for the antibacterial medicine amoxicillin/clavulanate potassium.⁹⁶ A similar finding initially was made in Australia in 2011 in relation to the rheumatoid arthritis medicine leflunomide. The Federal Court found that copyright subsisted in product information documents. However, later in 2011, the Australian parliament approved an amendment to Australia's Copyright Act establishing that use of already approved product information in other pharmaceutical products text, in any manner including a direct reproduction, is not an infringement of copyright. A subsequent court decision confirmed that generic pharmaceutical companies are now able to reproduce product information that has been approved by the Therapeutic Goods Administration, without infringing copyright in a range of prescribed circumstances.⁹⁷

(f) Enforcement

The value of the IP rules detailed above depends on the availability of an effective system of enforcement. As IPRs are private rights, their enforcement is generally the responsibility of the right holders themselves. Infringements are thus normally pursued by the right holders in civil actions. However, public interest is at stake when IP infringements takes place at a criminal level, for example, when a trader, without permission, knowingly and on a commercial scale manufactures, distributes or sells goods marked with another company's trademark. That said, the enforcement of IPRs is clearly distinct from the regulation of medicines for safety, quality and efficacy purposes, including any remedies against substandard and spurious/falsely-labelled/falsified/counterfeit (SFFC) products.

(i) *Link between intellectual property right enforcement and public health*

The meaning of "counterfeit" differs in the public health context and also in the IP context, just as the motivation to combat SFFC products also differs in the public health context and the IP context.⁹⁸ From the perspective of public health, which is driven by regulatory aspects, the term "counterfeit" is used in the broadest sense and should not be confused with trademark infringement. For this reason, it has been replaced in health policy discussions by the term SFFC.⁹⁹ The fight against substandard and SFFC products is exclusively motivated by the threat to public health, and

related concerns about consumer protection. From an IP perspective, using a trademark commercially without the authorization of its owner is the key condition to consider a product as counterfeit. In this context, the objective is to preserve the interest of the trademark owner in enforcing their rights and to protect the public interest by fighting infringements where they take place at a criminal level.

While the motivation may be different, the methods used to prohibit production, trade and distribution of all kinds of trademark infringing products and SFFC products have some similarities, with customs controls and criminal law figuring among the most frequently used means. For example, pharmaceuticals are regularly reported to figure among the top commodities suspended by customs authorities for IPR infringement.¹⁰⁰ This is because in international trade, a trademark plays an important role as a trade identifier and is an indication of trade source, which can help to identify fake products. Counterfeiters use trademarks without authorization to pretend, regularly but not always, that the product is a genuine product, thus falsely representing its identity and source. Therefore, some argue that IP enforcement measures to combat trademark counterfeiting can have positive side-effects, potentially supporting efforts to keep dangerous products out of the market. Others argue that public health considerations should be kept strictly separate from IP enforcement so as to avoid blurring the objectives between promoting the enforcement of private rights and serving public health objectives, especially against the background of detention of generic products in transit in Europe.¹⁰¹

(ii) *Enforcement under the TRIPS Agreement*

The TRIPS Agreement sets out the only comprehensive multilateral framework within which to enforce IPRs. It contains a set of minimum standards that safeguard the rights of IP owners while avoiding barriers to legitimate trade. These standards include civil court procedures and remedies that should be made available, such as injunctions, damages and orders for the disposal of goods that are infringing trademarks. These remedies must be available for all the IPRs covered by the TRIPS Agreement, including patents, test data protection, trademarks and copyright. Administrative – procedures, such as actions before administrative authorities, are optional and have to conform to the principles applicable to civil procedures. A wider range of procedures, including customs measures and criminal procedures, must be available for counterfeit trademark goods, as defined in the TRIPS Agreement, including medical products, and for pirated copyright goods. The TRIPS Agreement also includes certain general obligations or performance standards which provide that WTO members must ensure that these specific enforcement procedures permit effective action, including expeditious remedies to prevent and deter infringement. The application of these procedures must avoid the creation of barriers to legitimate trade and must provide for safeguards against their abuse. The TRIPS Agreement clarified that WTO

members are not under any obligation with respect to the distribution of resources between the enforcement of IPRs and law enforcement in general.¹⁰²

(g) Flexibilities under the TRIPS Agreement and the Doha Declaration

Determining a nation's optimal choices from within the available range of options is a central consideration in the design of a national IP regime. However, many of these policy options, often referred to as "TRIPS flexibilities", have long formed part of the mechanisms used in patent systems to maintain a balance of public and private interests – well before the TRIPS Agreement was negotiated, and before the Doha Declaration was framed.

(i) *Flexibilities in the IP system*

The adoption of the TRIPS Agreement standards resulted in creating diverse options for WTO members to implement their TRIPS obligations, while taking into account different considerations such as the country's stage of development and specific national interests (e.g. public health). However, despite repeated references to "flexibilities" in the policy debate, neither the TRIPS Agreement nor any of the later instruments have formally defined the exact meaning of this term. The TRIPS Agreement makes only limited use of the term. In fact, although flexibilities are available on a much broader scale, including for developing countries and developed countries, explicit reference to "flexibility" is exclusively made in relation to the special requirements of LDC members to create a sound and viable technological base, thus explaining the motivation for the additional transition period accorded to LDCs (see the Preamble and Article 66.1 of the TRIPS Agreement). The expression "flexibilities" only became part of the wider IP community's glossary in the lead-up to the Doha Declaration and especially following the conclusion of these negotiations.¹⁰³

In articulating the role of "flexibilities", the Doha Declaration clarified the importance of specific national choices in the implementation of the TRIPS Agreement. It referred to flexibilities in a much more prominent way. This can be explained by the central importance that the debate about policy options to promote public health assumed from the time preparatory work for the Doha negotiations got under way, culminating in the adoption of the Doha Declaration in 2001. The TRIPS Agreement highlights the existence of flexibilities and their importance for the pharmaceutical sector, and the Doha Declaration confirms "the right of WTO Members to use, to the full, the provisions in the TRIPS Agreement, which provide flexibility" to protect public health. The Declaration lists a number of such flexibilities relating to compulsory licensing and exhaustion. The subsequent decision of 30 August 2003 on the implementation of Paragraph 6 of the Doha Declaration (2003 Decision)

once more confirms "the rights, obligations and flexibilities that Members have under the provisions of the TRIPS Agreement".¹⁰⁴

Based on the Agreement between the World Intellectual Property Organization and the World Trade Organization of 22 December 1995,¹⁰⁵ WIPO provides legal and technical assistance relating to the TRIPS Agreement. Government offices in charge of drafting laws frequently request advice from WIPO regarding how to use the TRIPS flexibilities in their countries. Advice is provided after careful consideration of the flexibilities, consistency in relation to the TRIPS Agreement and their legal, technical and economic implications. However, the ultimate decision regarding the choice of legislative options lies exclusively with each individual member state. Four clusters of flexibilities have been identified in WIPO's work:

- the method of implementing TRIPS obligations
- substantive standards of protection
- mechanisms of enforcement
- areas not covered by the TRIPS Agreement.

The use of flexibilities is also addressed in a number of recommendations contained in the WIPO Development Agenda (see Box 2.9). Following the request of the Committee on Development and Intellectual Property (CDIP), WIPO prepared a preliminary study on patent-related flexibilities in the multilateral legal framework and their legislative implementation at the national and regional level.¹⁰⁶ The study presents a non-exhaustive number of flexibilities in the patent area, accompanied by a conceptual development for each, as well as annexes and tables reflecting corresponding legal provisions and practices in a substantial number of countries.

The report showed a diverse approach to the implementation of TRIPS flexibilities into national laws, including compulsory licensing, research exemptions, exhaustion of rights, and regulatory review exemption – also called the "Bolar" exemption.¹⁰⁷ A second paper extends this research to other flexibilities, namely: transition periods, the patentability of substances existing in nature, disclosure-related flexibilities, aspects related to substantive examination and the ex-officio control by IP offices of anti-competitive clauses in patent licensing agreements (see Box 2.10).¹⁰⁸

(ii) *Background to the Doha Declaration*

The negotiators of the TRIPS Agreement aimed to ensure that countries would make patents available for pharmaceutical products while at the same time retaining the right to qualify, limit or even exclude patents, including for public health purposes. However, the extent to which the Agreement was supportive of public health became highly controversial, particularly around the time when most of the substantive obligations of the Agreement for developing countries came into force

Box 2.9. Definition of flexibilities according to WIPO

According to the WIPO CDIP report,¹⁰⁹ the term “flexibilities” means that there are different options through which TRIPS obligations can be transposed into national law, so that national interests are accommodated and TRIPS provisions and principles are also complied with. This definition would effectively delimit the scope of the concept through the following elements:

- It highlights the idea of using various options as a means of implementation.
- It refers to the legislative process of implementation, reflecting the view that the first step needed in order to take advantage of a given flexibility consists of incorporating that flexibility into national law.
- It refers to the reason for flexibilities, which is to accommodate national interest.
- It reflects that a given flexibility needs to be compatible with the provisions and principles of the TRIPS Agreement.

These flexibilities can be categorized in different ways, including by grouping them according to the lifetime of the respective IPR. Flexibilities can thus be exercised regarding the:

- process of acquisition of the right
- scope of the right
- enforcing and using the right.

Box 2.10. TRIPS flexibilities highlighted in the GSPA-PHI

The WHO GSPA-PHI refers explicitly to the flexibilities reaffirmed by the Doha Declaration. It urges member states to consider implementing TRIPS flexibilities, including those recognized in the Doha Declaration, by incorporating them into their national laws (Element 5.2a). Regarding more extensive IP protection than that required under the TRIPS Agreement, member states are urged to take into account the impact on public health when considering the adoption or implementation of such obligations (Element 5.2b). Member states should also take into account flexibilities when negotiating other (bilateral or regional) trade agreements (Element 5.2c). In addition, the GSPA-PHI highlights a number of flexibilities and public policy options available to member states, which are designed to facilitate research and access to medical technologies:

- Research exception (Element 2.4e).¹¹⁰
- Voluntary patent pools of upstream and downstream technologies (Element 4.3a).¹¹¹
- For countries with manufacturing capacities, consider taking measures to implement the WTO Paragraph 6 System (Element 5.2d).¹¹²
- Develop effective and sustainable mechanisms in LDCs in order to improve access to existing needs, acknowledging the transitional period until 2016 (Element 6.1b).¹¹³
- Regulatory exception or Bolar-type exemption (Element 6.3a).¹¹⁴

in 2000. In a landmark legal action, a pharmaceutical industry association and 39 of its affiliate companies filed complaints at the Pretoria High Court, alleging, among other things, that South Africa's law on medicines allowed for parallel importation of (HIV/AIDS) medicines and was inconsistent with the TRIPS Agreement. The lawsuit triggered an active campaign led by non-governmental organizations (NGOs) and AIDS activists. During the court procedure, it was revealed that the South African law was based on a WIPO model law and in the end, the companies withdrew their complaints unconditionally in 2001. By that time, many governments and others were convinced that the relationship between the TRIPS Agreement and public health needed to be clarified.

In April 2001, the WHO and WTO Secretariats convened a workshop on differential pricing and financing of essential drugs in Høsbjør, Norway. Following the publication of the

report on that workshop,¹¹⁵ the African Group proposed that the WTO convene a special session of the Council for TRIPS to initiate discussions on the interpretation and application of the relevant provisions of the TRIPS Agreement, with a view to clarifying the flexibilities to which members are entitled and, in particular, to establish the relationship between IPRs and access to medicines. The proposal to hold the special session was supported by all members.¹¹⁶ This was followed in June 2001 by a detailed written proposal prepared by a group of developing countries calling for the WTO to take action to ensure that the TRIPS Agreement did not in any way undermine the legitimate right of WTO members to formulate their own public health policies and implement them by adopting measures to protect public health. At the Fourth WTO Ministerial Conference in Doha, Qatar on 14 November 2001, ministers adopted by consensus the Doha Declaration, addressing the concerns that had been expressed.

(iii) Content of the Doha Declaration

In articulating the general role of the TRIPS Agreement in promoting access to medicines, and in clarifying specific flexibilities to that end, the Doha Declaration has provided a clearer context for specific operational choices for the use of policy options under the TRIPS Agreement.

The Doha Declaration recognizes the gravity of the public health problems afflicting many developing countries and LDCs, and, in particular, the public health problems resulting from HIV/AIDS, TB, malaria and other epidemics. This defining statement was followed by a number of important statements signalling to all members that they are free to use the provisions of the TRIPS Agreement in a manner that is supportive of public health. Paragraph 4 confirmed that “the TRIPS Agreement does not and should not prevent Members from taking measures to protect public health”, that it “can and should be interpreted and implemented in a manner supportive of WTO Members’ right to protect public health and, in particular, to promote access to medicines for all”, and, in addition, that WTO members have the right “to use, to the full, the provisions in the TRIPS Agreement, which provide flexibility for this purpose”.

Paragraph 5 of the Doha Declaration specifically confirms four aspects in which the provisions in the TRIPS Agreement provide flexibility for this purpose:

- The first clarification concerns the way in which the TRIPS Agreement is interpreted. Each provision of the TRIPS Agreement shall be read in the light of the object and purpose of the Agreement as expressed, in particular, in its “objectives” and “principles”. These terms are not otherwise defined in the Doha Declaration, but there is a parallel with the respective titles of Articles 7 and 8 of the TRIPS Agreement – although objectives and principles can also be found elsewhere in the Agreement.
- The second and third clarifications concern compulsory licensing. Each WTO member has “the right to grant compulsory licences and the freedom to determine the grounds upon which such licences are granted”. These clarifications dispelled a misconception that compulsory licences were only available in national emergencies. Each WTO member also has the right to determine what constitutes a national emergency or other circumstance of extreme urgency. These clarifications have practical relevance, because in such situations countries are exempted from first attempting to negotiate a voluntary licence with the patent holder. In terms of examples of what these types of emergency might include, the Doha Declaration cites “public health crises, including those relating to HIV/AIDS, tuberculosis, malaria and other epidemics”.

- Finally, the Doha Declaration also confirms the freedom of each WTO member “to establish its own regime for such exhaustion without challenge”, subject to the rules against discrimination according to nationality. This allows a WTO member to choose between national, regional or international exhaustion.¹¹⁷ Exhaustion governs the extent to which an IPR holder can prevent the resale and importation of genuine goods placed on the market with its consent in the same or in another country. Countries are thus free to determine whether or not they want to allow parallel importation of patented goods, including medical products.

Paragraph 6 of the Doha Declaration prompted the commencement of work which subsequently culminated in the adoption of an additional flexibility designed to help countries with insufficient or no manufacturing capacities in the pharmaceutical sector to make effective use of compulsory licensing.¹¹⁸

Paragraph 7 of the Doha Declaration reaffirmed the commitment of developed country WTO members to provide incentives to their enterprises and institutions in order to promote and encourage technology transfer to LDC members, as set out under Article 66.2 of the TRIPS Agreement, thus confirming that technology transfer to LDCs is also a public health issue. In addition, paragraph 7 contained an instruction to the TRIPS Council to extend the transition period for LDCs, with respect to their obligations regarding patents and test data protection for pharmaceutical products (including enforcement procedures and remedies), until 1 January 2016.

(iv) Implementation of the Doha Declaration

Unlike TRIPS itself, the Doha Declaration does not oblige any specific legislative enactment. Even so, some countries have referred to its statements in a legal measure. The Doha Declaration has also been referenced in the work of other international organizations, notably the WHO Global Strategy and Plan of Action on Public Health, Innovation and Intellectual Property (GSPA-PHI), in many other WHO resolutions, the WIPO Development Agenda, and also in UN General Assembly resolutions 65/1 and 65/277¹¹⁹ addressing the MDGs and HIV/AIDS, respectively.

(v) Least-developed country transition period

The TRIPS Agreement provides for a number of transition periods so that countries can engage in a phased implementation of their TRIPS obligations. Some of these transition periods specifically target the patenting of pharmaceutical products. While these transition periods have now expired for developed- and developing-country WTO members, least-developed countries (LDCs), based on the Doha Declaration and subsequent TRIPS Council

Decision benefit from an extended transition period, until 1 January 2016, with regard to pharmaceutical patents and test data protection for pharmaceutical products (including enforcement procedures and remedies).¹²⁰ The WTO General Council also approved a waiver for LDCs from the obligation under Article 70.9 of the TRIPS Agreement and this also extended the transition period until 1 January 2016.¹²¹ As a result, LDCs are not obliged to grant exclusive marketing rights for pharmaceutical products while patent applications are pending – even for products that otherwise fall within the very specific circumstances set out in Article 70.9. These decisions are separate from the general extension of the LDC transition period, with respect to most of their other TRIPS obligations, until 1 July 2013.¹²² Further extensions of the LDC transition periods, are possible upon duly motivated request by LDC members. In this regard, ministers attending the Eighth WTO Ministerial Conference, in December 2011, invited the TRIPS Council “to give full consideration to a duly motivated request from LDC Members for an extension of their transition period”.¹²³ In November 2012, the LDC Group submitted a request for a further extension of the transition period. According to the proposed draft decision, LDCs would be exempted from applying the TRIPS Agreement for as long as they retain LDC status.¹²⁴ No decision has been taken in the WTO as of the time of writing.

At the national level, therefore, LDCs may, for the moment, maintain their existing legal standards of protection and enforcement without having to comply with the patent and test data protection obligations specified in the TRIPS Agreement, with respect to pharmaceutical products. However, if LDCs wished to lower their standards of patent protection for pharmaceutical products, which would be permitted under the above extension decision, they normally would still need to take action to incorporate these changes into their national laws. This is what happened in Rwanda in 2009, when a new law on the protection of IP was adopted. It excludes from patentability “pharmaceutical products, for the purposes of international conventions to which Rwanda is party”.¹²⁵ Under Rwanda’s previous patent legislation, pharmaceutical products were patentable subject matter. Alternatively, LDCs may leave their laws unchanged and simply declare that until the end of the transition period, they will not enforce legal provisions relating to test data protection or patents in the area of pharmaceuticals. For any of these measures, the LDCs concerned would, in any event, also need to check the conformity of the intended action within their own legal system and with the legal obligations that result from their membership of regional organizations or from bilateral trade agreements or other treaties to which they are a party.

The transition period potentially offers opportunities for these countries to attract investment for the local production of pharmaceutical products.¹²⁶ While some LDCs exclude pharmaceutical products from patent protection during

the transition period, others, such as LDCs which are members of the African Intellectual Property Organization, have foregone this option because the Bangui Agreement provides for the granting of pharmaceutical patents.¹²⁷

(h) Terms of accession to the WTO

Terms of accession to the WTO are another potential source of IP commitments in the WTO system. New WTO members have to negotiate their accession to the WTO under Article XII of the Agreement establishing the World Trade Organization.¹²⁸ The terms of accession are thus a matter of negotiation. These negotiations take place between the acceding member and interested existing members who choose to participate in the Working Party on the accession. At a minimum, terms of accession always provide for compliance with all multilateral WTO agreements, including the TRIPS Agreement, subject to possible transitional periods. In a number of cases in the past, existing members also requested additional commitments. If accepted by the acceding member, such additional commitments are noted in the Working Party report and referenced in the Protocol of Accession, which forms part of the WTO Agreement for that member. Newly acceding members may accept terms of accession that require higher levels of IP protection than those provided by the TRIPS Agreement. However, not all elements in the Working Party report are of equal legal status. While some amount to legally binding commitments, which are detailed in the report and in the Protocol of Accession, other elements are of a descriptive nature, merely reflecting the information provided to the Working Party by the acceding country. In such cases, no commitment is noted by the Working Party.

Issues relating to IP and pharmaceutical products have featured in a number of accession negotiations (see Abbott and Correa (2007) for a comprehensive overview of IP elements in WTO accession agreements). For example, when Ukraine acceded to the WTO in 2008, it recorded a commitment to notify the first applicants for marketing approval of originator pharmaceutical products about subsequent applications, in order to give the first applicants an opportunity to submit information regarding whether these later applications had permission to use the original test data and to grant exclusive rights to test data for at least five years.¹²⁹

With regard to LDCs, it was agreed in the 2001 Ministerial Declaration launching the Doha Development Agenda that WTO members would work to facilitate and accelerate negotiations with acceding LDCs. In 2002, the WTO General Council adopted guidelines for the accession of LDCs.¹³⁰ The guidelines provide, among other things, that transitional periods foreseen under specific WTO agreements must be granted – taking into account individual development, financial and trade needs – and that these transitional periods are to be accompanied by

Box 2.11. The example of Cambodia: an LDC's terms of accession to the WTO

Cambodia was the first least-developed country (LDC) to conclude WTO accession negotiations (many LDCs were original WTO members on its formation in 1995). Its Working Party was established in 1994 and met from 2001 until 2003, and Cambodia acceded to the WTO in 2004. In its terms of accession, Cambodia made a commitment to implement the TRIPS Agreement no later than 1 January 2007 – although an extension had been agreed for LDC members in the Doha Declaration until 1 January 2016 for patents and test data protection with respect to pharmaceutical products, and a general extension was later agreed for LDC members until 1 July 2013.

Cambodia's commitment to implement the TRIPS Agreement beginning in 2007 was made on the understanding that during the transition period it would, among other things, grant exclusive rights to test data for five years and provide for patent linkage to marketing approvals (WTO document WT/ACC/KHM/21, paras. 204-206 and 224). Cambodia thus accepted demands from existing members that went beyond the express obligations set out in the TRIPS Agreement. By doing so, Cambodia in its accession agreement appeared to have given away a number of the flexibilities under the Agreement that it would otherwise have benefited from under current transition periods.

However, immediately prior to adoption of the decision on Cambodia's accession, the WTO Deputy Director-General, speaking on behalf of the Chairman of the Working Party on the Accession of Cambodia, clarified that: "The results achieved in the case of Cambodia speak for themselves, and in this context I should also add that the terms of this accession do not preclude access to the benefits under the Doha Declaration on the TRIPS Agreement and Public Health to Cambodia as a (least developed country)" (WTO document WT/MIN(03)/SR/4).

action plans for compliance with the trade rules. In addition, a decision taken at the Eighth WTO Ministerial Conference, in December 2011, stipulated that "requests for additional transition periods will be considered, taking into account individual development needs of acceding LDCs".¹³¹ Subsequently, the WTO General Council decision of 25 July 2012 further streamlined and operationalized the LDC accession guidelines, among others, through enhanced transparency and the undertaking that additional transition periods be favourably considered on a case-by-case basis.¹³² Cambodia and Nepal acceded to the WTO in 2004, Cape Verde acceded in 2008, and Samoa and Vanuatu acceded in 2012 (see Box 2.11).

2. Competition policy

Among the policy instruments available to governments in addressing public health concerns, competition policy has an important role to play in ensuring access to medical technology and fostering innovation in the pharmaceutical sector. Competition is conducive to freedom of choice, low prices and good value for money, while serving as an important driver of innovation and productivity improvement.

(a) The dual function of competition policy

When examining policies which are designed to foster innovation and ensure access to medical technologies, competition policy can be considered as having two interrelated functions which complement each other (Hawkins, 2011).

First, competition policy is important in terms of informing regulatory measures and other relevant policy choices

relating to innovation in, and access to, medical technologies. Competition bodies can be given the mandate to undertake broad policy reviews of competition and regulation, pharmaceutical price regulation regimes, pharmacy regulation and wholesale/distribution arrangements. They can make policy recommendations for a range of policies affecting competition – not only the operation of competition and consumer protection laws, but also in areas directly affecting public health. Institutions such as the Organisation for Economic Co-operation and Development (OECD) and the World Bank have published studies on the interplay between competition policy and health regulation. Such interplay fosters, coordination between competition authorities and agencies that regulate the prices of medical products and the health sector generally.¹³³

Second, the enforcement of competition law also helps to correct anti-competitive behaviour that may take place in the various different business sectors involved in developing and supplying medical technology to patients who need them. It aims to prevent anti-competitive practices that can, for example: restrict R&D; limit the availability of resources needed for the production of medical technology; create unnecessary barriers to the entry of generic or inter-brand competition; and restrict available distribution channels and consumer choices generally. Practices that have been identified as detrimental in this regard include (but are not limited to): (i) abuses of IPRs because of refusal to deal with or imposition of overly restrictive conditions in medical technology licensing; (ii) preventing generic competition through anti-competitive patent settlement agreements; (iii) mergers between pharmaceutical companies that lead to undesirable concentration of R&D and IPRs; (iv) cartel agreements between pharmaceutical companies, including between manufacturers of generics; (v) anti-competitive behaviour in the medical retail and other related sectors;

and (vi) bid rigging in public procurement. These can be addressed on a case-by-case basis through competition law enforcement.

(b) The interface between competition policy and IP protection

In the area of innovation, the aims and effects of IP protection and competition policy can be complementary: both are aimed at fostering innovation by creating incentives to develop new products as an advantage over competitors. IP protection for novel medical technologies is generally considered to be an important means of promoting investment in R&D of new medical technology. This leads to competition between different originator companies with regard to the development of valuable new medical technologies, and therefore with regard to their earlier production and availability. This form of competition is generally not hindered by IPRs, rather it is enhanced by them. Competition policy also helps to maintain the innovative potential of the industry by regulating the market structure and providing countermeasures to anti-competitive behaviour. Competition authorities oversee mergers of pharmaceutical companies and may make them subject to divestiture of certain branches of research in order to prevent the abandonment of research for potentially competing future medical technology.¹³⁴ Ideally, this leads to so-called between-patent competition in pharmaceutical markets: alternative products of the same therapeutic class may be available, and producers of such drugs then compete in the same market.

In certain circumstances, however, IPRs, while aiming to stimulate innovation, can potentially prevent or diminish competition in the pharmaceutical sector at the manufacturing stage, as competitors are excluded from using the patented or otherwise protected medical technology. One important consideration in this regard is the extent to which alternative products are available. Where competitive alternatives are available, IPRs do not lead to the creation of economic monopolies.

Accordingly, policy-makers face the difficult task of finding an overall balance between the protection and enforcement of legitimate IPRs and the need to stimulate competition and prevent anti-competitive behaviour.

(i) *Addressing competition policy concerns in the legal framework for IP protection*

Competition policy has informed the legal framework for IP protection in that international agreements as well as national IP laws recognize the role competition policy has to play in providing “checks and balances” to IPRs. Legal provisions on competition can be considered an integral part of rules on IP protection.

At the international level, the relevance of competition policy in designing rules on IP protection has long

been recognized by the Paris Convention as grounds for granting compulsory licences to prevent the abuse of IPRs. It is also reflected in several provisions of the TRIPS Agreement.

Article 8.2 of the TRIPS Agreement stipulates that appropriate measures (consistent with the provisions of the Agreement) may be needed to prevent the abuse of IPRs by right holders, or the resort to practices which unreasonably restrain trade or adversely affect the international transfer of technology. On the face of it, this provision is not necessarily concerned only with competition law violations, but with the arguably more general concept of “abuse” of IPRs.

In a related area, but focusing on the specific issue of licensing practices that restrain competition, Article 40.1 of the TRIPS Agreement records the agreement among WTO members that some licensing practices or conditions pertaining to IPRs, which restrain competition, may have adverse effects on trade and may impede the transfer and dissemination of new technology. To address this concern, Article 40.2 of the TRIPS Agreement recognizes the right of WTO member governments to take measures to prevent anti-competitive abuses of IPRs. Article 40.2 of the TRIPS Agreement also contains a short illustrative list of practices which may be treated as abuses. These are exclusive grantback conditions, conditions preventing challenges to validity, and coercive package licensing.¹³⁵

Under Article 31 of the TRIPS Agreement, setting out certain conditions on the use of a patent without the authorization of the right holder, subparagraph (k) makes it clear that members are not obliged to apply certain of these conditions in circumstances where the compulsory licence is granted “to remedy a practice determined after judicial or administrative process to be anticompetitive” – namely, requirements to show that a proposed user has made efforts to obtain voluntary authorization from the right holder on reasonable commercial terms and conditions, and that such efforts have not been successful within a reasonable period of time, as well as the requirement that authorization for use of a patent under a compulsory licence be predominantly for the supply of the domestic market of the member authorizing such use. Moreover, authorities may consider the need to correct anti-competitive practices while determining the amount of remuneration due.

In many countries, national IP legislation implementing the TRIPS Agreement also recognizes the role of competition policy with regard to IPRs. For example, the Indian Patent Act provides for the grant of compulsory licences without prior attempt to obtain a licence from the patentee on reasonable terms and conditions in case of anti-competitive practices adopted by the patentee (Section 84.6(iv)), as well as the right to export any products produced under such licences, if necessary.

(ii) Enforcing competition law in the IP context

Competition law enforcement provides a useful tool for correcting abuses of IPRs on a case-by-case basis.¹³⁶ Generally speaking, no special principles of competition law apply to IP, and IP protection is not exempt from the application of competition law disciplines. Nor is IP protection presumed to confer market power or to indicate anti-competitive behaviour. Indeed, IPRs are considered useful in creating functioning markets and fostering innovation. Competition law does not, as a general rule, prevent IPR holders from exercising their exclusive rights. This general respect for IPRs under competition law is based on the assumption that IPRs were acquired legitimately through a system that does not confer overly broad IPRs.

The role of competition law enforcement therefore is to provide “corrective” measures only where needed. Enforcement action under competition laws may be warranted where the IP protection system itself is unable to prevent unwanted restrictions of competition.

3. Trade policy settings

All countries rely to varying degrees on imported goods to provide for the health care needs of their populations. In most countries, especially in smaller developing countries with little or no local production capacity in medical technologies, such imported goods make a unique contribution to these countries' national health systems. Countries are also increasingly engaging in trade in health care services. Trade policy thus affects the way in which markets for medical technologies are opened to competition from imported goods and services.

Rules for international trade are established at the multilateral level within the framework of the WTO. One of the cornerstones of the WTO is non-discrimination in international trade relations. This is implemented through the principles of national treatment and most-favoured-nation (MFN) treatment. These principles are enshrined in the General Agreement on Tariffs and Trade (GATT) in relation to trade in goods, in the General Agreement on Trade in Services (GATS) in relation to trade in services, and in the TRIPS Agreement in relation to IP. In the case of GATT and GATS, important exceptions apply, notably special and differential treatment in favour of developing countries, and free trade agreements (FTAs).

The WTO also guarantees its members the right to protect public health. Since its inception in 1947, GATT has given countries the right to take trade-restricting measures necessary to protect human, animal or plant life or health under certain conditions set out in Article XX(b). GATS contains a similar exception with regard to trade in services in its Article XIV(b). These

general exceptions can override WTO obligations and commitments, provided that the health measures, and the ways in which they are applied, satisfy certain conditions. Furthermore, Article 8 of the TRIPS Agreement recognizes the right of members to take measures to protect public health, as long as these measures are consistent with the TRIPS Agreement.

(a) Tariffs

Tariffs or customs duties on imported goods, are a traditional trade policy instrument and are preferred under WTO rules to quantitative restrictions, such as quotas, which are generally prohibited. Tariffs are relatively transparent and, unlike quotas, do not impose rigid restrictions on volumes of imports.

WTO members have agreed to certain maximum levels for their respective tariffs on all or most imported products, including pharmaceuticals. These maximum levels are called “tariff bindings” and vary according to each country and product. They are the result of decades of tariff negotiations that have gradually led to tariff bindings on more products, which create a more predictable and stable trading environment. Successive rounds of negotiations have also led to lower bound tariff rates and, in fact, WTO members frequently apply tariffs below the bound rate. For example, developing countries have bound their tariffs on formulations on average at 22.4 per cent *ad valorem* (calculated on the value of the imports), but they actually apply tariffs on average at 3.4 per cent *ad valorem*.¹³⁷

Tariffs make imported goods, including medicines, more expensive for consumers. Nevertheless, many countries apply tariffs to bolster the competitive position of locally based companies in the domestic market in an attempt to preserve employment or promote the development of the industry (e.g. the local production capacities of the pharmaceutical sector), or to maintain a certain level of independence from international markets. For consumers, tariff protection can result in costly outcomes. Tariffs also raise revenue for governments, although in the case of medicines, the revenue amounts raised are generally not significant.

In developed countries, the tariffs applied on medicines are very low, if not zero. A number of WTO members, mainly developed countries, concluded the Pharmaceutical Tariff Elimination Agreement in 1994. Under this agreement, they eliminated tariffs on all finished pharmaceutical products as well as on designated active ingredients and manufacturing inputs. Since 1994, the parties have periodically updated the agreement's coverage. Developed countries have applied tariffs on medicines of less than 0.1 per cent *ad valorem* on average since 2000. In the case of developing countries, over the past decade they have lowered their applied tariffs rates on medicines from 6.7 per cent to 4.2 per cent on average. Included in

these developing countries are a few countries with local manufacturing industries that apply relatively high tariffs on finished products. In the case of LDCs, the applied rates range from 4.5 per cent to 2 per cent on average.

Tariff exemptions can often be granted for certain medicines or certain purchasers. Public sector and private non-profit buyers often benefit from waivers from tariffs. Health Action International (HAI), in collaboration with the WHO, has undertaken a major project to identify the various costs associated with the prices of medicines in different countries. For some countries, the data include information on tariffs and exemptions.¹³⁸

(b) Non-tariff measures

The steady decrease of tariff rates through successive rounds of negotiations over the past 60 years has led to a shift in focus to other types of trade measures. Some experts argue that these other trade measures are increasingly used in place of tariffs to protect domestic industries. Non-tariff measures (NTMs) include, among others: sanitary measures; technical regulations; pre-shipment inspections; import licensing; price control measures; charges and taxes; restrictions on distribution and after-sales services. Several WTO agreements are dedicated to these types of NTMs. A basic objective of such agreements is to establish rules for the use of these measures so that they do not become unnecessary trade barriers. While all of these measures can affect trade in pharmaceuticals, the following two have a direct link to public health outcomes.

(i) *Sanitary and phytosanitary measures*

The WTO Agreement on the Application of Sanitary and Phytosanitary Measures (SPS Agreement) contains specific rules for countries which aim to ensure food safety and prevent the transmission of plant- or animal-carried diseases to humans via trade. This agreement aims to strike a balance between recognizing the sovereign right of members to determine the level of health protection they deem appropriate, and preventing SPS regulations that represent unnecessary, arbitrary, scientifically unjustifiable or disguised restrictions to international trade. The SPS Agreement requires that SPS measures are not more trade-restrictive than required to achieve the appropriate level of sanitary and phytosanitary protection, taking into account technical and economic feasibility. It therefore encourages members to follow international standards, guidelines and recommendations. Members are allowed to adopt SPS measures which result in higher levels of health protection, or measures for which international standards do not exist, provided that those measures are scientifically justified.¹³⁹

(ii) *Technical barriers to trade*

The TBT Agreement applies to technical product requirements that are not covered by the SPS Agreement.

It covers both those that are mandatory (“technical regulations”) and those that are voluntary (“standards”) as well as procedures to assess conformity with them, such as inspections. Technical regulations and standards include, for example, quality requirements for pharmaceuticals, labelling requirements for foods and safety standards for X-ray machines. The TBT Agreement incorporates the principle of non-discrimination, in terms of both national and MFN treatment. It also requires that technical regulations shall not be more trade-restrictive than necessary to fulfil a legitimate objective, taking account of the risks that non-fulfilment would create. The protection of human health or safety is listed as a legitimate objective. In other words, the TBT Agreement allows countries to regulate trade to protect health but requires that such measures do not unnecessarily restrict trade. Members are also encouraged to base their measures on international standards, although they may depart from them if they consider that their application would be ineffective or inappropriate for the fulfilment of legitimate objectives.¹⁴⁰

(c) Trade in services

Health services contribute significantly to the effective availability and proper use of many pharmaceuticals and other medical technologies, notably services concerned with prevention, diagnosis and treatment, but also ancillary and technical support. For many sophisticated diagnostic services or treatment regimes, there is no clear distinction between effective and appropriate access to a technology as such, and the supply of related services. Choices made in opening up health services to foreign providers may therefore affect access to medical technologies.

(i) *The multilateral legal framework*

GATS is the main multilateral legal instrument governing trade in health services. It defines trade in services as the supply of a service through four different “modes of supply”, each with bearing on the health sector:

- **Mode 1:** cross-border supply (e.g. telemedicine)
- **Mode 2:** consumption abroad (e.g. a patient seeking medical treatment in a foreign country)
- **Mode 3:** establishment of commercial presence (e.g. a clinic opens an overseas subsidiary or invests in an existing facility abroad)
- **Mode 4:** presence of natural persons (e.g. a physician moves abroad to work in a foreign-owned clinic).

(ii) *Scope of GATS commitments in health-related sectors*

GATS grants WTO members full flexibility when it comes to deciding which sectors and modes of supply to open to foreign competition, as well as the level of obligations that they are prepared to undertake. Health services fall

into several categories: (i) hospital services; (ii) other human health services; (iii) social services; (iv) medical and dental services; and (v) services provided by midwives, nurses, physiotherapists and paramedical personnel.¹⁴¹ Other services complement and facilitate access to medical technologies, such as: R&D on medical sciences; the pharmacy, wholesale and retail sale of various pharmaceuticals, medical and surgical goods and devices; maintenance and repair services for medical equipment; and technical testing and analysis services. GATS disciplines do not cover services “supplied in the exercise of governmental authority” (those supplied neither “on a commercial basis” nor “in competition with one or more service suppliers”). For this reason, many public-sector health services lie outside the scope of GATS.

Many countries have gradually liberalized their health services, thus creating more opportunities for private operators. However, such countries remain reluctant to make this opening binding under the terms of GATS. Apart from health insurance services, there are fewer GATS commitments on health services than there are for any other sectors (see Table 2.4). This is possibly due the major role played by public entities in providing public health services, coupled with the issue of political sensitivities and the lack of vocal business interests. Health services have not been the object of active bilateral negotiations, and commitments in this sector are mostly made as a result of a particular country’s own initiative (Adlung, 2010). It is important to note, in any event, that committing to open a service sector to foreign competition does not affect the government’s capacity to regulate the sector.

Across these six health sectors under consideration, there is generally reluctance to enter commitments on cross-border supply of health services. This is probably due to uncertainties on how to design and enforce appropriate regulation of service suppliers located abroad (a pattern observed across other service sectors). Commitments on health services consumed abroad account for the highest number of full commitments, perhaps reflecting governments’ reluctance – and inability – to prevent their nationals from leaving the state in order to consume services abroad (a practice that also occurs in all service sectors). Some members restrict the portability of insurance coverage for treatment abroad, possibly deterring patients from seeking treatment outside their country. Nearly half the commitments relating to the supply of health services through commercial presence are bound without limitations

at sectoral level, a result that seems above average for all sectors.¹⁴² Most commitments under this mode are subject to limitations, for example limits on foreign equity and requirements for joint venture or residency. Some list economic needs tests: criteria such as population density, existing medical facilities, degree of specialization, type of medical equipment, and distance or availability of transport infrastructure are taken into account before new hospitals and clinics are authorized.

Unlike the other modes of supply, commitments on health services supplied through the presence of natural persons have been undertaken on a “horizontal” basis by the vast majority of members, which means that these commitments apply to all covered services sectors. Most WTO members have closely restricted commitments on this mode, focusing on highly skilled persons or on individuals linked to a commercial presence, as opposed to the self-employed (WTO, 2009). Some add further restrictions to their commitments, referring to language, residency or nationality requirements, recognition of diplomas, strict time limits, economic needs tests or quotas, thus restricting further the already limited level of bindings. Evidence suggests, however, that health professionals benefit from better access conditions in practice than they would if they were exclusively limited to GATS bindings. Health services commitments are also limited as to the breadth of covered activities, such as exclusions of public suppliers, restrictions of commitments on hospital services to privately supplied or privately funded services, or types of medical specializations covered.

(iii) The growing economic importance of trade in health services and the impact of GATS commitments

According to Gottret and Schieber (2006): “Health care is probably the world’s largest single industry, with a combined turnover in excess of US\$ 3.2 trillion annually, equivalent to a tenth of global gross domestic product (GDP), and employing in excess of 59 million staff”. Health services continue to globalize, through cross-border movement of health care workers and patients, as well as through investments of health services companies (WHO/WTO, 2002; Blouin et al., 2006). Technological developments and dwindling telecommunication costs have contributed to the emergence of telemedicine across a range of health procedures (e.g. teleradiology, telediagnostic, telepathology, teleconsultation and telesurgery). It is almost

Table 2.4. Number of GATS commitments

	Medical and dental services	Nurses, midwives, etc.	Hospital services	Other human health services	Social services	Other	Health insurance services
Number of commitments	65	35	57	26	27	6	103

Source: WTO Secretariat (EU member states are counted individually).

Box 2.12. WHO Code of Practice on the International Recruitment of Health Personnel

In order to try and better regulate the migration and movement of health care workers from areas that need them the most, the WHO developed the Global Code of Practice on the International Recruitment of Health Personnel. Key components include:

- Greater commitment to assist countries facing critical health worker shortages with their efforts to improve and support their health workforce.
- Joint investment in research and information systems to monitor the international migration of health workers in order to develop evidence-based policies.
- Member states should meet their health personnel needs with their own human resources as far as possible and thus take measures to educate, retain and sustain their health workforce.
- Migrant workers' rights are enshrined and equal to domestically trained health workers.¹⁴³

impossible to measure the impact of GATS commitments on health services – and any other sector – because of limited data and the difficulty of distinguishing the effects of trade policy bindings from those of other policy and regulatory measures. However, studies suggest that the effects of GATS commitments – where such commitments exist – on trade patterns probably have been insignificant. GATS commitments do not entail additional liberalization, but (at best) they bind existing levels of market access. Consequently, the commercialization of health services has occurred irrespective of GATS obligations, and the main effect of GATS seems to have been to make national policies more predictable (Adlung, 2010).

The health sector has been virtually absent from the WTO Doha Round negotiations on services, with only about a dozen members, mostly developing countries, presenting offers in this sector. These offers were generally very restrictive (concerning only one mode or particular medical specializations). Others, including Canada, the European Union and Switzerland, explicitly excluded health and other social services from the WTO negotiations. This general lack of interest can be attributed to the dominant role of the public sector in providing health care, coupled with the strong social and public service dimension and a concern not to limit future policy options.

(iv) Challenges linked to the opening of trade in health services

Opening of trade in health services should not be seen as an end in itself, rather as a tool to generate distinct benefits if properly used in a broader policy context. From a public health perspective, increasing trade in services bears both opportunities for improving health service delivery and risks for equity if new cross-border health services are only available for those who can afford them. The concern is often expressed that opening health services may create a two-tier system – good services for the rich, bad services for the poor – thus jeopardizing equitable access for all. For example, exporting health services via the Internet from delocalized centres

may boost employment opportunities in developing countries, and contain costs in developed countries. By attracting health care workers to financially more attractive opportunities, this may leave gaps in the local health sector.

A strong regulatory system with credible implementation is necessary to ensure that competing private suppliers operate in ways that contribute to address broader public policy concerns, such as equitable and affordable access for all. Publicly owned and operated health facilities also generate regulatory challenges. Thus, the appropriate regulatory framework is required in order to ensure that more open trade in health services benefits all sections of the population. An impact assessment on the supply of health services should precede binding commitments under GATS or any other trade agreement. The migration of health workers is a key issue, with workers tending to move from the poorest regions to richer cities within a country, and from there to high-income countries (see Box 2.12). Demand for foreign health workers has increased in high-income countries as a result of insufficient numbers of health professionals being trained locally, and also due to ageing populations in these countries. Governments wishing to contain brain drain remain free to do so, as such measures are not subject to GATS disciplines which relate – particularly for Mode 4 – only to the temporary inward migration of foreign health workers. The limited scope of Mode 4, both its definition and specific commitments, means that GATS probably plays an insignificant role in the international migration of health personnel.

4. Government procurement

Government procurement refers generally to the purchasing of goods, services, and construction services, or any combination thereof, by, or on behalf of, government bodies in fulfilment of their public service responsibilities, including in areas of socially vital importance, such as health care. This section addresses the positive impact which a well-designed framework for government procurement can be expected to have on the health sector. It also sets

Box 2.13. Evidence of cost reduction/improvements in value for money in the health care sector made possible through transparent and competitive tendering

A 2011 study, published by the National Bureau of Economic Research, in the United States (Danzon et al., 2011), examined the determinants of prices for originator and generic drugs across a significant number of countries. The study mainly focused on drugs to treat HIV/AIDS, TB and malaria in LMICs. It analysed the effect on drug prices in cases where the drugs were sold through the retail pharmacy channel, as opposed to cases where the drugs were acquired in tendered procurements such as those, for example, carried out by the Global Fund and the Clinton Foundation.

The study shows that tendered procurement attracts generic suppliers and significantly reduces prices for originators and generics when compared with the prices that apply in retail pharmacies. Specifically, it finds that: “The evidence from HIV/AIDS, TB and malaria drugs shows that procurement mechanisms lower originator and generic prices by 42% and 28%, respectively, compared to their retail pharmacy prices”.

A 2003 OECD study on the benefits of transparent and competitive procurement processes referred to the following examples of benefits achieved:

- A 43-per-cent saving in the cost of purchasing medicines in Guatemala, due to the introduction of more transparent and competitive procurement procedures and the elimination of any tender specifications that favour a particular tender.
- A substantial reduction in the budget for expenditures on pharmaceuticals in Nicaragua, due to the establishment of a transparent procurement agency accompanied by the effective implementation of an essential medicines list (OECD, 2003).

out the rules established for that purpose by the plurilateral Agreement on Government Procurement (GPA) under the WTO, and the size of procurement markets in health-related sectors covered by that agreement.¹⁴⁴

(a) The importance of a transparent and competitive procurement process for the health sector

The possibility of achieving significant savings through the introduction of better government procurement tools is especially relevant for the health sector, where, according to the World Bank, the procurement of medicines has been particularly prone to weak governance, contributing to stock-outs, wastage, poor quality and price inflation (World Bank, 2011). In a similar vein, a medicines pricing study found that, in the Africa, Europe and Western Pacific regions, governments paid an average of 34 per cent to 44 per cent more than necessary for medicines (Cameron et al., 2009). Such deficiencies in public procurement practices should be acknowledged as a significant failure of public health systems. Conversely, the introduction of more efficient, transparent and competitive procurement procedures in the context of public health systems has the potential to contribute substantially to improvement in the accessibility and affordability of medicines, thus helping to establish more efficient and cost-effective health delivery systems that minimize waste and prevent fraudulent and corrupt practices. A range of evidence relating to cost reductions that have been achieved through the application of transparent and competitive procurement processes in the health care sector is summarized in Box 2.13.

(b) Procurement of medical technologies and health services under the GPA

The GPA provides an appropriate framework for rules at the international level which are intended to promote efficient trade and best practices in the area of public procurement. The GPA is a plurilateral agreement, meaning that only those WTO members that have acceded to it are bound by its rules. As of 2012, 42 WTO members are parties to the GPA.

(i) *GPA coverage*

The GPA has important application vis-à-vis the public health care sector, specifically with regard to the areas it covers – the procurement of medicines, pharmaceutical products and health services. In principle, the GPA promotes transparency and fair competition and helps to deliver improved value for money for governments and their agencies. Unless otherwise explicitly excluded, the GPA covers all goods procured by covered entities in values above the relevant thresholds,¹⁴⁵ including medicines and pharmaceutical products (see Table 2.5 for details).

The GPA applies only to such goods and services and government agencies or entities that have been specifically committed by the parties and included in their respective schedules of commitments in Appendix I of the GPA. To determine the specific market access commitments undertaken by GPA parties in the health care sector, the following factors must be taken into consideration: (i) whether, and if so which, health-related entities are

Table 2.5. Coverage in the health sector by parties to the WTO GPA

Party to the WTO GPA	Coverage of health-related entities at the central government level	Coverage of health-related entities at the sub-central government level	Coverage of goods (pharmaceutical products are generally considered to be goods)	Coverage of health-related services
Armenia ^a	✓		✓	✓
Canada	✓	✓	✓	X
European Union, including its 27 member states	✓	✓	✓	X
Hong Kong, China	✓	N/A	✓	X
Iceland ^b			✓	X
Israel ^c	✓	X	✓	X
Japan	✓	X	✓	X
Korea, Republic of	✓	X	✓	X
Liechtenstein			✓	X
Netherlands, with respect to Aruba	✓	N/A	✓	X
Norway ^a	✓		✓	X
Singapore	✓	N/A	✓	X
Switzerland	✓	✓	✓	X
Chinese Taipei	✓	✓	✓	X
United States	✓	✓	✓	✓

Notes: Names of parties to the WTO GPA are those used in the WTO. The symbols “✓” and “X” have been used respectively to indicate whether a party’s coverage is expressly stated to include health-related entities or not. Where a party’s coverage has been presented in generic or descriptive terms and no additional details have been provided – for instance, by way of an illustrative list – the specific entry has been left blank. In addition, a footnote is provided indicating that the item is neither expressly covered nor expressly excluded. It should also be noted that the following do not have sub-central level of government and accordingly have scheduled no commitments in this regard: Hong Kong, China; Netherlands with respect to Aruba; and Singapore. ^aIn Norway’s and Armenia’s Annex 2, health-related entities are neither expressly covered nor excluded. ^bHealth-related entities are neither expressly covered nor excluded. ^cIsrael has expressly excluded the following goods procured by its Ministry of Health: insulin and infusion pumps, audiometers, medical dressings (bandages, adhesive tapes excluding gauze bandages and gauze pads), intravenous solution, administration sets for transfusions, scalp vein sets, hemi-dialysis and blood lines, blood packs and syringe needles. It should be noted that a number of these exclusions have been deleted as a result of the conclusion of the GPA negotiations.

covered in a GPA party’s schedule of commitments; and (ii) whether, and if so which, health-related products and services are covered by the GPA.

In relation to the first aspect, health-related entities are covered by GPA parties at various levels of government (see Table 2.5). More precisely:

- Almost all parties expressly cover such entities at the central government level (e.g. federal entities and ministries).
- The majority of parties that have a sub-central level of government (e.g. states, provinces, cantons and municipalities) cover them at this level or do not expressly exclude them.
- Three parties cover other types of health-related government entities (e.g. hospitals).

It should also be noted, as is made clear in the revised GPA text, that the GPA does not apply to goods or services procured with a view to commercial sale or resale.

In addition, the European Union has undertaken binding commitments under the GPA for health-related entities at the central government level for all of its 27 member states and for a significant number of such entities at the sub-central government level. For its part, the United States is covered by the Federal Department of Health and Human Services, and health-related entities in a number of its states.

Another key point is that under the GPA, pharmaceutical products are generally considered to be goods, and accordingly, unless otherwise specified, are normally considered to be covered by the GPA when purchased by entities listed in the parties’ schedules, in values above

the relevant thresholds. Furthermore, none of the GPA parties currently incorporates a general exclusion of such products in its schedules. One smaller party has excluded a number of goods procured by its Ministry of Health. With regard to the coverage of health-related services under the GPA, the United States is the only GPA party currently covering them. In summary, the GPA provides relatively broad coverage for entities in the health care sector, particularly with respect to goods (including medicines); on the other hand, its coverage of health services is limited.

(ii) *The magnitude of GPA parties' health-related procurement*

The GPA is the pre-eminent international instrument regulating trade in government procurement markets, with the total value of covered procurement under the GPA estimated at around US\$ 1.6 trillion in 2008.¹⁴⁶ In order to appreciate the importance of the government procurement markets covered by the GPA in health-related fields, it is necessary to quantify the potential value of these market access commitments. An important source of statistical information on the size of covered procurement markets is now available from recent statistical reports that have been submitted by the GPA parties to the Committee on Government Procurement. Although these statistical reports are not necessarily consistent in all respects (efforts are under way to ensure greater consistency in methodological approaches), they nevertheless represent a very useful source of information regarding the magnitude of the market access commitments under the GPA.¹⁴⁷

These official sources make clear that the size of government procurement markets in health-related sectors covered by the GPA is substantial.¹⁴⁸ For example, the United States notes in its statistical reports that the total general expenditure, by function, of the 37 states covered under the GPA in 2008 was US\$ 40 billion for hospitals and US\$ 50 billion for health.¹⁴⁹ In addition, the United States reports that the value of goods and services covered by the GPA and procured by the US Department of Health and Human Services in 2008 was estimated to be around US\$ 30 billion. The European Union also notes in its statistical report for 2007 that its covered entities had procured an estimated EUR 11 billion of medical and laboratory devices, pharmaceuticals and

related medical consumables covered by the GPA.¹⁵⁰ Finally, Japan reports that the value of contracts covered by the GPA awarded by the Japanese Ministry of Health, Labour, and Welfare in 2010 was estimated at US\$ 1.8 billion.¹⁵¹

5. Free trade agreements

(a) Current trends in trade negotiations beyond the multilateral arena

There is a worldwide trend for countries to enter into economic integration arrangements in various bilateral and regional configurations (see Box 2.14), in parallel with multilateral agreements – a development that is presenting significant systemic challenges for the multilateral system outlined in this chapter (and analysed in WTO, 2011). These agreements have been dubbed regional trade agreements (RTAs), free trade agreements (FTAs), bilateral trade agreements (BTAs), or (the term used in recent reports by the World Bank and the WTO) preferential trade agreements (PTAs), reflecting the fact that many agreements are not “regional” but can cover countries which are geographically dispersed, and that such agreements provide for preferential tariffs on many goods. These terms often overlap, and several can, in effect, apply to the same agreement, depending on the characteristics of the agreement being considered. For the purposes of this study, the term “FTAs” is used in reference to any kind of trade agreement.

In the past, integration arrangements often focused on trade in goods and the elimination of tariff duties and other restrictions between parties to an agreement. However, WTO (2011) notes that in recent years, trade agreements have frequently taken the form of deep integration processes that include provisions on a wide range of behind-the-border or regulatory policy areas, such as services and IP and include a wider range of different players. The trade openness resulting from such processes creates pressures to reconcile divergent national practices and produces demands for governance and the rule of law that transcend national borders. In the area of IP law and policy, this trend may manifest itself in important changes in national laws, which in turn directly affect the framework governing access to, and innovation in, medicines and medical technologies – a set of processes that have recently been more dynamic than norm setting at the multilateral level.

Box 2.14. The changing geography and FTA coverage

PTAs may be FTAs or customs unions with common external tariffs. This most recent “wave” of regionalism covers a much wider network of participants – including bilateral, plurilateral and cross-regional initiatives – and encompasses countries at different levels of economic development – including “developed–developed”, “developing–developing”, and “developed–developing” alliances. Although these new agreements, like previous PTAs, involve preferential tariff reductions, they focus even more on other issues, such as capital flows, standards, IP, regulatory systems (many of which are non-discriminatory) and commitments on labour and environmental issues.

Many factors are at play in here. WTO (2011) refers to: (i) neutralizing beggar-thy-neighbour trade policies that seek benefits for one country at the expense of others; (ii) increasing market size; (iii) enhancing policy predictability; (iv) signalling openness to investors; and (v) the expansion of international production networks. WTO (2011) concludes that, for developing countries, common policies with advanced economies may create benefits by allowing them to import regulatory systems that are “pre-tested” and represent “best practices”. On the other hand, developing countries may also be pressurized to adopt common rules which are inappropriate for their level of development, or which could be used by advanced economies to protect vested interests.

Increasing market size can be a reason for establishing FTAs, since it enables companies from signatory states to exploit economies of scale and to gain a relative advantage over excluded competing companies. In addition, preferential access to a larger market may increase a country’s attractiveness as a destination for foreign direct investment (FDI). Both reasons are particularly valid for small economies, which may help to explain why these countries agree to make concessions on other more controversial issues, such as IPRs or environmental standards, when negotiating FTAs with large economies (WTO, 2011).

(b) Bilateralism and regionalism: the question of preferences

A key feature of FTAs is the idea of preferential treatment and benefits for parties to the agreement that may not be automatically extended to other parties. For some other areas beyond the traditional scope of agreements on trade in goods, such as government procurement or competition policy, negotiators also have the option to provide preferences that only benefit parties to the agreement. However, the situation is different for most aspects of IP standards.

Unlike other WTO trade agreements, such as GATT and GATS, the TRIPS Agreement does not provide for broad exceptions to the principle of MFN in the case of FTAs. This can have important implications for access to medicines and medical technologies, as well as for the innovation of new products. In concrete terms, if two WTO members agree to accord each other’s nationals higher standards of IP protection than provided in the TRIPS Agreement, they cannot, in principle, deny the same higher level of protection to nationals of any other WTO member. In other words, the agreed higher level of protection would not be limited to nationals of the FTA parties but would have to be extended to the nationals of all other WTO members as well. For example, if two countries agreed to provide patent term extensions for one another’s patent holders, the MFN principle under

the TRIPS Agreement would require them to provide the same patent term extensions to patent holders from all other WTO members. In contrast, if they agreed to abolish tariffs on pharmaceuticals or chemical ingredients imported from one another as part of a FTA or customs union, they would not need to abolish tariffs on imports from other countries.

(c) Intellectual property standards

As discussed in Chapter II, Section B.1(a), and Chapter IV, Section C.5, WTO members are free to incorporate into their national laws more extensive IP protection than the minimum standards required by the TRIPS Agreement, provided that this protection does not contravene TRIPS requirements. A number of FTAs provide for more extensive protection for patents and test data, as well as higher enforcement standards, which affect trade in pharmaceuticals and can have an impact on prices for medical technologies. Many of these agreements form “families” which are each grouped around a “hub”. EFTA, the European Union and the United States are the most important “hubs” in terms of the number of agreements containing such provisions. Each hub tends to use a consistent approach when negotiating agreements, so that the IP provisions (among others) of all agreements within each family often share many prominent characteristics. In effect, the process exports aspects of the regulatory regime of the hub to its trading partners. In this respect, WTO (2011) notes that, compared with the WTO agreements, this process has generally served to heighten commitment levels. The areas embodying legally enforceable commitments are relatively few and are to be found predominantly in the fields of investment, competition policy, IPRs and the movement of capital.

The impact of FTAs on national IP regimes can be far-reaching because, as indicated above, the more extensive protection that they require for IP, including patents and test data, must be made available without discrimination to the nationals of all other WTO members, and not just to the nationals of the other party to the FTA. Moreover, in areas that usually operate through the use of national regulations, such as IP, services and competition policy (WTO, 2011), it would, in any event, be costly in practice to tailor regulations in order to favour nationals originating from preferential partners, and this becomes even more difficult as the number of FTAs to which a country is a signatory increases. Thus, reasons of principle and practicality lead to a “ratcheting-up” effect on IP standards, in that they can lock in higher levels of protection, with potential effects on innovation and access to medical technologies. A number of guides on FTAs have been published. For example, the WHO Regional Office for the Eastern Mediterranean has published a policy guide for negotiators and implementers of IP provisions in bilateral FTAs (El Said, 2010).¹⁵²

(d) Commitments in other sectors

FTAs are, by their very nature, not limited to setting standards regarding IPR protection and enforcement. A thorough analysis of the potential effects of FTAs on innovation in, and access to, medical technologies must therefore also take into account the commitments and standards agreed in other key policy areas which directly relate to the pharmaceutical sector, such as tariffs, government procurement and competition law.

With respect to tariffs, however, while earlier FTAs were motivated by lowering relatively high tariffs applied on an MFN-basis, the achievement of such tariff reductions, including for pharmaceutical products, is likely to have lost some of its initial relevance in recent years, and may therefore only occasionally play a role in FTAs. As WTO (2011) notes, this is due to the average applied tariff

of merely 4 per cent across products and countries in 2009, implying that there is usually not much room left for exchanging preferential tariff concessions in trade agreements.

On the other hand, matters including investment, competition policy and government procurement have increasingly made their way into the more recent generation of FTAs, complementing the reduction of trade barriers and reflecting the trend towards the globalization of policies which previously were addressed at the national level. Related disciplines may either be addressed in stand-alone FTA chapters or, as is often the case for the competition sector, they become an integral part of chapters, for example, on IPRs or government procurement. WTO (2011) estimates, for example, that about 20 per cent of IPR chapters incorporate provisions preventing the abuse of IPRs or anti-competitive behaviour.

C. Economics of innovation and access to medical technologies

Key points

- Knowledge or new, useful information possesses the characteristics of what is commonly called “a public good”.
- The financing of new medical knowledge is particularly challenging. Factors to be taken into account include long product development times, the need for stringent regulatory standards, the high risk of failure and low marginal costs of production.
- The pharmaceutical sector stands out in terms of its dependence on patents to capture returns to research and development (R&D).
- Several policy options exist within and outside the patent system to attenuate the negative price and welfare effects of product patents, especially on pharmaceuticals. Economists have pointed out that some options may benefit traders/manufacturers more than consumers; that differential pricing could play a role in lowering prices in poorer countries; and that the lack of intellectual property (IP) protection and stringent price regulation could delay the launch of medicines in certain markets.

The past decade has seen more systematic efforts to use the tools of economic analysis to support discussions on health policy, particularly in developing economies. The WHO Commission on Macroeconomics and Health (WHO, 2001a) was a major milestone along this road. The present study does not attempt to advance economic analysis and the theoretical understanding of the economics of technology innovation and access issues. Rather, it recognizes the growing importance of economic concepts in policy debate, and it briefly reviews the main economic concepts and the current body of literature dealing with the IP aspects of these issues.

In the economics of innovation and IP, knowledge or new, useful information has been considered to have, to some extent, the classical characteristics of a public good: non-excludability and non-rivalry. Non-excludability means that it is not possible to exclude others from using the knowledge once it is made public. Non-rivalry means that one person's use of the knowledge does not restrict or diminish the amount of it available or its value for use by others. Its non-rivalrous character means that knowledge can be easily shared and replicated. In the absence of some kind of protection against unauthorized sharing or replication, it is difficult to see how private entities would invest in the creation of knowledge, since others could benefit for free from their efforts once the knowledge is public. Therefore, for the original private investors, generating a reasonable level of return on their investments might prove difficult. Consequently, no protection at all would lead to chronic underinvestment in the creation of knowledge, or in other words, markets would fail to produce knowledge in socially optimal quantities.

Economists wrestle with the question of how best to finance the creation of new knowledge, particularly when

private investment is involved. Special challenges arise in the area of medical technologies in general and medicines in particular, given the long product development times, the necessarily stringent regulatory burden, and the relatively high risk of failure (such as when pharmaceuticals fail tests on safety and efficacy at a late stage in their development) and the comparatively low marginal costs of production.

While patents may increase costs to society in the short term by restricting competition, they should generate greater and more dynamic benefits as a result of encouraging more innovation in the long term. The requirement to disclose the invention fully in patent applications helps to disseminate scientific and technical information that could otherwise be kept secret. Society therefore benefits from research conducted by those “standing on the shoulders of giants” to create additional new and useful inventions. Patents can also be useful instruments for obtaining finance (venture capital).

Costs associated with research in the pharmaceutical sector are high, but production costs often are very low and thus it is relatively easy for other companies to enter the market with generic versions of a new medicine at much lower prices, as these companies do not bear any of the R&D costs. Several studies have shown that when an array of different choices are examined – patents, trade secrets, lead times and other business strategies – the pharmaceutical sector stands out as the one that depends most on patents as a means of capturing returns on R&D investments. This finding has also been borne out by large-scale, multi-sector industry surveys conducted in the United Kingdom (Taylor and Silberston, 1973), the United States (Mansfield, 1986; Levin et al., 1987; Cohen et al., 2000) and in many other countries (WIPO, 2009).

Even where patent protection is in place, the actual period of effective market exclusivity is typically much shorter than the patent term. It has been estimated that the effective patent term of a new chemical entity (NCE), which is the balance remaining in the patent term after obtaining the relevant regulatory approvals, is an average of 8 to 12 years in the US market (Office of Technology Assessment, 1993; Grabowski and Kyle, 2007).

Despite this, the pharmaceutical sector also stands out for its high accounting rate of profit, which is between two and three times higher than the average rate for Fortune 500 companies. However, it should also be borne in mind that the pharmaceutical sector's profit growth rate corresponds with the growth rate of R&D in this sector (Scherer, 2001). Indeed, US pharmaceutical companies invest as much as five times more in R&D, relative to their sales, than the average US manufacturing firm. However, despite the steeply rising costs of R&D in recent decades, the number of NCEs introduced worldwide, particularly those that deliver a significant therapeutic advance, has not increased proportionately. Factors such as increasingly complex disease targets and growing technological complexity may play a role in this decrease (USCBO, 2006). OECD (2011) observes that "rising patenting activity has been accompanied by an average 20% decline in patent quality over the past two decades" with the quality of pharmaceutical patents rating below than average and below that of other less mature areas of technology.

In order to understand the effect of pharmaceutical product patents, several attempts have been made by economists to simulate the effect on prices and welfare of the introduction of pharmaceutical patents.¹⁵³ One such study concludes that the introduction of product patents on pharmaceuticals in just one therapeutic subsegment in India would lead to significantly higher prices and welfare losses which are estimated to range from US\$ 145 million to US\$ 450 million per year (Chaudhuri et al., 2006). Most of this loss would be borne by consumers, in terms of lower consumer surplus. This outcome in reality would of course depend on the way policies were implemented, the extent of price regulation and the degree to which foreign multinationals responded to patent protection. These companies could either maintain exclusivity in marketing or use licensing more extensively.

Medical innovation benefits patients around the world, whereas R&D into medical technologies is only undertaken in a few countries. This raises the issue of equitable sharing of the burden of R&D in this sector. Several solutions are advocated, and have been attempted, to attenuate the effects of high prices of patented medicines. Among these solutions are price controls, parallel imports and compulsory licensing. Price regulation, whether in terms of direct cost-plus or indirect price reimbursement models, including those based on reference pricing, can be efficient means to lower prices, but they have to be worked out carefully

in order not to result in medicine shortages in the market.¹⁵⁴ Compulsory licences have also been reported as having resulted in substantially reduced prices of patented medicines during the patent term (see Chapter IV, Section C.3(a)(iii)). However, compulsory licences are not an easy solution for more complex technologies, as they do not oblige the patent owners to cooperate in transferring the additional know-how that might be required. In addition, while compulsory licensing can be effective at reducing prices, if used widely, it can undermine the equitable burden sharing of R&D costs. There is, however, not much empirical evidence so far on this question.

In addition to compulsory licensing, parallel imports of medicines may allow poorer countries to benefit from lower prices elsewhere.¹⁵⁵ However, it has been demonstrated that while parallel imports result in a reduction in prices, they deliver considerably higher benefits for traders involved in such imports than they do for consumers (Ganslandt and Maskus, 2004). Furthermore, it needs to be borne in mind that the possibility of parallel importing is not determined solely by the IP regime chosen by a country. Rather, it also depends on the conditions in the individual contract between the manufacturer and the wholesaler, as well as on the differences in the market authorization granted, including, for example, the trade name of the product, which may vary from one jurisdiction to another.

Another potential solution is differential or tiered pricing, under which lower prices are applied in poorer countries (see Chapter IV, Section B.2). In order to maximize profits, a monopolist selling under different market conditions could use a form of price discrimination based on differing willingness and ability to pay for the product. The counterfactual to differential pricing is uniform pricing, whereby the seller sets one price, adjusted for transport, distribution and other costs, for all consumers in all countries. It should be noted that in such circumstances there would be no scope for parallel importation.

A medicine protected by patents should, in principle, lend itself to differential pricing. In such circumstances, both consumers in poorer countries and patent-owning companies would be better off. It would also seem that, in these circumstances, the market itself could move closer to solving the problem of equitable sharing of R&D costs. In order for differential pricing to occur, three conditions would need to be fulfilled (WTO, 2001):

- The seller must have some control over price, such as some degree of market power.
- The seller must be able to identify and segregate consumers according to varying price sensitivities.
- The seller must be able to limit resale from low-priced markets to high-priced markets or, in other words, must be able to segment the market.¹⁵⁶

In addition to concerns about the price or affordability of patented medicines, concerns have been raised about delays in the availability of these medicines in other countries from the date of first approval in the first country. One study (Lanjouw, 2005) found that while for high-income countries, patents unambiguously encourage the introduction of new drugs, price regulation deters such entry. The picture is mixed for the other countries. For low- and middle-income countries (LMICs) with a high capability to imitate new drugs, introducing strong IP protection may mean having fewer new drugs on the market, as patent owners may delay entry due to expectations of low prices, and generic producers cannot enter due to patent protection. On the other hand, while price regulation makes it less likely that new drugs will be available quickly in LMICs, such regulation does not appear to prevent new products from being launched eventually.

This research has been taken further by others including, more recently, by Berndt et al. (2011), who demonstrate that key developing countries have been shown to have slower diffusion of new drugs, even in a post-TRIPS era. While the data in this study are new and interesting, the researchers' conclusion that slower diffusion of new drugs

is due to lack of IP enforcement is more controversial. Some countries provide incentives to originator companies to introduce their products soon after first marketing anywhere in the world by counting the term of test data exclusivity from the date of first approval globally, as opposed to from the date of first approval in that country. For example, Chile has implemented such a system following the US–Chile FTA (Fink, 2011).¹⁵⁷ For countries with a weak regulatory framework, somewhat delayed introductions, on the other hand, have the advantage of avoiding adverse events associated with withdrawals for safety reasons.

Finally, it is important to note that patents and other IPRs are meant to be market-based instruments. They play a limited role in providing incentives to develop new medicines for “neglected diseases” or “diseases of the poor” in regions where there are small markets. Thus, the ongoing debate on access to medicines, has generated a debate on alternative non-price linked mechanisms for incentivizing innovations such as prizes or advance market commitments, and it has spawned new business models such as private–public partnerships.¹⁵⁸

D. Traditional knowledge and traditional medicine

Key points

- Traditional medicine contributes significantly to the health status of many communities, and is increasingly used within certain communities in developed countries. Appropriate recognition of traditional medicine is an important element of national health policies.
- The growth in the trade of health products based on traditional knowledge (TK), coupled with growth in the use of TK as a lead for biomedical research and product development, have provoked a policy debate about the misappropriation of TK and the development of, and compliance with, appropriate protocols for access to, and use of, TK, especially traditional medical knowledge. The related issues of prior informed consent (PIC) and equitable benefit-sharing (EBS), while ensuring continued R&D, have also formed part of this debate.
- Respect for both the economic value and the social and cultural significance of TK is of key importance.
- Documentation of traditional medical knowledge, such as databases and national inventories, can be used as evidence of prior art in patent procedures.
- As developing countries increasingly look to their indigenous TK as the basis for new products with significant export potential, this creates a need for the regulation of quality, safety and efficacy of such products, thus posing challenges for regulators and producers.

Traditional medicine has long been used as a mainstay of health care for many populations. This section reviews a number of issues concerning traditional medical systems with respect to IP, regulatory systems and trade.

1. Traditional medicine knowledge systems

Traditional medicine is the sum total of the knowledge, skills and practices based on the theories, beliefs and experiences indigenous to different cultures, whether explicable or not, used in the maintenance of health, as well as to prevent, diagnose, improve or treat physical and mental illnesses (WHO, 2000b).¹⁵⁹ It is used as a comprehensive term to refer both to traditional medicine systems such as Traditional Chinese Medicine (TCM), Ayurvedic medicine and Unani medicine, and to various forms of indigenous medicine being practised traditionally. It is thus best understood as a set of distinct systems of knowledge that include different therapeutic philosophies, products and practices. Traditional medicine that has been adopted by other populations (outside its indigenous culture) is often termed “complementary and alternative medicine” (CAM) (WHO, 2002b).

Traditional medicines can be of different composition, including herbs, herbal materials and preparations, and finished herbal products (herbal medicines). They may also use animal materials or mineral materials. Their active ingredients are therefore substances derived from

plants, animals or minerals.¹⁶⁰ Traditional medicine is used widely throughout the world, but especially in developing countries. In some Asian and African countries, 80 per cent of the population depend on traditional medicine for primary health care. In many developed countries, up to 80 per cent of the population has used some form of CAM, such as acupuncture.¹⁶¹

Herbal treatments stand out as the most popular form of traditional medicine. International trade in traditional medicines is growing, with the China Chamber of Commerce for Import and Export of Medicines and Health Products reporting exports of US\$ 1.8 billion in 2010.¹⁶² Traditional medicines are increasingly being used outside the confines of traditional cultures and far beyond traditional geographical areas without proper knowledge of their use and the underlying principles. They are also being used in different doses, extracted in different ways and used for non-traditional indications (WHO, 2004a).

The WHO, in cooperation with its member states, promotes the rational use of traditional medicine for health care.¹⁶³ The WHO monitors the status of traditional medicine around the world and has published a worldwide review on how traditional medicines and CAM are recognized and regulated at a national level. This work aims to facilitate the development of legal frameworks and the sharing of experiences between countries (WHO, 2001b). The WHO has also published a report on a WHO global survey on national policy on traditional medicine and regulation of herbal medicines (WHO, 2005b).

The WHO is currently updating its traditional medicine strategy and, for this purpose, is undertaking a second global survey. The WHA has also adopted a number of resolutions relating to traditional medicine:

- In 1988, referring to the Chiang Mai Declaration, the WHA resolution on medicinal plants placed medicinal plants, their rational and sustainable use, and their conservation, firmly in the arena of public health policy and concern.¹⁶⁴
- In 2003, a WHA resolution on traditional medicine, referring to the WHO traditional medicine strategy, requested the WHO to collaborate with other organizations in the UN system and NGOs in various areas related to traditional medicine, including research, protection of traditional medical knowledge and conservation of medicinal plants resources.¹⁶⁵
- Regarding the GSPA-PHI, the WHO identified traditional medicine as one of the areas to be addressed in its Quick Start programme. The programme aims “to support research and development and to promote standard-setting for Traditional Medicine products in developing countries”.¹⁶⁶
- In 2009, a resolution on traditional medicine referred to the Beijing Declaration, which urges national governments: to respect, preserve and widely communicate traditional medicine knowledge while formulating national policies and regulations to promote appropriate, safe and effective use; to further develop traditional medicine based on research and innovation; and to consider the inclusion of traditional medicine in their national health systems.¹⁶⁷

2. Traditional medical knowledge in international health and IP policy

In international debates, the term “traditional knowledge” (TK) has been used in a broad sense in many contexts, notably in policy discussions on the environment and biodiversity, health, human rights and the IP system. The term itself has no agreed international legal definition (WIPO, 2001).¹⁶⁸ In this study, “traditional medical knowledge” is used in a specific context, referring to the content or substance of TK, skills and learning, with specific application to human health, wellness and healing. It may apply to traditional medicines as such, or to knowledge systems relating to medical treatment (such as healing massage or yoga postures).

Traditional medicine systems can be categorized as follows:¹⁶⁹

- **Codified** systems which have been disclosed in writing in ancient scriptures and are fully in the public domain. These include the Ayurvedic system of medicine, the Siddha system and the Unani Tibb tradition. TCM,

which is disclosed in ancient Chinese medical texts, is another example of a codified system.

- **Non-codified** traditional medicinal knowledge which has not been fixed in writing often remains undisclosed by TK holders and is passed on in oral traditions from generation to generation.

The past decade has seen greater attention paid to traditional medical knowledge in several international policy contexts. For example, the United Nations Declaration on the Rights of Indigenous Peoples,¹⁷⁰ which was adopted in 2007, states: “Indigenous peoples have the right to their traditional medicines and to maintain their health practices, including the conservation of their vital medicinal plants, animals and minerals”. It also cites medicines within the context of the “right to maintain, control, protect and develop their cultural heritage, TK and traditional cultural expressions, as well as the manifestations of their sciences, technologies and cultures”.

3. Traditional medicines regulation

The high prevalence of traditional medicines throughout the world, coupled with efforts to integrate traditional medicines in modern national health systems, has increased the demand for information on the safety, efficacy and quality of these medicines. As with other medicines for human use, traditional medicines should be covered by regulatory frameworks to ensure that they conform to required standards of safety, quality and efficacy, according to the status and position of traditional medicine in the country’s national health policy and health system. The regulation of traditional medicines takes many different forms around the world. Depending on the national legislative and regulatory framework, they can be sold as prescription or non-prescription medicines, dietary supplements, health foods or functional foods.

Additionally, the regulatory status of a particular product may differ in different countries. The same herbal product can be considered differently if it is traded between two countries which have different regulatory approaches and requirements. Herbal products which are categorized as something other than medicines and foods are becoming increasingly popular, and there is potential for adverse reactions due to lack of regulation, weaker quality control systems and loose distribution channels (including mail order and Internet sales) (WHO, 2004a).

In 2006, the International Regulatory Cooperation for Herbal Medicines (IRCH), a global network of regulatory authorities responsible for the regulation of herbal medicines which operates in conjunction with the WHO, was established. Its mission is to protect and promote public health and safety through improved regulation of herbal medicines.¹⁷¹

Currently, over 120 WHO member states regulate herbal medicines. To support the efforts of member states in establishing and implementing effective regulation of herbal medicines, the WHO has published key global technical guidelines, in terms of their quality, safety and efficacy and sustainable use. Several other sets of guidelines are in development, including guidelines on the assessment of herbal medicines, the methodology for research and evaluation of traditional medicine, good manufacturing practices (GMPs) for herbal medicines as well as conservation and sustainable use of medicinal plants, such as good agricultural and collection practices (GACP) for medicinal plants.¹⁷²

In addition, the WHO has developed a series of volumes of WHO monographs on selected medicinal plants, which aim to provide scientific information on the safety, efficacy and quality control of widely used medicinal plants. The WHO provides models to assist member states in developing their own monographs or formularies for these and other herbal medicines, and it also facilitates information exchange among member states.¹⁷³

Growth in international trade in traditional medical products has sparked discussions on the trade impact of regulations. In recent years, WTO members have notified the WTO Committee on Technical Barriers to Trade (TBT Committee) in relation to a range of regulations that have a direct bearing on traditional herbal medicines. Such regulations include: GMPs for the production of herbal remedies (Mexico); regulation of herbal medicines for the protection of public health (Peru); inspection of herbal medicines for the protection of consumers and the promotion of public health (Republic of Korea); and regulations on the preparation of herbal medicine for human consumption (Kenya).¹⁷⁴ Reflecting the TBT Agreement principle that countries are encouraged to apply international standards, a number of these notifications refer to various WHO guidelines on herbal medicines.¹⁷⁵

The trade interest of countries such as China, Ecuador and India in traditional medicines has been apparent in the continuing TBT Committee discussions on the impact on these countries' exports to the European Union. The Directive 2004/24/EC on traditional herbal medicinal products¹⁷⁶ provides a simplified regulatory approval process for traditional herbal medicines through a single approval which has effect across the European Union.

4. Concerns about misappropriation of traditional medicines

Research is continuing on traditional medicines and traditional medical knowledge in various different areas, each generating a multitude of policy issues:

- Traditional health practitioners develop their expertise through observation, building on empirical

understanding about the use of traditional formulations. Many countries increasingly seek to preserve and promote traditional medicine systems.

- Research efforts are being made to scientifically and clinically validate traditional medicines, to integrate them into countries' health systems.
- Traditional medicine and medical knowledge provide leads for the development of new treatments. Many existing modern medicines are originally based on herbal products. For example, oseltamivir, used to treat various influenza infections, is based on shikimic acid, which is isolated from Chinese star anise, a cooking spice used in TCM.¹⁷⁷ Current malaria treatments contain synthetic derivatives of artemisinin, which is derived from a plant, sweet wormwood, or *Artemisia annua*. This is an ancient Chinese medicine still used in modern practice that was used to treat malaria-stricken soldiers during the Viet Nam War and was developed through international partnership into a widely used pharmaceutical product for malaria treatment (Rietveld, 2008).
- Reflecting the clinical significance of traditional medicine, some programmes undertake an "integrative" approach, looking for synergies between "traditional" and "conventional" medical research. One such example is a research programme on good practice in TCM Research in the post-genomic era (Uzuner et al., 2012) and initiatives to integrate traditional and contemporary cancer care in the Middle East (Ben-Ayre et al., 2012).

The use of genetic resources (GR) and associated TK is primarily regulated by the Convention on Biological Diversity (CBD) and the Nagoya Protocol on Access to Genetic Resources and the Fair and Equitable Sharing of Benefits Arising from their Utilization to the Convention on Biological Diversity (Nagoya Protocol). National biodiversity policies frequently reference traditional medicines and medical research. Many other national policies seek to create medical R&D programmes on the basis of their heritage of GR and associated TK.

The essential effect of the CBD and the Nagoya Protocol is to confirm national sovereignty over GR and to establish a right of prior informed consent (PIC), approval and involvement, over the access to, and use of, associated TK. Many of the issues highlighted in this debate concern genetic materials used as the basis for medical research, and traditional medical knowledge that is either used directly to produce new products or is used as a lead in researching new treatments. The principal shift in focus has been to recognize that: (i) the custodians and practitioners of traditional medical knowledge may have legitimate rights; (ii) their knowledge cannot be assumed to be in the public domain, free for anyone to use; and (iii) as financial and non-financial benefits from R&D are shared along the product development pipeline, an equitable portion should also be provided to the origin or source of the material

used in research. The Commission on Intellectual Property Rights, Innovation and Public Health (CIPRH) has called for benefits derived from TK to be shared with the respective communities (WHO, 2006b).

How to apply PIC and equitable benefit sharing (EBS) has sparked a wide-ranging debate.¹⁷⁸ With regard to IP, however, the policy issues can be distilled into two broad themes:

- First, whether patents and other IPRs can and should be obtained over inventions derived from TK and GR. In particular, what mechanisms, if any, should be put in place to ensure that patents are not erroneously granted over TK and GR and that patent holders comply with the principles of PIC and EBS. Strategies to ensure that third parties do not gain illegitimate or unfounded IPRs over TK subject matter and related GR are known as “defensive protection”, such as measures to pre-empt or to invalidate patents that claim pre-existing TK as inventions.
- Second, how to recognize and give legal and practical effect to positive IPRs that owners or custodians of TK and GR may have, whether through the existing IP system or through *sui generis* rights. This is referred to as “positive protection”. Positive protection involves preventing unauthorized use of TK by third parties as well as active exploitation of TK by the originating community itself.

Concerns about improving patent examination in the TK area, in order to avoid erroneous patents on traditional medicines in particular, have led to initiatives at international and national levels. A leading example is the Traditional Knowledge Digital Library (TKDL), a collaborative project in India between the Council of Scientific and Industrial Research (CSIR), the Ministry of Science and Technology, and the Ministry of Health and Family Welfare. An interdisciplinary team of Indian medicine experts, patent examiners, information technology experts, scientists and technical officers have created a digitized system enabling consultation of existing literature in the public domain relating to Ayurveda, Unani, Siddha and Yoga. Such literature is generally available in traditional languages and formats. The TKDL therefore provides information on traditional medical knowledge in five international languages and formats which are understandable by patent examiners at international patent offices. The aim is to prevent the grant of erroneous patents,¹⁷⁹ while at the same time not newly publishing TK in a way that would facilitate its misappropriation. The WHO GSPA-PHI urges governments and concerned communities to facilitate access to traditional medicinal knowledge information for use as prior art¹⁸⁰ in the patent examination procedures, where appropriate, through the inclusion of such information in digital libraries (Element 5.1f). The WTO TRIPS Council has discussed how to preclude erroneous patents using

GRs and associated TK through the use of databases. This included a submission by Japan that had been previously submitted to the WIPO Intergovernmental Committee on Intellectual Property and Genetic Resources, Traditional Knowledge and Folklore (IGC).¹⁸¹

5. New approaches to IP protection of traditional medical knowledge

Parties to the CBD, WIPO and the WTO have considered the concept of a disclosure requirement in the patent system, put forward by its proponents as a means of ensuring that patents on inventions derived from TK and GR are consonant with the principles of PIC and EBS. The proposals and the debate are diverse and cover areas other than medicine, although patents in the medical area have been the major focus of the debate. The essential thrust of the proposal to implement a disclosure requirement in the patent system would be to require the patent applicant to notify the source or origin of TK/GR used in claimed inventions and to document compliance with PIC and EBS requirements. A number of countries have implemented such provisions in their national laws, but there is no agreed international standard. An alliance of developing countries has proposed a revision to the TRIPS Agreement to make such provisions mandatory,¹⁸² but other countries continue to question the usefulness and effectiveness of this kind of disclosure mechanism.¹⁸³

The cultural, scientific, environmental and economic importance of TK has led to calls for it to be preserved (safeguarded against loss or dissipation) and protected (safeguarded against inappropriate or unauthorized use by others), and there are many programmes under way at national, regional and international levels to preserve, promote and protect different aspects of TK. Such measures include: first, preserving the living cultural and social context of TK, and maintaining the customary framework for developing, passing on and governing access to TK; and second, preserving TK in a fixed form, such as when it is documented or recorded.

WIPO is primarily concerned with “protection” in the IP sense (i.e. the protection against copying, adaptation and use by unauthorized parties). The objective, in short, is to ensure that the materials are not used wrongly. Two forms of protection – positive protection and defensive protection – have been developed and applied, as outlined above.

The IGC is working on the development of an international legal instrument for the effective protection of TK. It is also working on ways to address IP aspects of access to, and benefit-sharing of, genetic resources. The WTO TRIPS Council has also extensively debated the protection of TK,¹⁸⁴ including an African Group proposal for a formal decision to establish a system of

TK protection, but this discussion has not led to any conclusions. The IGC work on TK¹⁸⁵ is concentrating on positive protection and the IP aspect of protection – the recognition and exercise of rights to preclude others from illegitimate or unauthorised use of TK. As WIPO member states are continuing efforts to negotiate on these issues, no final agreement has been reached. The text of an international legal instrument for the effective protection of TK is, therefore, in flux and new drafts continue to become available on a regular basis. The information set out below seeks to provide a broad and informal description of the nature of the discussions under way in the WIPO negotiations.

(a) Why protect traditional knowledge?

The IGC has considered the policy objectives for international protection,¹⁸⁶ including to:

- recognize the holistic nature of TK and its intrinsic value
- promote respect
- meet the actual needs of TK holders and empower TK holders
- promote conservation and preservation of TK
- support customary practices and community cooperation
- contribute to safeguarding TK
- repress unfair and inequitable uses and preclude unauthorized IPRs
- promote innovation and creativity, community development and legitimate trading activities
- ensure that PIC and exchanges are based on mutually agreed terms, and promote EBS.

(b) What is to be protected, and for whose benefit?

There is as yet no accepted definition of TK at the international level. In principle, TK refers to knowledge as such, in particular knowledge resulting from intellectual activity in a traditional context, and includes know-how, practices, skills and innovations. It is generally accepted that protection should principally benefit TK holders themselves, including indigenous peoples and local communities. However, there is no agreement on whether families, nations, individuals and others (such as the state itself) could be beneficiaries. While TK is generally regarded as collectively generated, preserved and transmitted, so that any rights and interests should vest in indigenous peoples and local communities, in some instances beneficiaries may also include recognized individuals within communities, such as certain traditional health practitioners (with a specific reference to traditional medical knowledge). Some countries do not use the term indigenous peoples or local communities and consider that individuals or families maintain TK.

(c) What is it to be protected from?

One problem confronting TK holders is the commercial exploitation of their knowledge by others, which raises questions of legal protection of TK against unauthorized use, the role of PIC and the need for EBS. TK holders also report lack of respect and appreciation for such knowledge. For example, when a traditional healer provides a mixture of herbs to cure a sickness, the healer may not isolate and describe certain chemical compounds and describe their effect on the body in the terms of modern biochemistry, but the healer has, in effect, based this medical treatment on generations of clinical experiments undertaken by healers in the past, and on a solid understanding of the interaction between the mixture and human physiology.

(d) How to protect traditional knowledge?

The diversity of TK means that no “one-size-fits-all” solution could suit all countries and communities. It is also a significant challenge to establish how protection under a national system could be enforced regionally and internationally.

Existing IPRs have been successfully used to protect against some forms of misuse and misappropriation of aspects of TK. Several countries have adapted existing IP systems to the needs of TK holders, including through specific rules or procedures to protect TK. For example, the Chinese State Intellectual Property Office has a team of patent examiners specializing in TCM. Other countries have developed new, stand-alone *sui generis* systems to protect TK. Thailand's Act on Protection and Promotion of Traditional Thai Medicinal Intelligence, B.E. 2542 (1999)¹⁸⁷ protects “formulas” of traditional Thai drugs and “texts on traditional Thai medicine”. It defines “traditional Thai medicinal intelligence” as “the basic knowledge and capability concerned with traditional Thai medicine”. The Act confers on the right holder – “those who have registered their IP rights on traditional Thai medical intelligence under the Act” – “the sole ownership on the production of the drug and research and development”. Peruvian Law No. 27811 of 24 July 2002, Introducing a Protection Regime for the Collective Knowledge of Indigenous Peoples Derived from Biological Resources,¹⁸⁸ is a *sui generis* regime for the protection of collective knowledge of indigenous peoples that is connected with biological resources. The Swakopmund Protocol on the Protection of Traditional Knowledge and Expressions of Folklore, within the Framework of the African Regional Intellectual Property Organization (ARIPO), adopted by ARIPO member states in August 2010,¹⁸⁹ aims: “(a) to protect traditional knowledge holders against any infringement of their rights as recognized by this Protocol; and (b) to protect expressions of folklore against misappropriation, misuse and unlawful exploitation beyond their traditional context”. The international legal

instrument for the effective protection of TK, which is being negotiated in the IGC, is a *sui generis* system. Other options are also available, such as contract laws, biodiversity-related laws, and customary and indigenous laws and protocols.

(e) Documentation

Documentation is especially important because it is often the means by which people beyond the traditional circle get access to TK. It does not ensure legal protection for TK, which means that it does not prevent third parties

from using TK. Depending on how the documentation process is carried out, it can either promote or damage a community's interests. IPRs may be lost or strengthened when TK is documented. WIPO has developed the *World Intellectual Property Organization (WIPO) Traditional Knowledge Documentation Toolkit* to help holders of TK, in particular indigenous peoples and local communities, protect their interests should they decide to document their TK.¹⁹⁰ This toolkit focuses on management of IP concerns during the documentation process, and also takes the documentation process as a starting point for more beneficial management of TK as a community's intellectual and cultural asset.

Endnotes

- 1 UN document E/C.12/2000/4.
- 2 Ibid.
- 3 UN document E/C.12/GC/17.
- 4 OHCHR/WHO, "The Right to Health", Fact Sheet No. 31, 2008.
- 5 UN document A/HRC/RES/17/14.
- 6 Ibid.
- 7 UN document A/HRC/RES/16/28.
- 8 UN document E/CN.4/RES/2004/26.
- 9 Source: United Nations (2012).
- 10 WHA, *Resolution: WHA49.14: Revised drug strategy*.
- 11 WHA, *Resolution: WHA52.19: Revised drug strategy*.
- 12 WHA, *Resolution: WHA56.27: Intellectual property rights, innovation and public health*.
- 13 WHA, *Resolution: WHA56.30: Global health-sector strategy for HIV/AIDS*.
- 14 WHA, *Resolution: WHA59.26: International trade and health*.
- 15 WHA, *Resolution: WHA60.30: Public health, innovation and intellectual property*.
- 16 For a list of relevant WHO and other intergovernmental organization publications, see www.who.int/phi/publications/category_ip_trade/en/index.html.
- 17 See Section 4(c) below.
- 18 WHA, *Resolution: WHA56.27: Intellectual property rights, innovation and public health*.
- 19 WHA, *Resolution: WHA59.24: Public health, innovation, essential health research and intellectual property rights: towards a global strategy and plan of action*.
- 20 For more on the CIPIH, see Chapter II, Section A.4(b).
- 21 WHA, *Resolution: WHA61.21: Global strategy and plan of action on public health, innovation and intellectual property*.
- 22 WHA, *Resolution: WHA61.21: Global strategy and plan of action on public health, innovation and intellectual property*, Annex, para. 7.
- 23 See Chapter III, Section C.3.
- 24 WHA, *Resolution: WHA61.21: Global strategy and plan of action on public health, innovation and intellectual property*, Annex, para. 14 (e).
- 25 Ibid, Annex Element 5.1(h).
- 26 WHA, *Resolution: WHA61.21: Global strategy and plan of action on public health, innovation and intellectual property*, para. 4(5).
- 27 See Chapter I, Section B.4.
- 28 WHA, *Resolution: WHA64.5: Pandemic influenza preparedness: sharing of influenza viruses and access to vaccines and other benefits*. See also Chapter III, Section E.
- 29 WHA, *Resolution: WHA64.14: Global health sector strategy on HIV/AIDS, 2011-2015*.
- 30 WHA, *Resolution: WHA65.19: Substandard/spurious/falsely-labelled/falsified/counterfeit medical products*.
- 31 UN document A/RES/66/2. See also WHA, Decision WHA65(8): Prevention and control of noncommunicable diseases: follow-up to the High-level Meeting of the United Nations General Assembly on the Prevention and Control of Non-communicable Diseases.
- 32 WHO (2007). See also Chapter IV, Section B and Figure 4.4.
- 33 See: NIH (2001); and www.who.int/ictrp/glossary/en/index.html. For information on the role of clinical trials in the drug development process, see Chapter III, Section B.5.
- 34 WHA, *Resolution: WHA58.34: Ministerial Summit on Health Research*.
- 35 See Chapter III, Section B.5.
- 36 See Sections (e)(vii) and (viii) below.
- 37 See Chapter IV, Section B.5.
- 38 See www.who.int/medicines/areas/quality_safety/regulation_legislation/icdra/en/index.html.
- 39 The supply of medicines and medical technologies within health systems, as well as procurement, price regulation and the funding of health systems are covered in Chapter IV.
- 40 The EMA has issued a number of scientific guidelines on biosimilar medicines. See www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/general/general_content_000408.jsp&mid=WC0b01ac058002958c.
- 41 See Anleitung für die Zulassung ähnlicher biologischer Arzneimittel (Biosimilars), www.swissmedic.ch/rechtstexte/00626/index.html?lang=de.
- 42 See www.who.int/biologicals/areas/biological_therapeutics/BIOTHERAPEUTICS_FOR_WEB_22APRIL2010.pdf.
- 43 See 42 U.S.C. § 262 Regulation of biological products.
- 44 For a review the economics of IP in the field of medical technologies, see Chapter II, Section C.5.
- 45 As discussed in Section B.5 below.
- 46 This effect of "multilateralizing" the scope of bilateral deals on IP is discussed in Chapter IV, Section D.
- 47 WIPO document SCP/12/3 Rev.2.
- 48 Ibid.
- 49 WIPO document MTN.GNG/NG11/W/24/Rev.1.

- 50 For further explanation on the patentability criteria, see Section (iii) below.
- 51 For details of the treaty, see www.wipo.int/treaties/en/registration/pct.
- 52 Article 27 of the PCT.
- 53 Notable regional agreements include: the European Patent Convention (EPC), the Eurasian Patent Convention, the Harare Protocol of the African Regional Intellectual Property Organization (ARIPO), the Bangui Agreement of the African Intellectual Property Organization, the Patent Regulation of the Gulf Cooperation Council (GCC) and Decision 486 on the Common Intellectual Property Regime of the Andean Community (CAN).
- 54 For an explanation on the term claim, see below in Section B.1(b)(vi).
- 55 See Chapter IV, Section C.1(b).
- 56 Rule 29 of the Implementing Regulations to the Convention on the Grant of European Patents, contained in the EPC, provides further clarifications regarding the patentability of inventions relating to the human body, the use of human embryos for industrial or commercial purposes and a number of other cases where the grant of European patents is excluded.
- 57 See G 002/06 (Use of embryos/WARF) of 25 November 2008, OJ 2009, 306, available at www.epo.org/law-practice/case-law-appeals/pdf/g060002ep1.pdf. See also T 1374/04 (Stem cells/WARF) of 7 April 2006, OJ 2007, 313, available at www.epo.org/law-practice/case-law-appeals/recent/t041374ex1.html.
- 58 See C-34/10 of the 18 October 2011, available at <http://curia.europa.eu/juris/liste.jsf?language=en&num=C-34/10>.
- 59 OJ 1998 L213/13.
- 60 WTO document IP/C/W/369/Rev.1.
- 61 This question is discussed further in Chapter III, Section D.3(a).
- 62 These issues are addressed in Chapter III, Section D.3(b).
- 63 Ibid.
- 64 Ibid.
- 65 WIPO document SCP/13/5.
- 66 See example of Supreme Court of Canada Decision of 8 November 2012, 2012 SCC, 60, *Teva Canada Ltd. v. Pfizer Canada Inc.*, available at <http://scc.lexum.org/decisia-scc-csc/scc-csc/scc-csc/en/item/12679/index.do>. The Supreme Court of Canada in its decision of 8 November 2012 [EN 70] held that the Canadian Patent 2,163,446 granted on an invention for the treatment of impotence was void because the patent application did not satisfy the disclosure requirements set out in the Canadian Patent Act, R.S.C. 1985, c. P-4. The court stated that adequate disclosure in the specification was a precondition for the granting of a patent. The specification, which included the claims and the disclosure, had to define the "precise and exact extent" of the right being claimed. The public, from the perspective of a person skilled in the art, had to be enabled only by the specification to make the same use of the invention as the inventor could at the time of the patent application. In this case the claims were structured as "cascading claims", with Claim 1 involving over 260 quintillion compounds, Claims 2 to 5 concerning progressively smaller groups of compounds, and Claims 6 and 7 each relating to an individual compound. The court stated that the practice of cascading claims was common and did not necessarily interfere with the disclosure requirement. The skilled reader knew that when a patent contained cascading claims, the relevant claim would usually be the one at the end concerning an individual compound. The compounds that did not work were simply deemed invalid with any valid claim surviving. However, in this case, the claims ended with two individually claimed compounds and there was no basis for a skilled person to determine, only from the disclosure in the specification, which of Claim 6 and Claim 7 contained the effective compound. Further testing would have been required to determine which of those two compounds was actually effective. Hence, the disclosure did not state in clear terms what the invention was, rather obscured it.
- 67 "Prior art" is, in general, all knowledge that has been made available to the public prior to the filing or priority date of a patent application under examination. Prior art is used to determine the scope of novelty and inventive step, two patentability requirements (WIPO document SCP/12/3 Rev.2).
- 68 WIPO documents SCP/12/3 and CDIP/7/3.
- 69 Patent grant procedures from an access to medicines perspective are addressed further in Chapter IV, Section C.1 and 2.
- 70 Further information on opposition Systems and other administrative revocation and invalidation mechanisms is contained in WIPO document SCP/18/4. Review procedures from an access to medicines perspective are addressed in Chapter IV, Section C.2.
- 71 Licensing is further addressed in Chapter III, Section D.4(c), and Chapter IV, Section C.3(d).
- 72 For further information, see Chapter IV, Section C.5(a)(vi).
- 73 See also WIPO documents SCP/13/3, SCP/15/3, SCP/16/3, SCP/17/3 and SCP/18/3. Exceptions and limitations and flexibilities in the patent system from an innovation and access to medicines perspective are addressed in Chapter III, Section D.4, and in Chapter IV, Section C.3(a), respectively.
- 74 See Chapter III, Section D.4(b).
- 75 Compulsory licences are discussed in Chapter IV, Section C.3(i) and (ii).
- 76 Patent information is addressed in Chapters III, Section D.4(f), and IV, Section C.4, from an innovation and access to medicines perspective.
- 77 See the online WIPO publication, *Handbook on Industrial Property Information and Documentation*, www.wipo.int/standards/en/.
- 78 For a list of WIPO Standards, Recommendations and Guidelines, see www.wipo.int/standards/en/part_03_standards.html.
- 79 For more information, see: WIPO *Handbook on Industrial Property Information and Documentation* (available at www.wipo.int/standards/en/pdf/08-01-01.pdf); and the EPO

- patent family definitions (available at www.epo.org/searching/essentials/patent-families.html).
- 80 An overview about freedom to operate issues is provided in Chapter III, Section D.4(g).
- 81 One WIPO technical study (WIPO document CDIP/4/3 REV./STUDY/INF/3.) examined the availability of legal status data from primary sources and secondary sources, and described the challenges associated with the availability, reliability and comparability of such data. A total of 87 patent authorities contributed information to the study, which confirmed the sometimes deficient situation regarding availability of reliable legal status data and their comparability. The study includes recommendations for improvement, which would require considerable commitment from national authorities. For further information on the WIPO Project on Patent Legal Status Data, see www.wipo.int/patentscope/en/programs/legal_status/index.html.
- 82 The book's full title is the *Approved Drug Products with Therapeutic Equivalence Evaluations* and is available at www.fda.gov/Drugs/InformationOnDrugs/ucm129662.htm.
- 83 See www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/CFRSearch.cfm?fr=314.53.
- 84 See www.hc-sc.gc.ca/dhp-mps/prodpharma/patregbrev/index-eng.php.
- 85 Source: The Medicines Patent Pool, available at www.medicinespatentpool.org/patent-data/.
- 86 See Chapters II, Section B.5, and IV, Section C.5.
- 87 This is explained in Chapter IV, Section C.3(iii).
- 88 Ibid.
- 89 Directive 2004/27/EC of the European Parliament and of the Council of 31 March 2004 amending Directive 2001/83/EC on the Community code relating to medicinal products for human use.
- 90 See www.wipo.int/madrid/en/.
- 91 See www.who.int/medicines/publications/druginformation/innlists/en/index.html. In addition, the INN Extranet, MedNet, grants free access to the INN searchable database: <http://mednet.who.int/>.
- 92 WIPO document SCT/19/4.
- 93 Other countries, such as Australia, Canada, Japan, Mexico and South Africa have established their own reviews of proprietary names under their ministries of health.
- 94 The FDA Division of Medication Error Prevention and Analysis (DMEPA) and the EMA (Invented) Name Review Group (NRG).
- 95 The NRG rejected 47 per cent of all proposed names in 2011. See EMA, "Overview of Invented Names Reviewed in November 2011 by the Name Review Group (NRG)", Press Release EMA/802336/2011, 2011. DMEPA rejects "roughly one-third of all proposed proprietary names" (Scheib and Witherell, 2011).
- 96 Case No. 594/2000: Delivered in March 25, 2002, by Pretoria's High Court in favour of Beecham Group plc and SmithKline Beecham Pharmaceuticals (Pty) Ltd acting as Plaintiffs, against Biotech Laboratories (Pty) Ltd acting as Respondent. The Court considered the Plaintiffs had demonstrated that the package insert qualified as a literary work according to the definition of the South African Copyright Act, and interdicted Biotech from infringing the copyright. Biotech Laboratories (Pty) Ltd appealed the Court's decision, which was dismissed with costs.
- 97 Case No. FCA 1307: Delivered in November 18, 2011 by the Federal Court of Australia, not entitling to any relief in respect of copyright infringement to the Plaintiffs: Sanofi-Aventis Australia Pty Ltd, Sanofi-Aventis Deutschland GmbH and Aventisub II Incorporated, against the Respondent Apotex Pty Ltd.
- 98 See Chapter IV, Box 4.10.
- 99 Ibid.
- 100 See: WTO documents IP/C/W/570 and IP/C/W/571; and European Commission (2010).
- 101 See Chapter IV, Section C.3(e).
- 102 Developments regarding IP enforcement and the link with access to medical technologies, including the impact of higher enforcement standards resulting from either national or interregional frameworks, such as the Anti-Counterfeiting Trade Agreement (ACTA), are discussed in Chapter IV.
- 103 WIPO document CDIP/5/4 Rev.
- 104 WTO document WT/L/540. See Chapter IV, Section C.3(iii), and Annex II.
- 105 See www.wipo.int/treaties/en/agreement/trtdocs_wo030.html.
- 106 WIPO document CDIP/5/4 Rev.
- 107 Ibid.
- 108 WIPO documents CDIP/7/3 and CDIP/7/3 Add.
- 109 See www.wipo.int/treaties/en/agreement/trtdocs_wo030.html.
- 110 See Chapter III, Section D.4(b).
- 111 See Chapter III, Box 3.8.
- 112 See Chapter IV, Section C.3(iii).
- 113 See Chapter II, Section B.1(g)(v).
- 114 See Chapter IV, Section C.3(a)(i).
- 115 The report is available at <http://whqlibdoc.who.int/hq/2001/a73725.pdf>.
- 116 For records of the special session, see WTO document IP/C/M/31.
- 117 For an explanation, see Chapter IV, Section C.3(c).
- 118 See Chapter IV, Section C.3(a)(iii).
- 119 UN documents A/RES/65/1 and A/RES/65/277.
- 120 WTO document IP/C/25.

- 121 WTO document WT/L/478. *Research and Development under the Antimonopoly Act is available at www.jftc.go.jp/en/legislation_guidelines/ama/pdf/jointresearch.pdf.*
- 122 WTO document IP/C/40.
- 123 WTO document WT/L/845. 137 For more details on tariff data, see Chapter IV, Section D.1.
- 124 WTO document IP/C/W/583. 138 See www.haiweb.org/medicineprices.
- 125 Article 18(8), Law No. 31/2009 of 26/10/2009 on the Protection of Intellectual Property. 139 For further details, see WHO/WTO (2002).
- 126 See Chapters II, Section B.1(g)(v), and IV, Section B.6. 140 Ibid.
- 127 See www.wipo.int/wipolex/en/other_treaties/details.jsp?treaty_id=227. 141 These sectoral descriptions are found in the Services Sectoral Classification List (WTO document MTN.GNS/W/120), which WTO members have generally used for scheduling their GATS commitments. Sectors (i) to (iii) above are found in the section on "Health-Related and Social Services" sector; sectors (iv) and (v) under "Professional Services" and (vi) under "Financial Services".
- 128 WTO document LT/UR/A/2.
- 129 WTO document WT/ACC/UKR/152, paras. 425, 433 and 512. 142 If one takes into account horizontal limitations listed in some schedules (i.e. limitations applying across all scheduled sectors), partial commitments dominate.
- 130 WTO document WT/L/508.
- 131 WTO document WT/L/846. See www.wipo.int/wipolex/en/other_treaties/details.jsp?treaty_id=227. 143 WHO, "Migration of Health Workers", Fact Sheet No. 301, 2010.
- 132 WTO document WT/L/508/Add.1. 144 For additional details, see Müller and Pelletier (forthcoming).
- 133 See World Bank (2005, 2009). For a list of the OECD publications, see www.oecd.org/regreform/liberalisationandcompetitioninterventioninregulatedsectors/bestpracticetablesandpapersoncompetitionpolicy.htm. In particular, see the following Policy Roundtable papers: Generic Pharmaceuticals (2009); Competition, Patents and Innovation II (2009); Competition, Patents and Innovation (2006); Competition in the Provision of Hospital Services (2005); Enhancing Beneficial Competition in the Health Professions (2004); Competition in the Pharmaceutical Industry (2000); and, more generally, Relations Between Regulators and Competition Authorities (1998). 145 For the full content of GPA parties' schedules (Appendix 1), including the relevant thresholds, see www.wto.org/english/tratop_e/gproc_e/gp_gpa_e.htm.
- 134 Recent mergers between pharmaceutical companies have been reported as resulting in reduced R&D activity in the sector. See, for example, LaMattina (2011). 146 See <http://shenyang.usembassy-china.org.cn/wto-gpa.html>.
- 135 "Exclusive grantback conditions" refer to any obligation on a licensee to grant an exclusive licence to the licensor in respect of its own improvements to, or its own new applications of, the licensed technology. "Conditions preventing challenges to validity" are those that impose an obligation on a licensee not to challenge the validity of IPRs held by the licensor. "Coercive package licensing" refers to an obligation on a licensee to accept a licence on several different technologies when the licensee's interest is limited to only part of these technologies. 147 Additional statistical information is available at www.wto.org/english/tratop_e/gproc_e/gp_gpa_e.htm.
- 136 In that regard, several national or regional competition agencies have published guidelines providing solid foundation for their analysis of IP and antitrust cases: US Department of Justice/Federal Trade Commission (1995); European Commission, Guidelines on the application of Article 81 of the EC Treaty to technology transfer agreements, EC document 2004/C 101/02; for Canada, see Competition Bureau (2000); an unofficial translation of the Japanese Fair Trade Commission, *Guidelines for the Use of Intellectual Property under the Antimonopoly Act* is available at www.jftc.go.jp/en/legislation_guidelines/ama/pdf/070928_IP_Guideline.pdf, *Guidelines on Standardization and Patent Pool Arrangements* is available at www.jftc.go.jp/en/legislation_guidelines/ama/pdf/Patent_Pool.pdf and *Guidelines Concerning Joint* 148 It should be noted that the following analysis focuses only on the market access opportunities available under the GPA. It does not consider barriers to market access that could arise outside the scope of the GPA (e.g. IPRs).
- 149 WTO document GPA/102/Add.3. It is recalled that the GPA applies to the entities, goods and services that are specified in each individual party's schedules. 150 WTO document GPA/94/Add.4.
- 151 WTO document GPA/108/Add.4. The reported value was expressed Special Drawing Rights (SDRs) and has been converted to US dollars. The estimate may be affected by variations in exchange rates and related problems of conversion. 152 Some of the specific features of the FTAs relevant to pharmaceuticals are discussed in Chapter IV, Section C.5.
- 153 Economics teaches us that, under certain assumptions, static social welfare is maximized when consumers and producers are able to achieve the maximum surplus possible in a given market, such as a market for a specific medicine. Consumer surplus is the difference between the price a consumer pays for this medicine and the price he would be willing to pay rather than do without it. Producer surplus is the difference between the amount that a producer of the medicine receives and the minimum amount that he or she would be willing to accept for the medicine (or marginal cost). 154 For examples of these kinds of measures, see Chapter IV, Section B.1.

- 155 Exhaustion and parallel imports are discussed in Chapter IV, Section C.3(b).
- 156 For further details, see Chapter IV, Section B.2.
- 157 For other examples on the national implementation of test data, see Chapter II, Section B.1(c)(iii).
- 158 See Chapter III, Section C.4.
- 159 WHO, "Traditional Medicine", Fact Sheet No. 134, 2008, available at www.who.int/mediacentre/factsheets/fs134/en/.
- 160 For a definition of herbal medicines, see <http://apps.who.int/medicinedocs/en/d/Jh2984e/>.
- 161 WHO, "Traditional Medicine", Fact Sheet No. 134, 2008, available at www.who.int/mediacentre/factsheets/fs134/en/.
- 162 China Daily, "TCM Exports Set to Rise at a Healthy Clip", 10 February 2012, available at www.china.org.cn/business/2012-02/10/content_24601720.htm.
- 163 WHO, "Traditional Medicine", Fact Sheet No. 134, 2008, available at www.who.int/mediacentre/factsheets/fs134/en/.
- 164 WHA, *Resolution: WHA41.19: Traditional medicine and medicinal plants*.
- 165 WHA, *Resolution: WHA56.31: Traditional medicine*.
- 166 WHA, *Resolution: WHA61.21: Global strategy and plan of action on public health, innovation and intellectual property*.
- 167 WHA, *Resolution: WHA62.13: Traditional medicine*.
- 168 See also WIPO documents WIPO/GRTKF/IC/3/9 and WIPO/GRTKF/IC/17/INF/9.
- 169 WIPO document WIPO/GRTKF/IC/3/6.
- 170 UN document A/RES/61/295.
- 171 See www.who.int/medicines/areas/traditional/irch/en/index.html. As of August 2009, member states include Armenia, Australia, Brazil, Canada, China, Ghana, Hungary, India, Indonesia, Japan, Malaysia, Mexico, Pakistan, the Republic of Korea, the Kingdom of Saudi Arabia, Singapore, the United Arab Emirates, the United Kingdom and the United States. The three regional/sub-regional bodies are the Association of Southeast Asian Nations (ASEAN), the European Medicines Agency (EMA) and the Latin American Parliament (PARLATINO).
- 172 Guidelines and other relevant documents can be found at http://apps.who.int/medicinedocs/en/cl/CL10.1.3/clmd,50.html#hICL10_1_3.
- 173 WHO Monographs can be found at http://apps.who.int/medicinedocs/en/cl/CL10.1.4.3/clmd,50.html#hICL10_1_4_3.
- 174 For more information, see the WTO TBT Information Management System, available at <http://tbtims.wto.org/>.
- 175 Guidelines and other relevant documents can be found at http://apps.who.int/medicinedocs/en/cl/CL10.1.3/clmd,50.html#hICL10_1_3.
- 176 Directive 2004/24/EC of the European Parliament and of the Council of 31 March 2004 amending, as regards traditional herbal medicinal products, Directive 2001/83/EC on the Community code relating to medicinal products for human use.
- 177 See www.roche.com/med_mbtamiflu05e.pdf.
- 178 For the political debate on access and benefit-sharing aspects regarding the sharing of viruses, see Chapter III, Section E.
- 179 See www.tkd.res.in/tkd/langdefault/common/outcome.asp?GL=Eng.
- 180 For more information on prior art, see Endnote 67 above.
- 181 WTO document IP/C/W/472. Japan has submitted this proposal originally to the IGC as WIPO document WIPO/GRTKF/IC/9/13. See also WIPO documents WIPO/GRTKF/IC/20/INF/9 and WIPO/GRTKF/IC/20/INF/11.
- 182 See WTO document IP/C/W/474 and addenda.
- 183 See WTO documents IP/C/W/368/Rev.1 and Corr.1, IP/C/W/370/Rev.1. Discussions are ongoing in the TRIPS Council. They are regularly reported in the minutes of the meetings. For the latest report, see WTO document IP/C/M/70.
- 184 WTO documents IP/C/W/368/Rev.1 and IP/C/W/370/Rev.1.
- 185 See www.wipo.int/tk/en/igc/index.html.
- 186 The latest version of the negotiating text is available at www.wipo.int/tk/en/igc/index.html.
- 187 See www.wipo.int/wipolex/en/details.jsp?id=5790.
- 188 See www.wipo.int/wipolex/en/details.jsp?id=3420.
- 189 See www.wipo.int/wipolex/en/other_treaties/details.jsp?treaty_id=294.
- 190 The Consultation Draft of the WIPO Traditional Knowledge Documentation Toolkit is available at www.wipo.int/tk/en/tk/TKToolkit.html.

III. Medical technologies: the innovation dimension

Chapter II has described the main elements of the policy framework for innovation and access. This chapter considers how this policy framework applies to innovation in medical technologies. It reviews the factors that have spurred innovation in medical technologies in the past, identifies how current models of research and development (R&D) are evolving, charting the role of established and new participants in the innovation process, including in the context of neglected diseases. It also covers issues raised in the area of intellectual property (IP), particularly the patent system.

The chapter reflects the fact that health policy-makers in the past decade have paid greater attention to the innovation dimension, considering in particular:

- the kind of collaborative structures, incentive mechanisms, sources of funding and informatics tools that are required in order to build more effective and more broadly-based and inclusive innovation processes
- how to ensure that medical research activities focus increasingly on areas neglected so far.

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A. Historical pattern of medical R&D

Key point

- R&D in the modern pharmaceutical sector evolved in typically large, privately-owned companies where both R&D and marketing were carried out in-house. Initially, production was widely licensed by originator companies. Later, however, marketing and the distribution of new medicines were generally undertaken through a system of exclusive rights to single suppliers.

1. Innovation for medical technologies in context

Innovation in medical technologies is distinct from innovation in general. It is characterized by several distinguishing features:

- The need for a rigorous regulatory framework to assess medical technologies in terms of their quality, safety, and efficacy or effectiveness.
- The high costs of research and development (R&D) and the concomitant high risk of failure.
- A high level of public-sector input, in terms of input from basic research, funding and infrastructure and also in terms of influencing the market for finished products.
- The inherent ethical component of medical research, and the potential negative impact on public health of closely held or overly restrictive management of technology and intellectual property (IP).

Historical trends in medical R&D and the development of the modern pharmaceutical industry provide context for the dynamics of current developments and the challenges facing the existing innovation system and overall R&D landscape and are therefore important to understand.

2. From early discoveries to “wonder drugs”

Despite important medical discoveries in the 18th and 19th centuries, at the beginning of the 20th century, few medicines were available to treat basic infectious diseases. Prior to the 1930s, the pharmaceutical industry did not invest in R&D to any great extent. However, the discoveries in Europe that certain chemicals and microorganisms could be used to treat infections led to the development of a range of derivative products which served as effective anti-bacterial agents. Producing at industrial scale proved to be another challenge. For example, it was only in 1939, ten years after Alexander Fleming discovered penicillin, that mass manufacture of penicillin got under way at US Department of Agriculture facilities. Subsequently, private pharmaceutical companies were enlisted to develop and market the drug. It is notable that while both penicillin and sulphanilamide formed the

basis of a generation of new “wonder drugs” or antibiotics, neither was patented. These medicines were developed and marketed in collaboration with teams of researchers from both not-for-profit organizations and private enterprises.

3. Growth and evolution of the modern pharmaceutical industry

The turmoil of war and migration, among other factors, led to the shift of leadership in the pharmaceutical industry from Europe, particularly Germany, to the United States, although trans-Atlantic rivalries continued to be sharp. The mid-1940s saw the rise of the US-based pharmaceutical industry, and several factors influenced this, including the introduction of regulation on prescription drugs and changes in how patent law was applied.¹ The interplay between these two specific factors helped develop the modern, vertically integrated pharmaceutical firm which undertakes both in-house R&D and marketing. From 1950 to 1970, the ratio of R&D investments to sales revenues in the US pharmaceutical industry more than doubled, while the ratio of advertising expenses to sales revenues was even higher. Most of the marketing expenditure comprised the cost of informing and influencing doctors on prescription medicines. The period from the late 1940s onwards saw an increase in the grant of both product and process patents for pharmaceuticals.² During the period 1950 to 1970, the pharmaceutical industry returned consistently higher levels of profits than most manufacturing companies at that time.

Tight control of R&D and marketing was necessary because these companies derived most of their revenues from a very small number of successful products (Comanor, 1986). The basis for competition among these companies changed from price factors to non-price factors, such as research and advertising outlays and outputs. This model helped to incentivize innovation – the US R&D-based pharmaceutical industry moved from an average of 20 new products per year in the 1940s to an average of 50 new products per year in the 1950s.

The period 1930 to 1960 saw the introduction of innovations in organic and natural products chemistry, which in turn led to the isolation and synthesis of vitamins, corticosteroids, hormones and anti-bacterial agents. The following years were marked by the industry moving from chemistry-based

R&D and manufacturing to pharmacology and life sciences-based activities. Also during this period, a phased system for developing new medicines was established – the so-called “Phase I – IV” system for clinical trials.³

4. From non-exclusive licensing to restricted production

In the period up to 1960, a key development was that innovative companies began to exclusively produce products themselves, without licensing them to others. This enabled them to restrict output and generate larger profits. A practice of licensing with high royalty payments could potentially have delivered the same profits to these innovator companies, but such royalty payment rates would have had to be very high in the face of inelastic demand (i.e. consumers’ demand for a product does not change appreciably in response to a one-per-cent increase in price). By one estimate, when demand is inelastic, the royalty rate required to yield a return equivalent to an exclusive, single supply model would be 80 per cent (Temin, 1979). Relatedly, one estimate of the wholesale price of tetracycline, before the introduction of generic versions of this medicine in the United States, was US\$ 30.60 per 100 capsules, whereas the production cost for the same quantity was just US\$ 3.00, thus generating a profit rate of 90 per cent. Such high royalty rates would have been commercially unacceptable as royalty rates at that time were typically just 2.5 per cent. Apart from being the rate at which streptomycin was licenced, the 2.5-per-cent rate would have also applied in a US Federal Trade Commission (FTC) decision relating to a compulsory licence for tetracycline. However, this FTC decision did not subsequently enter into force for other reasons (Scherer and Watal, 2002).

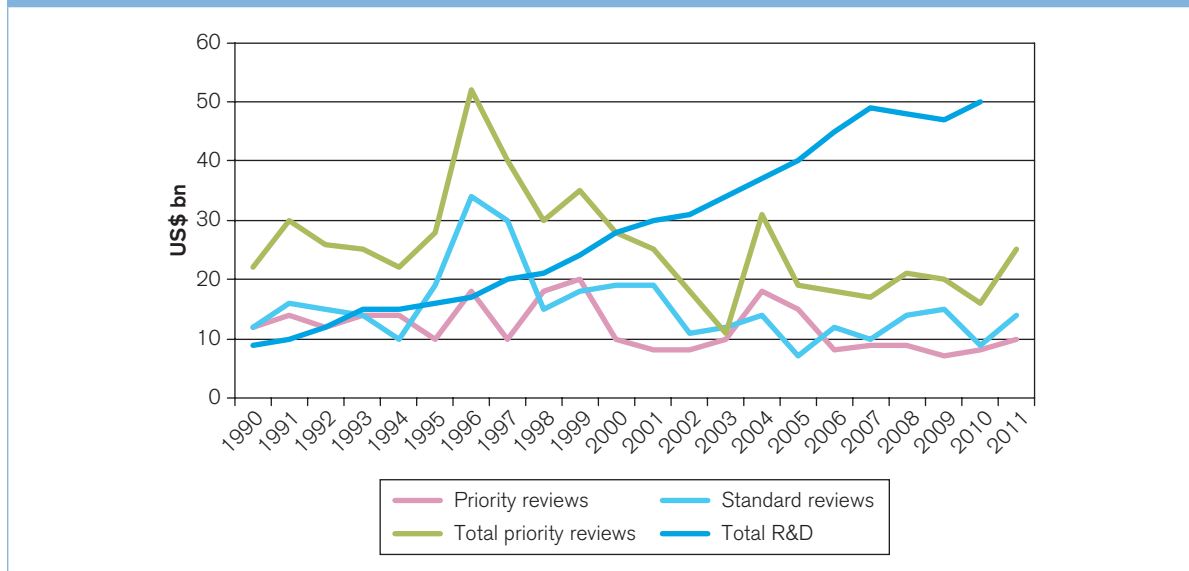
These conditions of exclusivity and product differentiation extended beyond antibiotics to all medicines obtained through R&D. For instance, the first generation of steroids was widely licensed, while the second generation of synthetic steroids was exclusively produced by patent-owning companies (Temin, 1979).

5. R&D productivity: early gains, regulatory concerns

Between 1961 and 1974, the world’s pharmaceutical companies introduced some 83 new molecular entities (NMEs) per year. By the late 1980s, this had declined to 50 NMEs per year. Between 1961 and 1990, 2015 NMEs were successfully marketed (Ballance et al., 1992, p. 86). More than 90 per cent of all new drugs were discovered and developed by pharmaceutical companies operating in Belgium, France, Germany, Italy, Japan, the Netherlands, Sweden, Switzerland, the United Kingdom and the United States (Ballance et al., 1992, p. 108).

This period was marked by the availability of several competing new drugs to treat the same disease, largely a consequence of the introduction of “me-too” drugs to compete with breakthrough, new drugs. In order to finance their investments in R&D and marketing, companies had to have a steady stream of new, improved drugs which could attract a price premium globally. That there have been relatively few new drug approvals, and even fewer new important breakthrough drugs in relation to the R&D expenditures, can be seen from the total priority and standard reviews approved in the US Food and Drug Administration. This is despite the fact that R&D expenditure in the private sector rose fivefold between 1990 and 2010 (see Figure 3.1).

Figure 3.1. Number of new drug approvals and expenditure on R&D, as reported by PhRMA, in the United States, 1990-2011



Source: WHO (2012a).

As early as 1959, the Kefauver Committee report accused the industry of price gouging through duplicative research and molecule manipulation to create therapeutically equivalent products. Sceptical views expressed in the current global debate about the benefits of competition, and the appropriate level of returns for innovation in the context of biomedical R&D, echo some of these early criticisms. The 2006 Congressional Budget Office report summed up the situation as follows: “The more accurately a drug’s price reflects its value to consumers, the more effective the market system will be at directing R&D investment toward socially valuable new drugs. However, prices can only serve that directing role to the extent that good information exists about the comparative qualities of different drugs and that consumers and health care providers use that information” (USCBO, 2006, p. 5). Certain criticisms of the industry notwithstanding, there is little doubt that modern medicines and technologies have contributed to longevity, especially in countries that have access to newer medicines (Lichtenberg, 2012).

B. The current R&D landscape

Key points

- The conventional innovation model in medical technologies is facing considerable challenges, including changing markets, higher costs, and more stringent regulatory standards.
- The public sector significantly impacts the innovation cycle at various stages, directly providing key R&D inputs, helping to shape private companies' R&D priorities, and influencing how health products are procured and disseminated.
- Developing pharmaceutical products and bringing them to market is usually costly and time consuming. However, limited data make it difficult to produce a reliable, independent assessment of the true costs of medical research.
- There are many different mechanisms for promoting innovation. Intellectual property rights (IPRs) are a useful incentive mechanism, but it is debatable whether the IP system can incentivize inventions in areas where there is no market.
- The WHO Commission on Intellectual Property Rights, Innovation and Public Health (CIPIH) found that the innovation cycle is self-sustaining in industrialized countries which have a large market, thus enabling companies to recoup their investments in innovation. This is not the case in low-income countries, where markets are small and health services are underfunded.
- Innovation policy instruments can differ to the extent that they address publicly funded and executed research, publicly funded but privately executed research, or privately funded and executed research.
- Vaccines are different from medicines in many respects. As there are no generic vaccines, the process of proving the safety and efficacy of a vaccine, even if it is a "copy", always requires a full regulatory dossier. Recent years have seen a significant increase in the development of new vaccines, and new models of innovation, coupled with a growing number of vaccine manufacturers in low- and middle-income countries (LMICs).
- The WHO has established a clinical trials registry that makes clinical trial data publicly available. The publication of results of clinical trials is in the interest of both public health and science.

This section reviews the challenges faced by today's pharmaceutical industry, against the background of its evolution outlined in the previous section.

1. A time of challenge for the pharmaceutical industry

The conventional innovation model in the pharmaceutical industry faces considerable challenges, not only with regard to the way innovation is carried out through knowledge networks, but also with regard to the marketplace it is seeking to serve (Tempest, 2011). The structure of the industry itself is evolving, including through mergers and acquisitions among R&D-based companies, in a bid to strengthen innovative pharmaceutical pipelines. It is also evolving as a result of acquisitions of generic pharmaceuticals companies by R&D-based companies and vice versa, thus blurring the traditional boundary between R&D-based companies and generic drugs companies.

Additional drivers of change in business models and in industry structure include:

- Growing diversity in innovation models and pathways to product development – with dynamic competitive pressures growing not merely between individual companies but also between distinct innovation strategies. For example, the exploration of the use of virtual R&D by leading R&D-based pharmaceutical companies – in terms of information and communications technology (ICT) that would involve the use of collaborative models (PwC, 2008).
- Regulatory processes, including more stringent safety standards and post-marketing surveillance, due to lower acceptance of risk.
- Expiry of patents on key blockbuster drugs ("patent cliffs"), one estimate is that, between 2012 and 2018, patent expiry and consequent generic entry will reduce revenues of R&D-based pharmaceutical companies by about US\$ 148 billion (PwC, 2012).
- A greater concentration on emerging economies – both as a rapidly growing market for medical technologies and as an increasingly viable base for research, development and effective commercialisation of research. For example, non-OECD economies accounted for

18.4 per cent of the world's R&D, up from 11.7 per cent in 1996 (PwC, 2008).

- Emergence of biologics that cannot be replicated as easily as can new small molecule pharmaceuticals (see further explanation below).
- Slowing demand in developed-country markets due to the recession and competing pressures on government budgets, and the shift in focus to emerging markets due to higher growth in demand there.

The latest wave of innovation in medical technologies, gathering pace from around 1980, is based on advances in the discovery and application of biotechnology. The growing use of bioinformatics in virtual R&D to create computer models of organs and cells offers significant potential for tailored drug discovery and development (PwC, 2008). The decoding of the human genome in the late 1990s spurred hopes of a new wave of innovation in personalized medicine. However, the promise of genomics delivering more precise diagnostics and medicines, also dubbed "precision medicines", has yet to be fully realized (Pray, 2008).

Changes are also occurring in the way innovation is taking place. The increasing importance of emerging economies markets for the industry, for example, leads the medical devices industry to adapt their innovation models to the specific demands of these markets (see Box 3.1).

2. Public-sector researchers play a key role in medical R&D

In the first phase of modern medical R&D, most products were developed by private companies, with little attention paid to understanding the causes of particular illnesses and diseases, or to understanding metabolic pathways. It required a determined effort on the part of governments to bring the insights from public-sector research to bear on the product development priorities of the private sector. The division of labour between the private sector and the public sector during these later "waves" of innovation was such

that the public sector began to concentrate on upstream research that provided basic scientific knowledge on the mechanisms of disease and immune reactions. As a result of the concentration on this area, researchers identified the entry points for effective medications. Companies then focused on downstream applied research and the development of products and, by doing so, they translated basic research into medical products. The main reason for this division of labour was that, globally, the vast majority of early stage research – which is essentially not marketable or profitable as such – is funded by governments and other public-sector institutions. The public sector thus significantly influences the innovation cycle by shaping research priorities, at least with regard to basic research (WHO, 2006b; USCBO, 2006).

Today, public-sector bodies continue to have an impact on early-stage drug development, but they also play an important role in the innovation cycle at subsequent stages. Governments, for example, control the quality of health products through their regulatory frameworks, which determine whether a product gets to the market and, if so, how quickly. Additionally, the public sector plays a critical role in the delivery phase of health products because governments are usually the main purchasers of health products and they often organize the distribution and delivery of such products.

In order to support biomedical sciences, and also to facilitate research at universities, some governments set up dedicated research institutes in the late 19th and early 20th century. Thus began the interaction between universities and government research institutions, which carried out the basic research, and the private sector, which developed and commercialized medicines based on this research. In recent years, a number of universities have developed extensive patent portfolios and many of the new companies focusing on biotechnology are originally spin-offs from universities. Non-profit entities play an important role in the funding of biomedical research, principally in high-income countries – the Howard Hughes Medical Institute in the United States and the Wellcome Trust in the United Kingdom are good examples of this type of initiative. In the developing

Box 3.1. Adapting innovation to local needs in the medical devices industry

Increasingly, private-sector medical devices companies are seeking to specifically design new devices and health care delivery models which can be adapted to the needs of LMICs. These actions reflect a growing level of commitment among companies to serve long-neglected markets; they also reflect companies' greatly increased interest in the commercial opportunities arising from addressing the health needs of people who inhabit the middle and bottom of the socio-economic pyramid. As a result, companies are committing greater resources towards evaluating local and regional barriers, and are creating tailored products and services to meet specific cultural or geographic needs. One of the outcomes of this development is devices that are more adapted to the needs of LMICs. Such devices are also less costly than those designed for markets in high-income countries and are thus more affordable. The design of the devices may also serve to enhance accessibility. The development of a portable and more affordable version of the common electrocardiograph – aimed at increasing access to health care in low-income rural areas – is an interesting example.⁴

Box 3.2. The case of paclitaxel

Screening of the Pacific yew tree for therapeutic effect was initiated as a cooperative venture between the US Department of Agriculture and the National Cancer Institute (NCI) at the NIH. In 1964, extracts from the bark of the Pacific yew tree were tested against two cancer cell lines and were found to have promising effects. In 1969, following research on extracts from the bark of the tree, the active compound, paclitaxel, was isolated. In 1979, the pharmacologist Susan Horwitz and her co-workers at the Albert Einstein College of Medicine at Yeshiva University reported a unique mechanism of action for paclitaxel. In 1983, the NCI supported clinical trials with paclitaxel, and in 1989, NCI-supported clinical researchers at Johns Hopkins University reported very positive effects in the treatment of advanced ovarian cancer. Also in 1989, the NCI reached an agreement with a pharmaceutical company to increase the production, supply and marketing of paclitaxel. Paclitaxel began to be marketed for the treatment of ovarian cancer in 1992. Subsequently, the pharmaceutical company adopted a semi-synthetic process for manufacturing the product.⁵

world, research institutions are also beginning to build up substantial patent portfolios. For example, in January 2013, the Council for Scientific and Industrial Research in India held 702 patents on medicines and 450 patents in biological sciences.⁶ The US government provides significant funding for medical R&D, especially through the National Institutes of Health (NIH).

The story of the development and marketing of paclitaxel provides an example of how public and private enterprise can cooperate in the development of new discoveries and new drugs (see Box 3.2).

A recent study suggests that public-sector research has had a more immediate effect on improving public health than might be expected (Stevens et al., 2011). According to the study, of the 1,541 US Food and Drug Administration (FDA) approvals between 1990 and 2007, a total of 143 (9.3 per cent) related to drugs developed as a result of public-sector research. However, of the 348 priority reviews, 66 drugs (19 per cent) had resulted from public-sector research. In other words, public-sector research accounted for twice the overall priority reviews rate. Viewed from another perspective, 46.2 per cent of new-drug applications from public-sector research received priority reviews. This compares with 20 per cent of new drug applications, which were developed solely as a result of private-sector research, thus representing an increase by a factor of 2.3. Therefore, products resulting from public-sector funded research apparently have a greater therapeutic effect than those resulting from private sector research.

3. Medical R&D costs

One of the main arguments put forward by industry with respect to the need for strict protection of IPRs is the high cost of R&D for new medical products. Developing a pharmaceutical product from laboratory stage to marketing stage takes a long time and entails the additional burden of complying with stringent regulatory approval processes, thus resulting in a small number of successful products. There are, however, few sources of data available that enable the true costs of medical research to be assessed.

According to the report on the European Commission pharmaceutical sector inquiry covering the period 2000 to 2007, European originator companies spent an average of 17 per cent of turnover generated from sales of prescription medicines on R&D. Approximately 1.5 per cent of turnover was spent on basic research to identify potential new medicines, while 15.5 per cent of turnover was spent on developing the identified potential medicines through clinical trials on products. As in earlier decades, marketing and promotional activities exceeded R&D costs, accounting for 23 per cent of originator companies' turnover during this period.⁷

While these figures reveal the costs of research in relation to originator companies' overall turnover, a number of estimates have been made about the average absolute costs of R&D for new medicines. Costs greatly depend on the type of medicine in question. There is a huge difference in costs between a medicine based on a new chemical entity (NCE) not previously used in any pharmaceutical product, and an incremental modification of an existing medicine. However, even for NCEs the stated costs differ widely.

In 2007, the Pharmaceutical Research and Manufacturers of America (PhRMA) estimated that it takes between 10 and 15 years to bring a new medicine (based on an NCE) from discovery to market at an average cost for R&D of US\$ 800 million to US\$ 1 billion. This estimate included the costs of failed research projects (PhRMA, 2007). In 2011, PhRMA estimated the average cost at more than US\$ 1.2 billion.⁸ Such figures are derived from a study carried out by DiMasi et al. (2003), who estimate that the average cost per NCE was US\$ 802 million in 2000 for small-molecule drugs, and US\$ 1,318 million in 2005 for biologics (DiMasi and Grabowski, 2007). Included in these costs are substantial opportunity costs. A more recent publication, Munos (2009), suggests that current research costs are higher than the average costs cited by DiMasi et al. (2003).

A systematic overview, which involved assessing publications dealing with the cost of developing pharmaceuticals, found that estimations of R&D costs varied more than ninefold – from US\$ 92 million (US\$ 161 million capitalized) to

US\$ 883.6 million (US\$ 1.8 billion capitalized). Some of these variations can be explained by different methods, data sources and time periods, but the authors emphasize that there is a lack of transparency, as confidential information provided by unnamed companies about unspecified products formed all or part of the data for most of the studies referred to in the publications assessed as part of the overview process (Morgan et al., 2011).

All of these estimations rely on many variables, such as the estimated average length of development, the average size and costs of clinical trials, and the probability of success that products will finally make it to market. In addition, it is difficult to verify the underlying data, as this is not disclosed. These figures have been widely discussed and challenged (Love, 2003; Light and Warburton, 2011). There are also doubts about the usefulness of such estimations, as costs vary widely between companies and also between the private sector and the public sector.

While there is no agreement on precise costs, it is obvious that medical R&D is very costly and highly risky, and that many investments do not result in a return, due to product failures in the clinical trials phase. Rapidly drying up or non-existent pipelines for innovative blockbuster products is the reason for the increase in mergers and acquisitions in this sector, and is also the reason for the declining stock valuations of even the largest pharmaceutical companies in recent years.

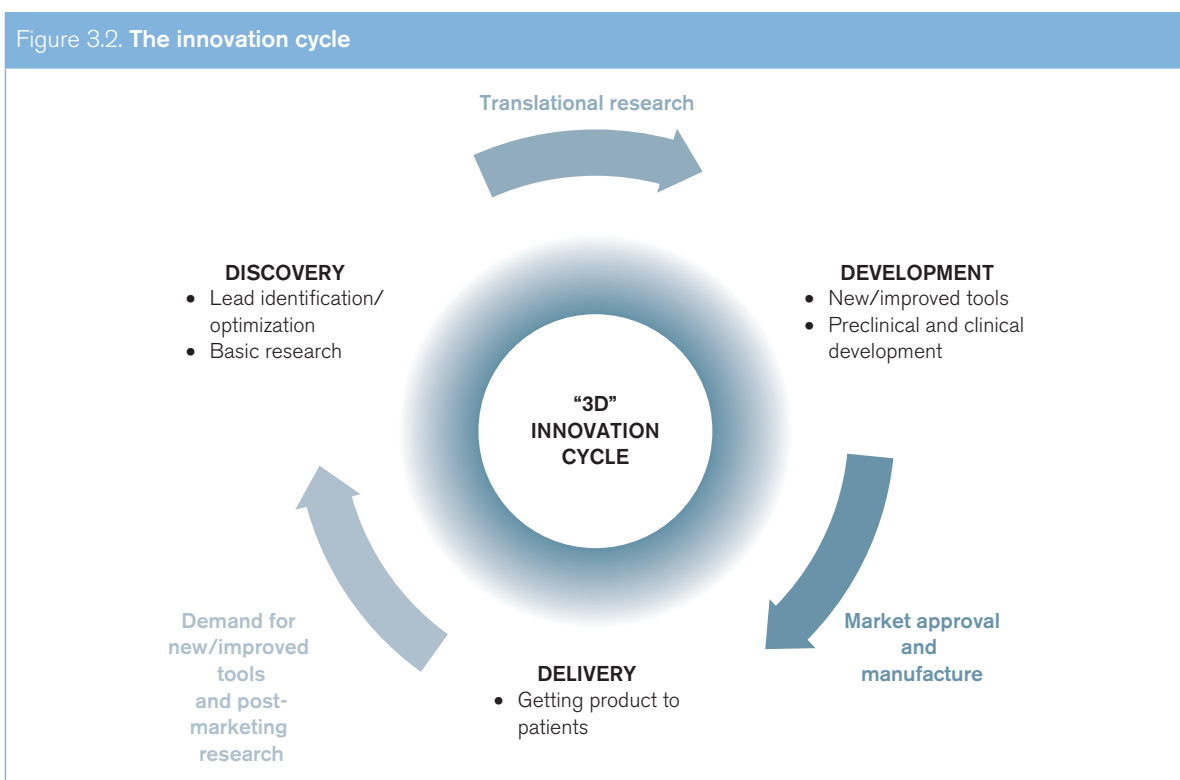
4. Incentive models in the innovation cycle

The 2011 World Intellectual Property Report (WIPO, 2011a) observes that “IP rights are a useful incentive mechanism when private motivation to innovate aligns with society’s preferences with regard to new technologies. But such an alignment does not always exist. In addition, it is unclear whether the IP system can incentivize invention that is far from market application, for example basic science research”. In reviewing the IP system in the context of the broad sweep of innovation policies, the report distinguishes three mechanisms for promoting innovation:

- Publicly funded innovation carried out by academic institutions and public research organizations.
- Publicly funded research undertaken by private firms – notably through public procurement, research subsidies, soft loans, R&D tax credits and innovation prizes.
- Privately financed and executed R&D, financed through the marketplace rather than government revenues and incentivized through the IP system, which is one mechanism of government policy that promotes innovation.

(a) The innovation cycle

Innovation is often presented as a linear process that culminates in the launch of a product, but innovation in health can also be seen as a cycle (see Figure 3.2).



Source: WHO (2006b, p. 23).

This cycle goes from R&D of new, basic compounds to the testing and development of new products, up to the delivery of these products, and then returning to the R&D of new products (or to the optimization of existing products) through systematic post-marketing surveillance and the development of an increasingly effective demand model based on health needs.

The circular model of health innovations illustrates a critical reality: the current market-driven innovation cycle works better for developed countries where effective demand for health products is matched by the ability to pay for them. In contrast, for diseases that predominantly affect patients in developing countries, there is a critical gap in the availability of incentives that fuel the conventional innovation cycle. While there is an urgent need for new medications for diseases that predominantly affect developing countries, that market is characterized by limited purchasing power, coupled with the lack of health insurance systems in many countries.

(b) Absence of self-sustaining innovation cycle in the case of small markets, low incomes

The CIPIH in this context observed that the IP system needs a certain type of environment in order to deliver expected results. In low-income countries, the innovation cycle is not self-sustaining due to small markets, underfunded health services and generally weak upstream research capacity. In this type of environment, IPRs alone do not provide an efficient incentive for medical research (WHO, 2006b). Member states subsequently confirmed this finding in the WHO Global Strategy and Plan of Action on Public Health, Innovation and Intellectual Property (GSPA-PHI).⁹

This gap – between the specific needs of developing countries and the medical research effort – has sparked policy debate on the effectiveness of current medical innovation structures for the needs of developing countries, both in terms of the disease burden addressed and in terms of how appropriate the solutions found are for those suffering from disease. Equally, the compelling need to address this gap has, over the past decade, prompted an array of practical initiatives to find new ways of combining the diverse inputs, infrastructure and resources needed for product development. These initiatives have explored new ways of integrating these different inputs and steering candidate products through the innovation process, culminating in the delivery of safe and effective new technologies. This approach has typically made use of more collaborative structures, a wider range of non-exclusive and segmented technology licensing models, the development of pre-competitive technology platforms, as well as product development partnerships (PDPs) that harness private-sector capacities and deploy them towards the attainment of not-for-profit public health objectives. Such practical initiatives both respond to, and

help to influence, the dynamics of medical innovation today, both in terms of making new technologies available and illustrating in practice the possibilities for a wider range of innovation models.¹⁰

While it is important to trigger the requisite innovation for neglected diseases, it is also important to ensure that any new medical technologies emerging from such initiatives are affordable for the people who need them. In the existing patent-driven innovation ecosystem, the returns for investment in innovation are generally factored into the price of new generation products. In contrast, new and innovative finance mechanisms and initiatives aim not to finance the cost of R&D through the price of the end product, thus delinking the cost of research from the price of the product.¹¹

There have been a few successful cases of tailoring innovation to meet identified medical needs. An example is the development of a meningitis vaccine for Africa (see Box 3.3).

(c) Building innovation networks

The CIPIH stressed that the formation of “effective networks, nationally and internationally, between institutions in developing countries and developed countries, both formal and informal” is an “important element in building innovative capacity” (WHO, 2006b). Among current initiatives to build such collaborative networks for innovation is the African Network for Drugs and Diagnostics Innovation in Africa (ANDI) (see Box 3.4).

(d) Overview of innovation structures

A broad range of diverse innovation structures are used in the development of medical technologies. As Figure 3.3 illustrates, these structures can be characterized according to two factors – the degree of market-based incentives involved, and the extent to which some leverage or exclusivity is exercised over the technology. Often innovation processes are neither situated in an entirely non-commercial context with no leverage at all maintained over technologies, nor a rigid, highly exclusive and entirely private model of technology development. Legal instruments alone, particularly at the international level, do not generally determine where a practical innovation strategy for a specific new technology is, or should be, located on this spectrum, and other factors typically guide choices about the mix of public and private inputs, and the management of technology.

One key feature of the innovation landscape, however, is the dividing line between “pre-competitive” and competitive inputs to innovation. Landmark research projects such as the Human Genome Project¹² and the International HapMap Project¹³ have sought to define a pre-competitive body of data that is openly shared for wide use in research

Box 3.3. New innovation models in practice: tailoring a meningitis vaccine for Africa

The successful 2010 MenAfriVac launch highlights the role of new approaches to innovation and product development in order to address the health needs of developing countries. Prior to this, vaccines were available for various strains of meningitis, but they were too expensive for those living at risk of the disease in the so-called African meningitis belt. Moreover, they did not offer an appropriate solution for resource-poor settings. Against a background of recurrent epidemics and increasing death rates, stakeholders faced a significant innovation challenge in order to ensure the production of a vaccine that would be suitable from a clinical point of view, and would also be sustainable and affordable. The Meningitis Vaccine Project, a consortium led by the WHO and the Programme for Appropriate Technology in Health (PATH), a not-for-profit health technology organization, set about producing a vaccine for the A strain of meningitis that would cost no more than US\$ 0.50 per dose. A review of options led to a decision to develop a production process and to transfer the relevant technology to a low-cost producer in the developing world, rather than subsidizing a vaccine manufacturer in the industrialized world to undertake development and production. An innovative model for vaccine development was established, with key raw materials sourced in India and the Netherlands. The technology developed by the US FDA Center for Biologics Evaluation and Research, and the technology and know-how, was transferred to Serum Institute of India Ltd to produce vaccines for clinical trials and, ultimately, for full-scale production. This development model reportedly cost one tenth of the conventional estimate for producing a new vaccine. The development and introduction of this new vaccine marks a huge step towards the elimination of epidemic meningitis in sub-Saharan Africa.¹⁴

Box 3.4. African Network for Drugs and Diagnostics Innovation

ANDI is an African-led innovation network that provides a time-efficient and cost-effective approach to achieving the overarching goal of linking innovation to development in the field of pharmaceuticals and health (Nwaka et al., 2010).¹⁵ Its vision is to create a sustainable platform for R&D innovation in Africa, in order to address Africa's specific health needs. The implementation of ANDI is linked to the GSPA-PHI. In this context, ANDI is developing a focused strategy for the management of IP, both in the context of training and in the area of specific projects.

Specific goals:

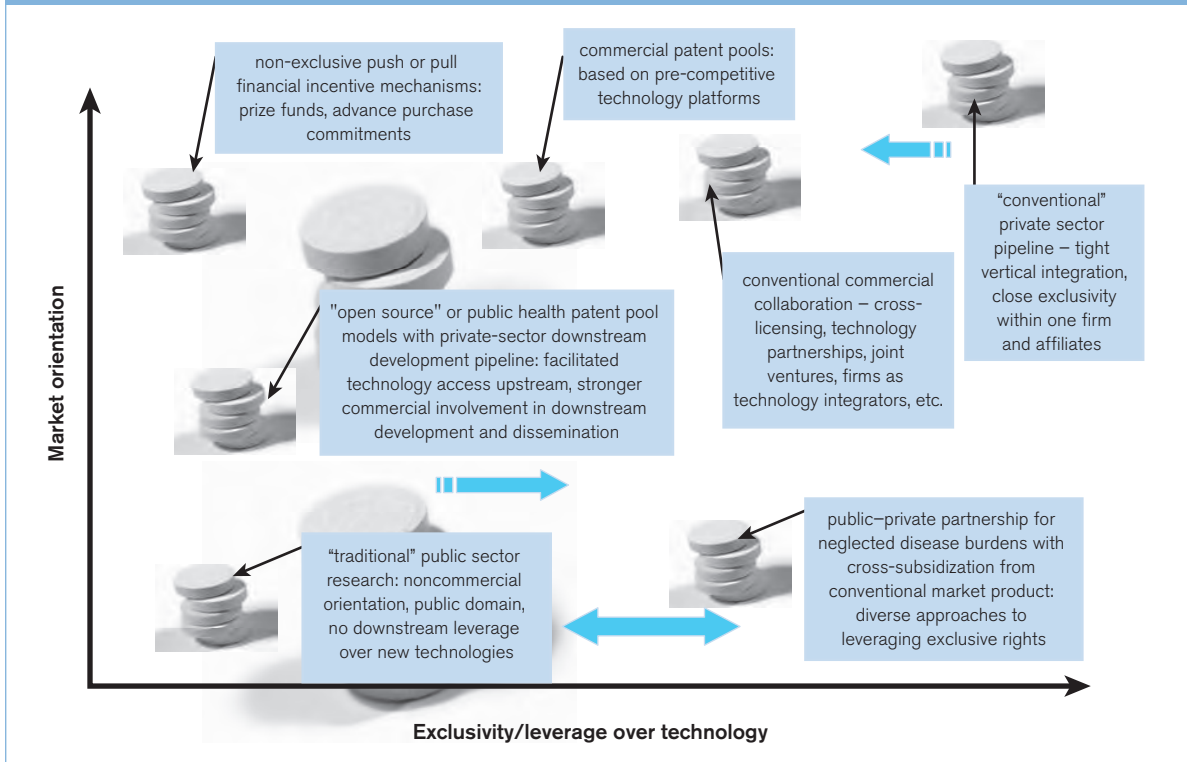
- increase R&D collaboration among African institutions and countries, including through the management of centres of excellence in health innovation
- fund and manage a portfolio of health R&D projects
- support and promote public-private partnerships (PPPs) and new companies in Africa, in order to enable the development and manufacture of new drugs, diagnostics and other health products
- encourage and reward local innovation, including research that draws on traditional medicine and IP
- support South-South and North-South collaboration
- promote long-term economic sustainability through supporting R&D and access to health products in Africa.

Highlights of progress to date:

- development and endorsement of the ANDI strategic business plan, based on local priorities
- identification of United Nations Economic Commission for Africa (UNECA) as the host agency in Africa, and the transfer of the ANDI Secretariat from the WHO Special Programme for Research and Training in Tropical Diseases (TDR) in Geneva to UNECA in Addis Ababa, Ethiopia
- establishment of a ministerial-level governance board which recognizes the important role of ministries of health and science and technology in the work of ANDI
- implementation of the first pan-African centres of excellence
- successful launch of first call for product R&D projects, with over 200 proposals received.

The establishment of ANDI is supported by several African institutions, the WHO through TDR, the WHO Regional Office for Africa (AFRO) and the WHO Regional Office for the Eastern Mediterranean (EMRO), UNECA, the European Commission and the African Development Bank.

Figure 3.3. Mapping market incentives and leverage over technology in innovation structures



Source: Taubman (2010).

and in the development of inputs at an early stage in the product development pipeline – so as to provide a common platform for companies to compete in the development of finished products. At a later stage along the R&D pipeline, a degree of competition and differentiation between companies can promote a greater diversity of available technologies (Olson and Berger, 2011). While the idea of a “pre-competitive” information platform of knowledge was a common theme in public-sector innovation models around 2000, the same concept has increasingly formed part of the innovation strategies of established private-sector research-based companies.

Policy instruments have significant impact on how innovation takes place. Table 3.1 sets out the different characteristics of the main innovation policy instruments, and illustrates how they differ according to whether they are addressing publicly funded and executed research, publicly funded but privately executed research, as well as privately funded and executed research.

(e) Vaccines: a distinct challenge for innovation

Vaccine development differs from the development of small-molecule, chemically synthesized pharmaceuticals. Vaccines are complex biological entities and there is no such thing as a “generic” vaccine. Proving the safety and efficacy of a

vaccine, even if it is a “copy” of an existing vaccine, requires a full regulatory dossier containing data on pre-clinical and clinical trials. This adds years, and complexity, to the process of making and copying even existing vaccines. Vaccines are typically given to healthy individuals and, in particular, to healthy infants as a prophylaxis against a subsequent infection. Safety is therefore paramount, and any remote suggestion of risk to the recipient can result in withdrawal or non-authorization of the vaccine.

The cost of establishing and gaining regulatory approval for a manufacturing facility partly explains the limited number of manufacturers entering the field of vaccines and the relatively small number of qualified products and producers. Other reasons include the lack of production know-how that can constitute an effective barrier to the viable reproduction of vaccine technologies. Vaccines also often require costly cold-chain infrastructure and only a relatively small number of doses are required to achieve immunization. Thus, profit margins can be relatively low in comparison with other pharmaceuticals.

These challenges mean that private manufacturers have long lacked the necessary incentives to invest in vaccines, particularly those that focus on the specific needs of developing countries. Almost all the important, innovative vaccines introduced during the past 25 years have resulted from initial discoveries made by public-sector research institutions (Stevens et al, 2011).

Table 3.1. Overview of innovation policy instruments

	Main features	Research direction	Financing of R&D	Push versus pull	Selecting entity	Selection criteria	Ownership of results	Main advantages	Main drawbacks
Publicly funded and executed									
Public research organizations	<ul style="list-style-type: none"> Public goods such as defence and health Does not undertake commercialization of knowledge 	<ul style="list-style-type: none"> Basic Generic 	<ul style="list-style-type: none"> Ex-ante financing of project cost 	<ul style="list-style-type: none"> Push 	<ul style="list-style-type: none"> Government 	<ul style="list-style-type: none"> Public interest Peer review 	<ul style="list-style-type: none"> Public Institution 	<ul style="list-style-type: none"> Advance fundamental scientific knowledge 	<ul style="list-style-type: none"> Uncertain impact
Academic research	<ul style="list-style-type: none"> Aimed at increasing basic scientific knowledge Does not undertake commercialization of knowledge 	<ul style="list-style-type: none"> Basic Generic 	<ul style="list-style-type: none"> Ex-ante financing of project cost 	<ul style="list-style-type: none"> Push 	<ul style="list-style-type: none"> Government University Philanthropy 	<ul style="list-style-type: none"> Public need Peer review 	<ul style="list-style-type: none"> Public Institution 	<ul style="list-style-type: none"> Advance fundamental scientific knowledge 	<ul style="list-style-type: none"> Uncertain impact
Publicly funded and privately executed									
Procurement	<ul style="list-style-type: none"> Government purchases of well-defined innovative goods – for example, military equipment 	<ul style="list-style-type: none"> Generic Applied 	<ul style="list-style-type: none"> Financing of project cost Timing depends on contract 	<ul style="list-style-type: none"> Combination of push and pull depending on design 	<ul style="list-style-type: none"> Government 	<ul style="list-style-type: none"> Ex-ante competition 	<ul style="list-style-type: none"> Depends on contract 	<ul style="list-style-type: none"> Mobilizes competitive market forces for the provision of public good 	<ul style="list-style-type: none"> Difficult to write perfect contracts
Research subsidies and direct government funding	<ul style="list-style-type: none"> Public support for targeted research 	<ul style="list-style-type: none"> Generic Applied 	<ul style="list-style-type: none"> Ex-ante financing based on estimated project cost 	<ul style="list-style-type: none"> Push 	<ul style="list-style-type: none"> Government Firm 	<ul style="list-style-type: none"> Competition Administrative decision 	<ul style="list-style-type: none"> Usually firm 	<ul style="list-style-type: none"> Mobilizes competitive market forces for public benefit 	<ul style="list-style-type: none"> Governments are imperfectly informed about success potential of R&D projects
Prizes	<ul style="list-style-type: none"> Prizes for targeted solutions to specific problems 	<ul style="list-style-type: none"> Generic Applied 	<ul style="list-style-type: none"> Ex-post financing based on ex-ante estimated project cost 	<ul style="list-style-type: none"> Pull 	<ul style="list-style-type: none"> Government 	<ul style="list-style-type: none"> Competition 	<ul style="list-style-type: none"> Usually public 	<ul style="list-style-type: none"> Mobilizes competitive market forces for public benefit Subsequent competitive provision of technology 	<ul style="list-style-type: none"> Difficult to write perfect contracts Requires private ex-ante financing of R&D
Soft loans	<ul style="list-style-type: none"> Subsidized provision of credit through below-market interest rates, government guarantees and flexible reimbursement provisions 	<ul style="list-style-type: none"> Applied 	<ul style="list-style-type: none"> Ex-ante financing based on estimated project cost 	<ul style="list-style-type: none"> Push Some pull depending on design 	<ul style="list-style-type: none"> Government Firm 	<ul style="list-style-type: none"> Administrative decision 	<ul style="list-style-type: none"> Firm 	<ul style="list-style-type: none"> Reduces risks associated with large R&D undertakings 	<ul style="list-style-type: none"> Governments are asymmetrically informed about success potential of R&D projects Does not address firms' appropriability problem
R&D tax credits and related fiscal incentives	<ul style="list-style-type: none"> Reduced taxation of profits linked to investment in R&D 	<ul style="list-style-type: none"> Generic Applied 	<ul style="list-style-type: none"> Ex-post financing dependent on actual investment expenditure 	<ul style="list-style-type: none"> Push Some pull depending on design 	<ul style="list-style-type: none"> Firm 	<ul style="list-style-type: none"> Proof of R&D investment 	<ul style="list-style-type: none"> Firm 	<ul style="list-style-type: none"> Decisions on R&D decentralized 	<ul style="list-style-type: none"> Does not address firms' appropriability problem Requires private ex-ante financing of R&D
Privately funded and executed									
IPRs	<ul style="list-style-type: none"> Market exclusivity 	<ul style="list-style-type: none"> Generic Applied 	<ul style="list-style-type: none"> Ex-post financing based on market value of innovation 	<ul style="list-style-type: none"> Pull 	<ul style="list-style-type: none"> Firm 	<ul style="list-style-type: none"> As specified in IP laws 	<ul style="list-style-type: none"> IP owner (firm or institution) 	<ul style="list-style-type: none"> Decisions on R&D decentralized 	<ul style="list-style-type: none"> Static misallocation of resources Requires private ex-ante financing of R&D

(i) New vaccine innovation in the 21st century

The first decade of the 21st century brought a record number of new vaccines, including vaccines for meningococcal meningitis, rotavirus, pneumococcal disease and cervical cancer caused by human papillomavirus. At the same time, the market for vaccines has grown dramatically. It has tripled since 2000, and had reached over US\$ 17 billion globally by mid-2008 (WHO/UNICEF/World Bank, 2009).

This increase in the development of vaccines is due to a number of key factors: more innovative technologies; improved understanding of immunity; investment by PDPs such as the GAVI Alliance,¹⁶ and, more recently, new funding sources and mechanisms such as advance market commitments, which contribute to public funding for vaccine development (see Box 3.5). These changes continue to shape the current landscape of vaccine manufacturers.

(ii) Role of developing-country manufacturers

The vaccine industry has undergone major changes in the past decades. The market share of a small number of multinational companies grew from approximately 50 per cent (in terms of sales revenue) in 1988 to about 70 per cent of sales revenue in 2005. Overall, there are fewer than 40 vaccine suppliers, with over 90 per cent of all vaccines produced by only 15 manufacturers (WHO, 2011c).

However, due to liability and regulatory compliance issues, or as a result of mergers and acquisitions, developed-country manufacturers are increasingly leaving the vaccine market. Small- and medium-sized companies, together with emerging companies in Brazil, India, Indonesia and the Republic of Korea comprise about 10 per cent of the market in terms

of value (Milstien et al., 2005). However, in terms of volume of production, developing country vaccine manufacturers contribute a larger share.¹⁷ Developing country vaccine manufacturers are also increasingly investing in research. For example, the Serum Institute of India has developed a meningitis A vaccine for use in sub-Saharan Africa (see Box 3.4), as well as a measles vaccine delivered by aerosol.¹⁸ Cuba has a vibrant research-based biotechnology industry that has developed a number of innovative vaccines, including a meningitis B vaccine and a synthetic haemophilus influenza B vaccine.¹⁹ It also has numerous innovative products in the pipeline. A Chinese company has developed a hepatitis E vaccine: this company is currently developing a cervical cancer and a genital warts vaccine.²⁰ In Brazil, the Oswaldo Cruz Foundation (Fiocruz), through its Immunobiological Technology Institute (Bio-Manguinhos), supplied 47 per cent of the vaccines acquired by the Brazilian National Immunization Program in 2007. Bio-Manguinhos currently has 25 projects under development: 13 involving bacterial or viral vaccines.²¹ Also in Brazil, the Butantan Institute, which held 51 per cent of the market share for vaccines in Brazil in 2010, has developed a novel adjuvant derived from a by-product of pertussis vaccine production.²²

5. Registration of clinical trials in pharmaceutical product development

Registration of clinical trials means making accessible to the public, by means of a registry, an agreed set of information about the design, conduct and administration of clinical trials.²³ A clinical trials registry is a publicly accessible database containing entries with information about the design, conduct and administration of clinical trials.

Box 3.5. Advance market commitment: saving lives through vaccines

Although vaccines are among the most effective public health interventions, few of the vaccines that have been developed address diseases that primarily affect the developing world. In the past, new vaccines typically reached low-income countries only decades after they had been rolled out in developed countries. A pilot project on an Advance Market Commitment (AMC) for pneumococcal vaccines was launched in 2007. It was funded by Canada, Italy, Norway, the Russian Federation, the United Kingdom and the Bill & Melinda Gates Foundation. Pneumococcal disease was selected for this project, as it claims 1.5 million lives each year, mostly children in Asia and Africa.

The AMC guarantees a market to manufacturers of a novel and suitable pneumococcal vaccine, with a high introductory price of US\$ 7 for each dose. This price is guaranteed for about 20 per cent of the doses that manufacturers commit to sell through the AMC and is designed to help them recover the costs of establishing production capacity. In return, manufacturers have accepted to provide additional doses at a “tail price” of US\$ 3.50 for at least a decade.

Under the oversight of the World Bank and the GAVI Alliance, the AMC, in conjunction with UNICEF, issued the first tender in September 2009. Since then, two pharmaceutical companies have committed to each provide 30 million doses of a pneumococcal conjugate vaccine (PCV) annually and the vaccines have been successfully launched.

In December 2010, Nicaragua became the first country to immunize its children with the new vaccine. Since then, 15 other countries – Benin, Burundi, Cameroon, the Central African Republic, the Democratic Republic of the Congo, Ethiopia, The Gambia, Guyana, Honduras, Kenya, Malawi, Mali, Rwanda, Sierra Leone and Yemen – have added the AMC-purchased vaccine to their national vaccination schedules.²⁴

The WHO maintains the International Clinical Trials Registry Platform (ICTRP).²⁵ The ICTRP Search Portal (222,000 records as of 29 October 2012) provides a searchable database containing the trial registration datasets made available by 14 national registries meeting criteria for content and quality control. These datasets constitute international standards for clinical trials registration. The platform also has the unique ability to link together (bridging) records registered in different countries (or multi-country trials). Currently, the ICTRP database has 63,203 records for recruiting trials. It is updated weekly.

The WHO considers the registration of all interventional trials a scientific and ethical responsibility. The rationale for the ICTRP includes the following considerations:

- Decisions about health care should be informed by all of the available evidence.
- Publication bias and selective reporting make informed decisions difficult.
- Improving awareness of similar or identical trials enables researchers and funding agencies to avoid unnecessary duplication.
- Describing clinical trials in progress can make it easier to identify gaps in clinical trials research and to define research priorities.
- Making researchers and potential participants aware of trials may facilitate recruitment and increase patients' active involvement in the clinical trial process.
- Enabling researchers and health care practitioners to identify trials in which they may have an interest could result in more effective collaboration among researchers, including prospective meta-analysis.

- Registries checking data as part of the registration process may lead to improvements in the quality of clinical trials by making it possible to identify potential problems early in the research process.

There are other national and regional initiatives for capacity-building in developing countries, such as the European and Developing Country Clinical Trials Partnership (EDCTP), which aims to accelerate the development of new or improved drugs, vaccines, microbicides and diagnostics against HIV/AIDS, malaria and TB, with a focus on Phase II and Phase III clinical trials in Africa. It supports projects which combine clinical trials, capacity-building and networking. Various European countries operate in partnership with over 40 countries in Africa (EDCTP, 2011).

Besides the registration of clinical trials, the publication of the results of clinical trials is equally important for public health. Patients take part in clinical trials in the hope that they will contribute to advances in medical science and they do this altruistically. Participants expect that results are used to further scientific research. Sponsors of clinical trials will often not provide details of clinical trials that have failed, although this is valuable knowledge and could be used help to prevent a repetition of such trials, and thus help to avoid exposing patients to unnecessary risks. It would be in the interest of public health if the details of all clinical trials were to become publicly available, allowing interested parties to verify the data. The European Medicines Agency (EMA) intends to provide access to clinical trial data, allowing interested parties to verify the data (see Box 3.6).

Box 3.6. European Medicines Agency to make available clinical trials data

In December 2010, the EMA adopted a new policy of public access to EMA documents.²⁶ In response to a number of safety-related requests received since 2010, the EMA has granted access to 1.5 million pages of clinical trial data. During the second phase of implementation, the EMA intends to proactively publish clinical trials data that applicants submit to the agency within the framework of the authorization process. The purpose of this initiative is to provide access to full datasets for interested parties, allowing them to verify the clinical data produced and submitted by companies in justification of the quality, safety and efficacy of products. The disclosure of such data is considered to be in the public interest, as it allows independent researchers and other interested groups to screen the raw data and to assess for themselves the efficacy and potential side effects of the product. The modalities of providing such proactive access to clinical trial data are under consideration (see EMA, 2012; Reuters, 2012). The new policy is expected to enter into force in January 2014.²⁷

C. Overcoming market failure: the challenge of neglected diseases

Key points

- Innovation in medical technologies for neglected diseases suffers from market failure as conventional IP-based incentives do not correspond with the nature of demand for treatments of these diseases. A key factor is the limited purchasing power of both governments and patients in the countries where such diseases predominate.
- While there is still a huge research gap, the neglected diseases R&D landscape is changing, and an increasing number of actors are engaged in funding and carrying out such research.
- Many new innovation mechanisms and models aimed at increasing R&D to find effective treatments for neglected diseases have been discussed and implemented at international and national levels. One such innovative model set up in cooperation between multiple stakeholders is WIPO Re:Search *Sharing Innovation in the Fight Against Neglected Tropical Diseases*.
- Assessments of many such proposals can be found in the reports published by the WHO Expert Working Group on Research and Development: Financing and Coordination (EWG) and by the Consultative Expert Working Group on Research and Development: Financing and Coordination (CEWG).
- The CEWG has recommended specific action points, including establishing a binding global instrument for R&D for developing countries.
- PDPs have significantly increased the number of products in development for diseases that predominantly affect developing countries.

There is a particular problem in incentivizing medical R&D for diseases that disproportionately affect poor people in developing countries as the market mechanisms, such as intellectual property rights (IPRs), do not work in this case. A key factor is the limited purchasing power of both governments and patients in the countries where such diseases predominate; unlike for other diseases, there is no positive spillover from drug development targeted at more affluent markets. These diseases are called neglected diseases, and this section deals with the challenges of medical innovation in this area.

1. Diseases disproportionately affecting people in developing countries: neglected diseases

Both the Commission on Intellectual Property Rights, Innovation and Public Health (CIPIH) (WHO, 2006b) and the WHO Global Strategy and Plan of Action on Public Health, Innovation and Intellectual Property refer to diseases that disproportionately affect people in developing countries. This concept is based on the three types of diseases distinguished by the Commission on Macroeconomics and Health (WHO, 2001a):

- **Type I diseases** are found in both rich and poor countries, and affect large numbers of vulnerable

populations in both. Examples of communicable diseases include measles, hepatitis B, and Haemophilus influenzae type b. Examples of non-communicable diseases include diabetes, cardiovascular diseases and tobacco-related illnesses.

- **Type II diseases** are incident in both rich and poor countries, but with a substantial proportion of cases in poor countries. Examples of such diseases include HIV/AIDS and TB. While both diseases are present in rich and poor countries, more than 90 per cent of cases occur in poor countries.
- **Type III diseases** are those that are overwhelmingly or exclusively incident in developing countries. Examples of such diseases include African sleeping sickness (trypanosomiasis) and African river blindness (onchocerciasis).

Type II and III diseases are often referred to as neglected diseases. These also include 17 neglected tropical diseases that are a specific focus of the work of WHO. These neglected tropical diseases currently impair the lives of an estimated one billion people (WHO, 2010f). They share a number of common features:

- They have an enormous impact on individuals, families and communities in developing countries in terms of disease burden, quality of life, loss of productivity and the aggravation of poverty, as well as the high cost of long-term care.

- They affect largely low-income and politically marginalized people living in both rural and urban areas. Such people cannot readily influence administrative and governmental decisions that affect their health, and often seem to have no constituency that speaks on their behalf. These people are therefore likely to be “neglected” by public policy-makers.

The distribution of these diseases is restricted by climate, in particular by its effect on the distribution of vectors and reservoir hosts. In most cases, there appears to be a low risk of transmission beyond the tropics. Unlike influenza, HIV/AIDS and malaria and, to a lesser extent, TB, most neglected tropical diseases present little threat to the inhabitants of high-income countries, thus triggering less attention. They are relatively neglected by the pharmaceutical research that is needed to develop new diagnostics and medicines, and to make accessible interventions to prevent, cure and manage the complications of these diseases (WHO, 2010f).

The unavailability of medical technologies to effectively address neglected diseases is one of the major problems associated with tackling this human health tragedy. The situation has been characterized by a chronic lack of investment in R&D to find effective treatments for neglected diseases. The innovation effort is starkly disproportionate to the public health challenge posed by such diseases. Since the diseases are concentrated in poor countries, and since poor people are affected the most, it is not just the diseases that are neglected; rather, the problem is one of neglecting patients who die of these diseases.

In 1990, the Commission on Health Research for Development found that of the US\$ 30 billion global investment in health research in 1986, only 5 per cent, or US\$ 1.6 billion, was devoted specifically to health problems of developing countries, although an estimated 93 per cent of the world’s burden of preventable mortality occurred in the developing world (Commission on Health Research for Development, 1990, Chapter 3). Later, based on this data, the Global Forum for Health Research coined the term “10/90 gap” to highlight the gap between the share of the global disease burden and the resources devoted to addressing it.

While a huge research gap for neglected diseases still exists today, both the health research landscape and the share of the global disease burden have been changing positively since 1990. The G-Finder reported that the funding of R&D for neglected diseases was more than US\$ 3 billion in 2011, with the three “top tier” diseases being HIV/AIDS (33.8 per cent), TB (17.3 per cent) and malaria (18.4 per cent). This leaves only slightly more than 30 per cent of funding in the neglected diseases area available for carrying out research on all other neglected diseases (Moran et al., 2012). Significantly more money is spent on development of new medicines than on vaccines. As little as under 5 per cent of the total annual

R&D budget spent on addressing neglected diseases is reported to be spent on diagnostics (BIO Ventures, 2010). Funding comes predominantly from the public sector. In 2011, the public sector provided almost two thirds (US\$ 1.9 billion, 64.0 per cent) of global funding with high-income countries contributing 95.9 per cent of this share. The philanthropic sector contributes US\$ 570.6 million (18.7 per cent) and industry invested US\$ 525.1 million (17.2 per cent) (Moran et al., 2012).

2. New approaches to innovation for neglected diseases

This section presents some of the currently discussed innovation models for neglected diseases. It includes information on various WHO developments, including the report of the CEWG (WHO, 2012a). This section also reviews the role of PDPs and the efforts of research-based pharmaceutical companies in this regard.

Recent years have seen a drive to find alternative and innovative ways to undertake needs-based research. New initiatives aimed at increasing R&D to find effective treatments for neglected diseases are under way, involving a diverse group of actors, and a large number of collaborative partnerships are at work to address the lack of medical innovation for neglected diseases. While many proposals are still under discussion, various new measures are already being used to fill the research gap. One such innovative model set up in cooperation between multiple stakeholders is WIPO Re:Search *Sharing Innovation in the Fight Against Neglected Tropical Diseases* (see Section C.6 below).

One important concept that evolved from this discussion is the concept of delinking price of the final product from the costs of R&D. This concept is based on the fact that patents allow developers to recoup the costs and make profits by charging a price in excess of the costs of production. This way of financing R&D is viewed as constituting a barrier to access to medicines in countries where populations pay out of their own pockets for medicines and thus cannot afford to pay high prices. The principle of delinking is based on the premise that costs and risks associated with R&D should be rewarded, and incentives for R&D provided, other than through the price of the product. This type of delinking is particularly advocated in the case of financing R&D for neglected diseases.

Delinking can be facilitated by push mechanisms and by pull mechanisms. Push mechanisms are incentives that include such initiatives as grant funding and tax credits for investment in R&D. Pull mechanisms are incentives that offer rewards for the final outcome of R&D of certain products. Mechanisms in the latter category include milestones or end prizes. The following section, while not exhaustive, describes some of these approaches. Assessments of many related proposals can be found in the reports of both the EWG²⁸ and the CEWG.

(a) Open source drug discovery and development

Open source drug discovery and development builds on two principles borrowed from open source software development. First, open source drug discovery is based on the idea of collaboration, i.e. organizing and motivating groups of independent researchers to contribute to research projects. Second, it is based on an open approach to IP which makes the outcome of that research generally available, either through the public domain or through the use of customized licences (Maurer, 2007; Masum and Harris, 2011).

The success of open source models in the information technology (e.g. web technology and the Linux operating system) and biotechnology (e.g. human genome sequencing) sectors highlights both the need and the potential to initiate a similar model in health care, such as an open source model for drug discovery. Several open source drug discovery projects are currently under way.²⁹ Most have secured financing either in the form of government grants or from philanthropic sources. These funds are used to cover administrative expenses and may also be used to fund access to laboratories, computer facilities and payment to researchers.

To date, open source initiatives have had only a minor impact on public health in developing countries. While they seem ideally suited to promote pre-competitive research, they do not as yet have the capacity to ensure delivery of finished health products to patients or to ensure that products are steered through costly development phases. Biopharmaceutical firms have used different organizational modes (i.e. licensing agreements, non-equity alliances, purchase and supply of technical and scientific services) to enter into relationships with different types of partners, with the aim of acquiring or commercially exploiting technologies and knowledge. These relationships can include large pharmaceutical companies, biotechnology product firms, biotechnology platform firms and universities. Box 3.7 describes one recent initiative in open innovation for drug discovery.

(b) Grants

A grant may enable a small or medium-sized enterprise to finance initial research for a medicine on a neglected disease and bring a potential new medicine through Phase I trials, at which stage it may be possible to attract commercial funding. Push mechanisms operate best in the initial or upstream phase of the R&D process.

While grants can be useful for stimulating R&D, like most push mechanisms, they provide no guarantee that a viable drug will ultimately be delivered. This is because grants are paid irrespective of the results achieved. The impact of grant schemes on the development of effective treatments in the area of neglected diseases is therefore uncertain. On the other hand, evidence from some US grants schemes suggests that 60 per cent of projects supported by way of grants do eventually make it to market. Evidence also shows that funding from such schemes enabled almost 80 per cent of grantees to raise additional capital subsequently.³⁰

(c) Prizes

Prizes work as a pull mechanism in R&D by increasing the rewards for success, thereby making investment more attractive and the delivery of a specific product more likely. Pull mechanisms are incentives that are likely to operate more successfully in downstream or later phase R&D. Prizes can also favourably impact the delivery of a product. For example, certain requirements relating to IP management may be imposed on the prize winner, including allowing free use of the technology by the public sector or developing countries, in order to promote competition for supply. There are two categories of prizes: the first is awarded for reaching a specified milestone in the R&D process; the second rewards the attainment of a specified endpoint (such as a new diagnostic, vaccine or medicine with a particular profile in terms of performance, cost, efficacy or other important characteristics). Prizes may be offered in the area of neglected diseases.

Box 3.7. The Council for Scientific and Industrial Research Open Source Drug Discovery Model

The Open Source Drug Discovery (OSDD) model of India's Council of Scientific and Industrial Research (CSIR) represents a consortium which aims to deliver affordable health care to the developing world by providing a global platform where researchers can collaborate and collectively try to solve some of the complex problems associated with discovering novel therapies for neglected diseases such as malaria, TB and leishmaniasis. In order to expedite the discovery of drugs, the consortium aggregates the biological and genetic information available to scientists. This provides a unique opportunity for scientists, doctors, technocrats, students and others with diverse expertise to work for a common cause. The CSIR has also joined forces with some research-based pharmaceutical companies in this model. The OSDD is a large community, comprising more than 4,800 registered users from 130 countries.

During the early stages of a discovery, the OSDD establishes a collaborative model with community participation. However, it collaborates with industry/contract research organizations and publicly funded organizations at the development stage.³¹

While the funds would provide incentives for drug development, they would also aim to delink R&D costs from the prices of medicines. The effect that such prizes could have on innovation and access would largely depend on the application and design of the medicines developed, and the manner in which they align research efforts with health priorities, while aiming to leverage access by keeping prices of finished products low.

(d) Advance market commitments

Advance market commitment (AMC) agreements aim to create greater incentives for the R&D of a specific product either through market creation or through risk reduction. AMC agreements operate as contracts between a purchaser (normally a government or an international financing agency) and suppliers. They usually contain some form of agreed guarantee with regard to price or volume. By effectively guaranteeing a market, pharmaceutical companies are incentivized to undertake R&D.³² Box 3.5 provides an example of how advance market commitments can be implemented.

(e) Tax breaks for companies

Many countries provide tax credits for R&D expenditures, enabling companies to account for expenditure on R&D against their tax liabilities. Some governments have introduced additional tax credits with the express goal of incentivizing research on specific neglected diseases, for example HIV/AIDS, TB and malaria (European Commission, 2003).

How much tax breaks could drive innovation in the field of neglected diseases R&D is open to debate. This is because tax credits cannot by themselves remedy the absence of an effective market. In other words, as long as a company has to recover a substantial amount of its investment in R&D for a drug through the selling price, tax

credits cannot effectively drive innovation for products for which there is no effective demand.

Tax credits also cannot help where companies are operating at a loss – as is the case with some biotechnology companies in their start-up phase, before they have launched any approved product on the market. Another disadvantage of the introduction of tax breaks is that they may simply subsidize R&D that a company would have undertaken anyway.

(f) Patent pools

A patent pool is an agreement between at least two patent owners to group their patent rights relating to a specific technology and to license the rights to use these patents to each other and to third parties, subject to certain conditions such as the payment of royalties. Pooling the relevant patents necessary to use a technology, or to produce downstream products, allows licensees to only enter into one licence agreement with one legal entity and has been advocated as a tool to be used in R&D for neglected diseases. Patent pools have been used since the 19th century in different industry sectors. Early patent pools were aimed at fixing prices and keeping competitors out of the market, and thus came into conflict with competition law. Today, most patent pools aim to enable access to new technologies and to foster downstream competition. By reducing transaction costs for licensees, patent pools provide easy access to all patented technologies needed to produce standardized products. The audio-visual industry, for example, has adopted pooling as an instrument to facilitate licensing of standard technology and has established a number of successful patent pools.³³ In the field of pharmaceutical inventions, with funding from UNITAID,³⁴ a Medicines Patent Pool Foundation was established to pool patents regarding ARVs (see Chapter IV, Section C.3(b)(i)).

Patent pooling was also discussed as a possible solution to clear patent thickets to facilitate a response to the severe acute respiratory syndrome (SARS) (see Box 3.8).

Box 3.8. Patent pools

After the outbreak of SARS in 2002, the WHO set up a collaborative network of laboratories to help determine the cause of the disease. Ultimately, this led to the identification of the responsible pathogen, a member of the coronavirus family.³⁵ Collaborating laboratories involved in the decoding of the genome of the virus filed a number of patent applications covering the genomic sequence of the SARS coronavirus. This caused concern that diverse ownership of patents claiming all or parts of the genomic sequence of the virus might impede development of medical products, including vaccines and diagnostic tests. To counter this concern, and also to facilitate the development of needed medical products, a patent pool was suggested. This involved placing all essential patents in a pool to be licensed among the participants in the pool and to third parties on a non-exclusive basis.³⁶ As a result of implementing this proposal, some of the entities who are expected to be granted a significant number of patents relating to the SARS virus have signed a letter of intent in relation to creating such a patent pool. The next step would have been to determine which patent applications were essential for the pool and to draft the patent pool agreement.³⁷ However, as no new SARS outbreaks were recorded, there was no economic driver for the patent pool and it was decided not to pursue the project any further.

(g) Priority review voucher

A priority review voucher (PRV) is a scheme which aims to reward companies that develop health products that address small markets or limited patient groups as is the case also with neglected diseases. The PRV entitles a company to receive priority review (i.e. quicker review by the responsible regulatory authority) for any additional health products that would not otherwise qualify for priority review. A company can use this scheme to advance the marketing date of a potential “blockbuster” product, thus generating increased and earlier revenues from that product.

A PRV scheme was introduced in the United States in 2007. Under this scheme, companies that obtain marketing approval from the FDA for a product to treat or prevent one of 16 neglected tropical diseases are entitled to receive a PRV. The PRV can be used by the recipient or it can be sold to another company.

The average difference in approval time between a priority review product and a standard review product was estimated to be about one year, and the average value of a PRV was thought to exceed US\$ 300 million (Ridley et al., 2006; Grabowski et al., 2008). Since this scheme was introduced in the United States, two PRVs have been issued – in April 2009 for the development of an antimalarial drug and in December 2012 for the first anti-TB drug in 40 years. The first company used the voucher in February 2011 to accelerate FDA review of a drug for arthritis. It is to be seen what the second company does with the voucher.

Some argue that the value of the voucher is too small to have meaningful impact on the allocation of R&D resources by large pharmaceutical companies. A voucher might be attractive for smaller companies, but these companies are less likely to progress a health product through to development phase in view of the large costs of that phase. The value of a voucher is uncertain since it does not guarantee that an additional company product will, in fact, ultimately be approved by the regulatory authority, nor does it guarantee that the time saved by a priority review will actually exceed one year (Noor, 2009).

(h) A global binding framework for R&D for neglected diseases

The proposal to negotiate an international treaty on R&D for neglected diseases has been discussed for some time. In 2005, the CIPIH received a proposal regarding an R&D treaty and it concluded that “recognising the need for an international mechanism to increase global coordination and funding of medical R&D, the sponsors of the medical R&D treaty proposal should undertake further work to develop these ideas so that governments and policy makers may make an informed decision” (WHO, 2006b).

In the GSPA-PHI, the World Health Assembly (WHA) called for “further exploratory discussions on the utility of

possible instruments or mechanisms for essential health and biomedical R&D, including, inter alia, an essential health and biomedical R&D treaty”.³⁸

Several different proposals have been made for an international treaty on R&D. One of the latest submissions regarding such a proposal was presented to the CEWG. The proposal was “to create a new global framework for supporting priority medical R&D, based on the fair and equitable sharing of costs, access to benefits of R&D, and incentives to invest in needs-driven R&D consistent with human rights and with the goal of all sharing in the benefits of scientific advancement” (WHO, 2012a).

3. WHO Expert Working Groups on R&D financing

The GSPA-PHI as well as WHA61.21 required the WHO to “establish a results-oriented and time-limited expert working group under the auspices of WHO and linking up with other relevant groups to examine current financing and coordination of research and development, as well as proposals for new and innovative sources of financing to stimulate research and development related to Type II and Type III diseases and the specific research and development needs of developing countries in relation to Type I diseases”.³⁹ Two WHO expert working groups (the EWG and the CEWG) have examined the current financing and coordination of R&D, as well as proposals for new and innovative sources of financing to stimulate R&D directed at the specific needs of developing countries.

The EWG assembled 109 proposals on how to increase the level of R&D on neglected diseases. It then developed a methodology to assess the feasibility of the proposals. The EWG report was presented to the WHA in 2010 (WHO, 2010g). Subsequently, member states decided to establish the CEWG to further progress the work of the EWG.⁴⁰

The CEWG carried out an in-depth analysis of the proposals contained in the EWG report, considered additional submissions and proposals from relevant stakeholders, and also examined the appropriateness of different R&D financing approaches and the feasibility of implementing these approaches in each of the six WHO regions. The CEWG agreed on criteria for assessing the proposals. Such criteria included: public health impact; efficiency/cost-effectiveness; technical, financial and implementation feasibility; IP, delinking, access, governance and accountability aspects, as well as capacity strengthening potential.⁴¹

The CEWG concluded that the proposals that came closest to meeting its criteria were: a global framework on R&D; open approaches to R&D and innovation; pooled funds; direct grants to companies; milestone prizes and end prizes; and patent pools. The proposals

Box 3.9. 2012 CEWG report: key recommendations

Approaches to R&D:

- Open knowledge innovation; pre-competitive R&D platforms, open source and open access schemes, and the utilization of prizes, in particular milestone prizes
- Equitable licensing and patent pools

Funding mechanisms:

- All countries should commit to spend at least 0.01 per cent of GDP on government-funded R&D aimed at addressing the health needs of developing countries in relation to product development.

Pooling resources:

- Between 20 per cent and 50 per cent of funds raised for health-related R&D aimed at addressing the needs of developing countries should be channeled through a pooled mechanism.

Strengthening R&D capacity and technology transfer:

- Address the capacity needs of academic and public research organizations in developing countries.
- Utilize direct grants to companies in developing countries.

Coordination:

- Establish a global health R&D observatory and relevant advisory mechanisms under the auspices of the WHO.

Implementation through a binding global instrument for R&D and innovation for health:

- Formal negotiations on an international convention on global health R&D should be initiated.⁴²

that did not meet the CEWG criteria included: tax breaks for companies; orphan drug legislation; green IP; PRVs; transferable IPRs; the Health Impact Fund; and purchase or procurement agreements. A detailed presentation and analysis on each of these proposals is set out in Annex 3 of the 2012 CEWG report (WHO, 2012a) (see Box 3.9).

The CEWG recommended that WHO member states negotiate a global convention or a treaty under the auspices of Article 19 of the WHO Constitution. The proposed convention would be aimed at providing effective financing and coordination mechanisms to promote R&D. It would bind all governments to invest 0.01 per cent of gross domestic product (GDP) in R&D for Type II and Type III diseases and in R&D for the specific needs of developing countries in relation to Type I diseases. Part of these contributions would be collected in a pooled fund at global level. The CEWG report was presented to the 65th WHA in May 2012 for further consideration by member states. In November 2012, an open-ended meeting of member states agreed to establish a global health R&D observatory within the WHO Secretariat in order to monitor and analyse relevant information on health R&D for neglected diseases. Member states also agreed to explore and evaluate existing mechanisms for contributions to health R&D for such diseases and, if there is no suitable mechanism, to develop a proposal for effective mechanisms, including pooling resources and voluntary contributions, as well as a plan to independently monitor their effectiveness.⁴³

4. Product development partnerships: new pathways to innovation

The term public–private partnership (PPP) is usually used to describe an initiative that consists of a partnership between government and at least one private-sector company. Today, such partnerships manage a large proportion of all neglected diseases drug development projects worldwide. PPPs have common characteristics:

- They integrate public-sector and private-sector approaches, and generally use industry practices in their R&D activities.
- They manage neglected diseases R&D portfolios and they target one or more neglected disease.
- They are created in order to pursue public health objectives rather than commercial gains, and also in order to provide funding to cover existing research gaps.
- They ensure that the developed products are affordable (WHO, 2006b).

It is difficult, however, to clearly identify the common denominator in all initiatives that are identified as “PPPs”. Some may not be true “public–private” partnerships, in the sense that they may not have partners from both private and public sectors (Moran et al., 2005). The broader category of product development partnerships (PDPs) embraces such initiatives that do not necessarily have a public-sector or private-sector partner, and thus do not qualify as PPPs in the strict sense. It therefore

encompasses equally public health-driven, not-for-profit organizations that use private-sector approaches to develop new products in conjunction with external partners. This study uses the term PDP, not PPP, as it is more descriptive of new structures for medical innovation.

The emergence over the last 15 years of PDPs drawing together actors from the public and private sectors has been a major development in efforts to focus R&D towards diseases that disproportionately affect low- and middle-income countries (LMICs). These new partnerships have been constituted in a number of ways, but usually with the involvement of non-profit organizations, foundations and industry. The non-profit philanthropic sector provides most funds for such PDPs, notably the Bill & Melinda Gates Foundation (Grace, 2010). These partnerships have significantly increased the number of products in development for diseases and conditions that predominantly affect developing countries, and they play an important role in identifying pathways and overcoming bottlenecks in research for neglected diseases.

A 2005 study, which examined the portfolios of five PDPs as well as the portfolios of a selected number of pharmaceutical companies, identified 63 new drug development projects for neglected diseases (including tropical diseases, malaria and TB). A significant finding was that one quarter of development projects came from the pharmaceutical industry working alone; one quarter from the pharmaceutical industry together with PDPs; and the balance from PDPs working with a diversity of small companies, developing country companies, academics and the public sector. Thus, PDPs were involved in three quarters of all identified neglected diseases drug development projects in 2005 (Moran et al., 2005).

PDPs form alliances with stakeholders drawn from the public and private sectors because PDPs and these entities have the potential to capitalize on the opportunities that each may offer the other. PDPs are performing the service of integrating inputs from different branches of a very diverse industry. PDPs also seem to have lower research costs than research-based pharmaceutical companies for a number of reasons. PDPs benefit from lower capital costs as a result of their capacity to leverage in-kind inputs. They also benefit from the fact that they do not have to fund a fully loaded development pipeline. Instead, they select their projects from a pool of existing public and private domain projects. On the other hand, their costs could be expected to increase substantially as more projects enter large-scale Phase III trials. In this case, the PDP cost-efficiency profile would probably change, since late-stage failures are more expensive than early-stage failures (Moran et al., 2005). Some examples of PDPs organized to tackle solutions for neglected diseases are given in Box 3.10. A concrete example of a needs-driven partnership is the Drugs for Neglected Diseases initiative (DNDi) (see Box 3.11).

Box 3.10. Public-private partnerships and product development partnerships

In 2011, funding to PDPs involved in research into neglected diseases totalled US\$ 451.4 million. This represented 14.8 per cent of global funding for research on neglected diseases. Four PDPs – Programme for Appropriate Technology in Health (PATH), Medicines for Malaria Venture (MMV), the International AIDS Vaccine Initiative (IAVI) and the Aeras Global TB Vaccine Foundation – accounted for over half of all PDP funding (Moran et al., 2012).

One of the first of such new PDPs was the IAVI, founded in 1996, but many more have been created since then, including:

HIV/AIDS

- IAVI
- International Partnership for Microbicides
- South African AIDS Vaccine Initiative

Malaria

- Malaria Vaccine Initiative
- MMV

TB

- Aeras Global TB Vaccine Foundation
- Foundation for Innovative New Diagnostics
- Global Alliance for TB Drug Development
- Tuberculosis Vaccine Initiative

Other partnerships include

- Drugs for Neglected Diseases Initiative
- Institute for OneWorld Health
- PATH
- International Vaccine Institute
- Infectious Disease Research Institute
- Innovative Vector Control Consortium
- Sabin Vaccine Institute
- European Vaccine Initiative.⁴⁴

5. Research for neglected diseases: a growing role for pharmaceutical companies

Research-based pharmaceutical companies are increasingly engaged in philanthropic research. Aggregated contributions make the industry in 2011 the second largest sponsor of research for neglected diseases, after the US National Institutes of Health and ahead of the Bill & Melinda Gates Foundation (Moran et al., 2012). A number of companies have established dedicated research institutes to develop new products targeting diseases that disproportionately affect developing countries, or participate in cooperative

Box 3.11. Drugs for Neglected Diseases initiative: a concrete example of a needs-driven partnership

DNDi is a collaborative patients' needs driven, non-profit R&D organization that aims at bridging gaps in existing R&D in essential drugs for neglected diseases.⁴⁵ To ensure access to medicines and medical technologies in endemic countries, DNDi negotiates non-exclusive licenses with any right holders to have the final product registered and sold on an affordable and equitable basis in all endemic countries. In addition, DNDi secures contractual commitments from its industrial partners to sell the products on a cost-plus basis (e.g. the costs of production plus a reasonable margin to sustain long-term production). By negotiating access commitments at a very early stage in the R&D process, DNDi is paving the way to access through delinking the costs of R&D (financed with DNDi funding) from the final price of the product (maintained at the lowest possible sustainable level by the manufacturing partner).

The example of ASAQ, a new fixed-dose combination of artesunate (AS) and amodiaquine (AQ) for the treatment of uncomplicated malaria, illustrates this approach. DNDi coordinated the development of ASAQ with various public-sector and private-sector partners while retaining ownership of the related IP. DNDi then licensed IP to a pharmaceutical company for the industrial production, registration and distribution of ASAQ in Africa and other developing countries. Under the agreement, the pharmaceutical company committed to supply ASAQ to the public sector of endemic countries at a "no-profit-no-loss" maximum price of US\$ 1 per adult treatment. In the private sector, the pharmaceutical company is free to sell the product at market price and pays a 3-per-cent royalty on sales to DNDi, which is reinvested in further research. The various public-sector and private-sector partners have agreed not to file any patent on ASAQ. As a consequence, ASAQ can be freely produced and distributed by any other pharmaceutical company in the world. The results of this approach are conclusive: ASAQ is registered in 30 countries in sub-Saharan Africa and India. It is pre-qualified by the WHO, and more than 130 million treatments have been distributed to date. In addition, DNDi is also facilitating technology transfer to an African manufacturer.

Table 3.2. Industry R&D centres dedicated to research on diseases that disproportionately affect developing countries

Company	Centre	Location	Disease	Since
AstraZeneca	Bangalore Research Institute	Bangalore, India	Tuberculosis Malaria	2003 2009
GlaxoSmithKline	Tres Cantos Medicines Development campus	Tres Cantos, Spain	Malaria Tuberculosis Kinetoplastids	2002
MSD/Merck & Co.	MSD Wellcome Trust Hillemann Laboratories	New Delhi, India	Rotavirus	2009
Novartis	Novartis Institute for Tropical Diseases (NITD)	Singapore	Dengue Fever Malaria Tuberculosis	2002
Novartis	Novartis Vaccines Institute for Global Health (NVGH)	Siena, Italy	Diarrhoeal diseases Salmonella	2008
Novartis	Genomics Institute of the Novartis Research Foundation (GNF)	La Jolla, USA	Chagas disease Leishmaniasis Malaria	2010
Novartis	Novartis Institutes for Biomedical Research (NIBR)	Horsham, UK	Infectious diarrhoea	2009

Source: IFPMA (2013).

projects and PDPs, thus sharing assets and knowledge. Table 3.2 gives details of some industry-supported R&D centres that are dedicated to research in neglected diseases. In total, research-based pharmaceutical companies were reported in 2012 to be engaged in 132 projects aimed at developing new medicines and vaccines for diseases which have been prioritized by the WHO Programme for Research and Training in Tropical Diseases (TDR). Of these projects, 112 are being carried out in collaboration with PDPs. A further 20 are being run by individual research-based pharmaceutical companies without the involvement of third parties (IFPMA, 2013).

On 30 January 2012, pharmaceutical companies together with a range of public and private partners met in London and agreed to unite for a new, coordinated push to accelerate progress toward eliminating or controlling 10 neglected tropical diseases. They confirmed their commitment to expanding current programmes that ensure the necessary supply of medicines and other interventions and advance R&D through partnerships and provision of funding to develop next generation treatments, and providing continued financial support to accelerate progress towards eliminating or controlling these diseases by 2020. These commitments were laid down in the "London Declaration on Neglected Tropical Diseases".⁴⁶

Box 3.12. WIPO Re:Search

In October 2011, WIPO, in collaboration with public-sector and private-sector researchers and BIO Ventures for Global Health, launched a new consortium called WIPO Re:Search. Public-sector and private-sector organizations share IP and expertise with the global health research community to promote development of new medicines, vaccines and diagnostics to treat neglected tropical diseases, malaria and TB. Selected IP assets are available under royalty-free licences to researchers anywhere in the world. As products come to market, licences for sale will be royalty-free in all least-developed countries, with royalties subject to negotiation for other developing countries.

This commitment of resources is expected to accelerate the development of medicines, vaccines, and diagnostics for neglected diseases, malaria and TB, and resources is aimed at facilitating new partnerships. The WHO supports the project through the provision of technical advice. WIPO Re:Search is grounded in voluntary agreements and operates on the basis of voluntary licenses. It is based on the belief that intellectual property and knowledge can be used creatively to stimulate more investment in R&D for new health solutions. By October 2012, WIPO Re:Search had 62 members and had facilitated 11 research collaborations or agreements between WIPO Re:Search members.⁴⁷

6. WIPO Re:Search: a new partnership to use intellectual property in public health

WIPO, working together with multiple stakeholders in the private sector, academia, and civil society, created a new partnership – WIPO Re:Search *Sharing Innovation in the Fight Against Neglected Tropical Diseases* (see Box 3.12). WIPO Re:Search provides an innovative model of IP sharing and management. It is based on the belief that IP and knowledge can be used creatively to stimulate the invention of new health solutions while ensuring access for the most disadvantaged populations and to demonstrate that IP can serve the needs of countries at all levels of development.

WIPO Re:Search aims to foster collaborations to advance and stimulate research and development for new and better treatment options for those suffering from neglected tropical diseases (NTDs, see Section C.1 above), malaria and TB. In addition to pharmaceutical companies, members of WIPO Re:Search include universities and research centres from all over the world. Of particular importance are the several research centres from the African continent whose participation is an important component to the development of new and better treatments for NTDs.

The approach of WIPO Re:Search is novel in that public-sector and private-sector organizations around the world are making valuable IP available to qualified researchers anywhere in the world seeking to develop new solutions for NTDs, malaria and TB. All licenses granted for R&D and manufacture must be royalty-free to any user anywhere in the world. Any products developed for these diseases under a WIPO Re:Search Agreement must be sold on a royalty-free basis in all least-developed countries (LDCs). Access terms for other, non-least developed, developing countries are subject to agreement between the parties. Services,

such as access to company research facilities, screening of compounds as well as the sharing of expertise and hosting of scientists, are also offered through WIPO Re:Search. The principal implementing tools developed by WIPO Re:Search are: *the Public Database*, to guarantee transparency and accessibility of information; and the *Partnership Hub* to facilitate collaboration and cross-sector partnerships.

The *Public Database* is composed of IP assets that providers have chosen to make available through WIPO Re:Search. All the information is publicly available and can be accessed without registration. Providers to the database submit summary information relevant to: hits, leads, lead series, pre-clinical candidates, clinical candidates, enabling technologies, IP, formulation, diagnostic tools, vaccines, new biological entities, know-how, or other services for the purpose of facilitating R&D.

Because collaborations are critical to success in science, the Partnership Hub is a key component of WIPO Re:Search. The Partnership Hub Administrator, BIO Ventures for Global Health (BVGH) is a non-governmental organization based in Seattle, United States. BVGH actively engages with members – including major pharmaceutical and biotechnology companies, academic and other non-profit research institutions, government, and non-governmental organizations – to facilitate NTD research collaborations among members.

Through the Partnership Hub, WIPO Re:Search connects providers and potential users so that assets and knowledge are shared to accelerate the development of products in the fight against NTDs. As WIPO Re:Search develops over time, WIPO and BVGH are collecting and analysing feedback in order to ensure that the consortium's operations, in particular the Database and related services, are useful to the global health research community.

For example, the first WIPO Re:Search agreements were made between industry and research institutions to study novel treatments for Chagas disease, sleeping sickness, schistosomiasis (snail fever), and TB. Specifically, these first agreements concern:

- Cathepsin inhibitors, originally developed for osteoarthritis, will be tested for activity in biochemical and phenotypic screens for two parasitic diseases: schistosomiasis and kinetoplastid diseases that include leishmaniasis, sleeping sickness and Chagas disease.

- Researchers will test a selection of glycogen synthase kinase (GSK)-3 inhibitors, which were originally developed for a potential treatment of Alzheimer's disease, against parasites responsible for Chagas disease, leishmaniasis and sleeping sickness.

- Isocitrate lyase inhibitors will be developed intended as a novel treatment for tuberculosis.

WIPO Re:Search is a results-oriented project that, through the creative and innovative use of IP, facilitates the research and development and technology transfer needed to find concrete solutions to one of the most challenging issues of global health today.

D. Intellectual property rights in the innovation cycle

Key points

- The international legal framework governing intellectual property rights (IPRs) and, possibly more importantly, the choices made within that framework at regional and national level can be essential determinants for the innovation cycle.
- The role of patent law in developing new medical technologies depends not only on the legal and administrative design of the patent system but also on specific decisions made by individual parties at different stages in the development process, in terms of whether and when to obtain patent rights, and how to exercise them.
- Biotechnology advances in the field of medical innovation have led to renewed debate about what should be considered patentable subject matter and how to identify the industrial applicability/utility in such cases.
- Incremental innovation can improve the safety, therapeutic effect or method of delivery of an existing medicine or vaccine. Whether such inventions merit the granting of a patent is judged on a case-by-case basis.
- While a patent on incremental innovation does not extend the term of the original patent, there are concerns about the negative effects of such patenting strategies on further innovation and access. These strategies are also referred to as “evergreening”, which remains a controversial issue.
- Some patent laws allow the granting of patent protection on a product for which a new medical indication has been identified, but only on condition that the proposed product fulfils all patentability criteria. In such circumstances, the product is regarded as new in respect of the new indication.
- The patenting of research tools have been particularly controversial in the biopharmaceuticals sector as it could hold up further downstream research.
- While the research exception is one of the most commonly found limited exceptions in national patent laws, no one single approach is used worldwide, and not all countries make use of such exceptions.
- Licences are tools for partnership building and cooperation and may allow public-sector entities to achieve public policy goals. Licences can be restricted to certain content or a degree of exclusivity, and may include know-how.
- Patent landscaping has evolved as a tool to search, analyse and illustrate the patent situation or patenting activity in a specific technology field, enabling policy-makers to follow trends in medical innovation.
- A freedom to operate (FTO) analysis provides the basis for a risk management decision in relation to R&D, product launch and commercialization.

Following the introduction to IPRs in Chapter II, Section B.1, this section looks at the impact of IPRs on innovation in the pharmaceutical sector, with a particular focus on patent-related issues. After having set out the interdependence of the international, regional and national framework, and the importance of choices made with respect to the management of IPRs, questions related to patentability in the pre-grant phase are then analysed, as well as issues related to the use of patents in the post-grant phase. To round up the section, an overview of issues regarding FTO is provided.

1. The role of international and national norms and IP management

While the international legal dimension of IPRs is critically important to the medical innovation ecosystem – and has garnered much attention in policy debate – it is essential to consider the various layers of IP law and policy which ultimately influence the directions that research takes. TRIPS provisions, for instance, can be understood as part of the interplay between international and domestic law and policy frameworks. Policy measures with bearing

on medical technologies range from the strategies of individual projects to the standards of international law:

- General policies and strategies for management of IP at institutional or project level, whether within the private sector, the public sector or the philanthropic sector, and including practical choices such as whether or not to file for a patent, and, if so, where; and how to exercise the ensuing rights.
- National innovation policy settings, including targeted incentive initiatives, and policies for the management of publicly funded medical research.
- National legislative settings, including IP laws and their interaction with other aspects of the regulatory system, such as competition policy and regulation of medicines.
- International cooperation on public health and specific international initiatives, including on neglected diseases research.
- The international legal framework, comprising a complex of so-called “hard law” and “soft law” instruments and standards spanning trade and investment, IP, public health, human rights, bioethics and related areas.

Consequently, while international legal standards can have a major impact on innovation systems (e.g. in requiring pharmaceutical inventions to be patentable), the choices made at regional and national level within the international legal framework can be possibly equally, if not more important (e.g. in determining and applying specific patentability criteria under national law). Similarly, the choices made by a public-sector research programme or a private-sector company regarding the management of IP can have a more immediate impact on R&D outcomes. These choices for IP management are often shaped by overall innovation structures, such as those discussed in Section B.4(e) above.

2. Intellectual property and the product development process

An overview of relevant IP issues that arise at each stage of the product development pipeline can help to clarify the linkages between specific issues and choices within a narrower operational context, and the overarching policy objective of improved public health outcomes. Table 3.3 sets out these issues. Each of these is not a narrow “technical” question that can be considered entirely in isolation. Rather, the successful development and diffusion of a new technology is a consequence of the combined impact of choices taken at each of these steps.

The debate on the value and practical impact of the patent system, in particular, in delivering needed medical technologies has highlighted two key points.

- First, patent law is not a stand-alone innovation system. It is only one element of the innovation process, and one which can be deployed differently in diverse innovation scenarios. Patent law has little bearing on many other factors that lead to the successful development of technologies, e.g. the nature and extent of demand, commercial advantages gained by marketing and ancillary services and support, commercial and technical viability of production processes, and compliance with regulatory requirements, including through effective management of clinical trials data.
- The role of the patent system in developing a new medical technology depends not only on legislative and regulatory settings, but also on a variety of choices made by individuals at different stages of the development process as to whether and when to obtain patent rights, and how to exercise them. They may rely on exclusive commercial positions, or may draw from a range of nonexclusive and open licensing structures, waivers of rights and specific non-assertion undertakings. Notably, in the case of not-for-profit initiatives in public health, these approaches are not necessarily aimed at securing financial advantages. Instead, they are aimed at leveraging access to complementary technologies.

Patents do not have the same importance to all industries. In addition, they have quite different impacts on markets, as is illustrated by the comparison between the medical devices industry and the pharmaceutical industry (see Table 3.4).

3. Pre-grant issues: questions of patentability

This section considers selective aspects of patent law that are especially relevant to the innovation dimension of medical technologies.

(a) Patenting material that exists in nature

While modern biotechnology plays an increasing role in pharmaceutical R&D and production, patents have been granted on biotechnological inventions since the 19th century.⁴⁸ For instance, German patent DE 336051 was granted in 1911 to Friedrich Franz Friedmann on the production of a therapeutic against TB involving the continued vaccination of tubercle bacilli obtained from turtles.

The maturing of genetic engineering has been accompanied by an intense public debate about the desirability and appropriateness of applying patent law to modern biotechnology. Important legislative and administrative steps have been taken to clarify some of these issues, such as Directive 98/44/EC of the European Parliament and of the Council on the legal protection of biotechnological

Table 3.3. Illustration of IP issues that arise at each stage of the product development pipeline

Innovation planning for health outcomes	Initiating research on unmet public health needs	Initial choices on presence and absence of IP protection	Beyond the initial research: proof of concept and scaling-up	Clinical trials and regulatory approval	Manufacture and distribution	Distribution and marketing phase
<ul style="list-style-type: none"> - Setting IP policies and management strategies, including clarifying questions of ownership, access and control over research outcomes. - Surveys of existing technology as research inputs and patterns of ownership (according to patent holder, and territorial effect of patents in force), so as to identify potential partners and possible barriers as well as avenues for productive new research. - Assessment of FTO, status of existing technology, in addition to prospects for technology partnering, access and pooling options. 	<ul style="list-style-type: none"> - IP or non-IP incentives for private investment in research and other contributions (including financial and other resources, background technology, infrastructure, scientific and technology management expertise, management of regulatory processes, risk exposure and opportunity cost). - Negotiation of terms and conditions covering R&D, including using IP when negotiating guarantees of development and access to finished product; negotiation or implementation of public interest safeguards so as to ensure adequate access to research outcomes. - Establishing and implementing publication and IP management policies for researchers. 	<ul style="list-style-type: none"> - Following initial research outcomes and their subsequent elaboration, the decision at an institution or company level whether or not to seek IP protection on particular innovations and in which jurisdictions, guided by an overall product development, commercialization and diffusion strategy. - Decisions at national and regional levels concerning the patentability of the research outcome according to patent grant criteria. - Management of know-how, confidential information and other forms of IP. 	<ul style="list-style-type: none"> - IP arrangements in negotiations on financing and conducting clinical trials, and in attracting further investment, philanthropic support or allocation of public resources. - Other incentives trigger innovation in certain fields, e.g. through "orphan disease" schemes. - Assessment of the IP implications of moving beyond a pure research phase into the preliminary stages of full drug development. 	<ul style="list-style-type: none"> - Arrangements for generating, protecting and accessing clinical trial data; incentives for investing in this process, and the laws and policy settings that govern this; mechanisms for facilitating or reducing the cost of regulatory approval, such as push and pull incentives, e.g. advance market commitments. - IP aspects of issues such as mutual recognition of regulatory approvals, sharing of data, negotiating or otherwise ensuring access to, and use of, clinical trial data. 	<ul style="list-style-type: none"> - Access to necessary manufacturing, excipient and adjuvant, drug delivery and platform technologies. - IP management strategies for effective global outcomes (including different ownership in different markets or jurisdictions; different approaches to control or licensing of IPRs in rich and poor countries; role of IP in tiered pricing; "march in" rights and other forms of guarantees of access to public or philanthropic-funded research). - Requirements of national competition policies. 	<ul style="list-style-type: none"> - Monitoring and enforcing access guarantees, such as licensing provisions providing for effective access for particular patient groups and requirements for timely introduction of medicines to specified markets. - Managing IP that may be relevant to improvements and new indications, and regulatory approval; fulfilling access commitments. - Assessing the implications of regulations governing the use of IP in the marketplace, e.g. measures against anti-competitive practices.



Table 3.4. The different role of patents in the medical devices industry and the pharmaceutical industry⁴⁹

Medical devices industry	Pharmaceutical industry
Characteristics: Medical devices are mainly based on mechanical/electrical technology, information technology and systems engineering. The trigger for innovation typically arises from a clinician's practice.	Characteristics: Pharmaceutical products are based on chemistry, biotechnology and genetics. Fundamental research, applied research, including that based on traditional knowledge, are the basis for innovation.
Patents: Given the interplay between many fields of art, technically complex devices may be protected by hundreds of patents covering the structure, function and/or methods of using the device.	Patents: Active ingredients/chemical compounds are usually covered by a small number of patents, with additional patents addressing variations of such ingredients/compounds, e.g. salts and esters, polymorphs, ways of delivery or formulations.
Design and invent around: In the field of medical devices, to opt for a not protected design and thus invent around patents is relatively common because alternative technical solutions can be found. This, in turn, enables the creation of greater competition in the market through alternative types of devices, with variations and continuous iterative improvements produced by other companies within the patent term. Competition, coupled with the continuous need and pressure for innovation, lead to relatively short commercial life cycles of about 18-24 months, which is much shorter than the potential patent term of 20 years. However, while the product may change frequently, the technology may be continuously used in successor products.	Design and invent around: In the pharmaceutical area, to invent around patents is often more difficult. Patents covering chemical compounds can exclude competitors from producing comparable products for the entire patent term. In general, pharmaceuticals, if proven efficacious and safe, can enjoy a long commercial life cycle of about 10-20 years or more without undergoing significant changes. Patents will thus be exploited until the end of the patent term.

inventions⁵⁰ and the United States Patent and Trademark Office (USPTO) revised *Guidelines For Determining Utility Of Gene-Related Inventions* of 5 January 2001.⁵¹ Some jurisdictions require that the function of a gene needs to be clearly identified and to be related to the claimed part of the gene sequence. For example, Section 1a(3) of the German Federal Patent Act stipulates: "The industrial application of a sequence or a partial sequence of a gene shall have to be specifically disclosed in the application by indicating the function fulfilled by the sequence or partial sequence". In relation to gene sequences, Swiss patent law limits the exclusivity rights stemming from the patent to those parts of the gene sequence that are strictly necessary to fulfil the functions described in the patent (Article 8c Swiss Patent Law).

A 2001 WIPO survey⁵² provides information about national legislation of WIPO member states related to the protection of biotechnological inventions under patent and/or plant variety protection systems, including information as to which countries might admit the patenting of genes, cells or plant varieties.

One specific biotechnology patent law issue that is relevant to pharmaceutical production relates to the patentability of material existing in nature or in synthesized or extracted chemical compounds, particularly if they are identical to a compound that already exists in nature. A distinction is made between a naturally occurring compound and an artificially extracted and isolated compound. The latter is considered to be a new entity and patentable subject matter in some jurisdictions.

In 1910, Japan granted a patent for an isolated, naturally occurring substance, aberic acid (now termed thiamine, or vitamin B1) from rice bran, that had been identified for the prevention of beriberi, a disease caused by a lack of vitamin B1. The same year, a United States court upheld a

patent granted to an inventor who had isolated adrenalin from the human suprarenal gland, had purified it, and had identified that it could be used in the treatment of heart disease.

While in many cases, patentability criteria are successfully applied by patent law practice and by the courts to determine the patentability of biotechnology inventions, two cases in US courts illustrate that controversy continues (see Boxes 3.13 and 3.14).

(b) First and second medical indications

In certain cases, a previously known substance, used for a certain purpose, may later be found effective in the treatment of a disease, and a patent application may be filed claiming the "first medical use" (also called "secondary use" or "new use") of the known product.⁵³ If the first or earlier use was already medical in nature, such claims are labelled "second medical indication". The Agreement on Trade-Related Aspects of Intellectual Property Rights (TRIPS Agreement) does not expressly address this question. National patent laws differ on this point. Some patent laws specifically rule out the patenting of first or secondary medical indications. For example, the Andean Community Decision 486, the common IP law for the Member States of the Andean Community, stipulates in Article 21: "Products or processes already patented and included in the state of the art... may not be the subject of new patents on the sole ground of having been put to a use different from that originally contemplated by the initial patent".⁵⁴ Some jurisdictions allow patents on a known medical substance for use in a new method of treatment if that use is not known. This is, for example, the case with Article 54(4) and (5) of the European Patent Convention (EPC) as revised in 2000.⁵⁵ It should be noted that all other patentability criteria under the EPC

Box 3.13. BRCA-1 and BRCA-2: the “Myriad case”

BRCA-1 and BRCA-2 are two genes linked to susceptibility to breast and ovarian cancer. The risk of getting cancer increases if these genes show certain mutations. Identifying the mutations is therefore important for diagnosis and for monitoring higher-risk women. Myriad Genetics Inc., in collaboration with the University of Utah, Cancer Institute of Japan and the Centre de Recherche du Chul in Canada obtained patents on the isolated DNA coding for two genes, BRCA-1 and BRCA-2, and on a related screening methods. As a product patent not only protects the functions disclosed in the patent, but also all other possible future therapeutic uses of the gene, concerns have been raised that any other patent for a different use of the genes would be dependent on the patents held by Myriad Genetics (Von der Ropp and Taubman, 2004) and this could serve as disincentive to carrying out further research on possible functions of this gene.

Where patents were in force, Myriad Genetics adopted a restrictive licence policy that in practice only allowed Myriad to perform the complete sequence analysis in their laboratories in the United States (Matthijs and Van Ommen, 2009). Public health concerns have been raised about the issue of having only one source for diagnostic testing.

In 2010, the US District Court for the Southern District of New York held that patents on the BRCA-1 and BRCA-2 genes were invalid on grounds of lack of novelty because the genes, even in isolated form, were not markedly different from what existed in nature. The judgement stated: “DNA’s existence in an ‘isolated’ form alters neither this fundamental quality of DNA as it exists in the body nor the information it encodes”. This decision was reversed by the US Court of Appeals for the Federal Circuit in 2011. The Court of Appeals noted that the distinction between a product of nature and a human-made invention depended on a change in chemical identity compared with what exists in nature. An isolated gene sequence (“a free-standing portion of a native DNA molecule”) could be claimed as a patentable invention, by contrast with purified DNA material. Further, it stated: “Purification makes pure what was the same material, but was previously impure. Although isolated DNA must be removed from its native cellular and chromosomal environment, it has also been manipulated chemically so as to produce a molecule that is markedly different from that which exists in the body”. The US Court of Appeals decision states “that biologists may think of molecules in terms of their uses, but genes are in fact materials having a chemical nature and, as such, are best described in patents by their structures rather than their functions”. Upon appeal to the Supreme Court, that court remanded the Myriad Genetics case back to the Federal Circuit Court in 2012 to reconsider it in light of the *Mayo v. Prometheus* decision (see Box 3.14).⁵⁶

The Federal Circuit Court, in its decision of 16 August 2012, confirmed its view that the claims directed to isolated DNA molecules were patent-eligible subject matter under 35 USC. § 101, and considered that the *Mayo v. Prometheus* decision would not change that result. However, the court reiterated that the issue was patent eligibility, not patentability, about which it did not express an opinion. The court held that some method claims were patentable subject matter and some not.⁵⁷

The US Supreme Court granted certiorari in November 2012 in this case, in effect agreeing to review the question whether human genes are patent-eligible or not.⁵⁸

Box 3.14. *Mayo Collaborative Services v. Prometheus Laboratories*

In the case *Mayo Collaborative Services v Prometheus Laboratories*, the Supreme Court decided unanimously on 20 March 2012 that *Prometheus Laboratories’* claims to methods of administering drugs to treat gastrointestinal autoimmune diseases are not sufficiently distinct from the laws of nature so as to meet the patentable subject matter standard of section 101 of the US Patent Act. The disputed claims covered a method of optimizing therapeutic efficacy for treatment of an immune-mediated gastrointestinal disorder comprising two steps:

- administering one of a class of drugs (thiopurines)
- determining the level of a specified metabolite in the blood, where a level below a certain threshold indicated a need to increase the amount of the drug to improve efficacy, and a level above the threshold indicated a need to decrease the amount of the drug to avoid toxicity.⁵⁹

Box 3.15. Secondary use patents: the case of Fluoxetine

Fluoxetine (better known as “Prozac”) was first marketed in the United States for the treatment of depression in 1987, and its US base patent expired about 14 years later, in 2001. However, fluoxetine was discovered to also be useful in the treatment of a second indication, premenstrual dysphoric disorder. A pharmaceutical company obtained a patent on this secondary use in 1990 (United States Patent No. 4,971,998) and secured regulatory approval for this indication in 2000 under the trade name Sarafem. Although both medicines contain the identical active ingredient (fluoxetine hydrochloride), at an identical dosage level (20 mg), the prices differ widely in the US: in one pharmacy, it was found that Prozac was US\$ 0.83 per pill for Prozac, while Sarafem was US\$ 9.26 per pill.

must be met before a patent on a known substance for a new medical use can be granted. The European Patent Office Enlarged Board of Appeal clarified that: “where it is already known to use a medicament to treat an illness, Article 54(5) EPC does not exclude that this medicament be patented for use in a different treatment by therapy of the same illness”.⁶⁰ This means that a known substance – if it meets the general criteria for patentability – can be patented for use in a different treatment for the same illness. Such a secondary use patent, however, does not extend the patent protection covering the already known medical use.

The case of fluoxetine as a secondary use patent illustrates how prices can differ widely for the same product used to treat a different medical use (see Box 3.15).

The patentability of secondary indications is a matter of debate, and therefore exemplifies the continuing challenge in patent law of balancing access against innovation. On the one hand, opponents of secondary use patents argue that such patents impede access to medicines, reward uninventive activities and unnecessarily prolong effective patent protection for a certain medical substance. On the other hand, proponents express the view that an additional medical use can itself be inventive, and that the development and clinical testing of a second use is no less in need of incentives than the first use, and in some cases may be more therapeutically valuable than the first use.

Some guidance about when the European Patent Office (EPO) grants patents for a second medical indication can be obtained from the guidelines for patent examination of the EPO.⁶¹

(c) Incremental and adaptive innovation

Patents can be granted on incremental innovations if they meet the patentability criteria. The application of the inventive step/non-obviousness criterion⁶² has implications for incremental innovation. Incremental innovation can improve the safety, therapeutic effect or method of delivery of an existing medicine or vaccine, or improve the efficiency with which it can be manufactured, with positive outcomes for public health.

(i) *Examples of incremental innovation*

Frequently, the first approved formulations of a drug are followed by changes in the formulation or route of administration that improve the effectiveness of the treatment. These incremental innovations include, for example:

- **New dosage forms which increase compliance:** Controlled-release formulations, which permit a single administration per day or even per week (as opposed to multiple administrations), can increase compliance due to decreased frequency of administration as well as a more stable drug level and decreased side-effects. There are many such examples. They include oral formulations for sustained delivery of antibiotics, injectable sustained-release formulations of hormones, topical sustained release formulations for hormones, among others. New dosage forms which increase compliance also include sublingual or rapid-dispersion tabs, which are easier to take than capsules and give a more rapid effect. Sublingual benzodiazepines are an example of one such dosage form.
- **New dosage forms with improved efficacy:** Frequently, the addition of an additive or a second active ingredient can improve the efficacy of a drug to treat a specific ailment. These can be taken separately as two drugs. However, combining them improves effectiveness since dosage compliance is assured. Packaging and prescription are also simplified. There are numerous examples of new dosage forms with improved efficacy, such as the inclusion of corticosteroids with antivirals, and the coformulation of antiretroviral drugs.
- **New formulations with improved storage characteristics:** Reliance on the cold chain is a barrier to access for many drugs which lose their activity when stored out of the cold chain. Numerous second-generation products with improved heat stability (or simply decreased storage volume) are easier to ship and to store, enabling access in resource-poor settings. Examples include vaccines that can be stored in a fridge rather than a freezer (oral polio vaccine, nasal influenza) and oral drugs that can be stored at room temperature.

- **New routes of delivery:** Many drugs are first approved for administration by injection, a route which limits ease of access. Alternative routes of administration (e.g. oral, nasal, topical patch) are then developed, thus greatly simplifying ease of administration, access and effectiveness. Examples include oral forms of antibiotics, nasal vaccines, among others.

Other incremental innovations related to a known, approved drug can have a significant impact on effectiveness. For example, improved processes for production can decrease the cost of manufacture. Improved processes for purification can decrease the contamination of the drug with residual potentially toxic substances.

(ii) *Patent clusters and evergreening*

Concerns have been raised that the patent clusters around an existing medicine, that is patenting of new forms or other minor variations of existing products that have no additional therapeutic value and display limited inventiveness, can be used to prolong patent protection in an inappropriate manner, thus creating a negative effect on access to medicines, as well as on further innovation – a strategy referred to as “evergreening”. The Commission on Intellectual Property Rights, Innovation and Public Health (CIPRH) defined evergreening as a term popularly used to describe patenting strategies “when, in the absence of any apparent additional therapeutic benefits, patent holders use various strategies to extend the length of their exclusivity beyond the 20-year patent term” (WHO, 2006b).

The European Commission has identified the creation of “patent clusters” by filing numerous additional patents for the same medicine as a common strategy employed by pharmaceutical companies. Companies reportedly file a significant number of these additional patents on variations of the same product, especially for blockbuster medicines, very late in the life cycle of a medicine, when the main patent is about to expire.⁶³ The Commission found that these patent clusters make it more difficult for generic competitors to evaluate whether they can develop a generic version of the original medicine without infringing one of the numerous patents filed around one medicine. The number of patents also increases the risk of potentially costly litigation for generic companies.

In reviewing the evergreening debate, the CIPRH commented that “demarcating the line between incremental innovations that confer real clinical improvements, therapeutic advantages or manufacturing improvements, and those that offer no therapeutic benefits is not an easy task. But it is crucial to avoid patents being used as barriers to legitimate competition”. The CIPRH recommended that governments “take action to avoid barriers to legitimate competition by considering developing guidelines for patent examiners on how properly to implement patentability criteria and, if appropriate, consider changes to national patent legislation”.⁶⁴

The central issue is: when does an adaptation or modification of a first patented invention itself become separately eligible for a patent? In this respect, it is important to judge every individual invention claimed in a patent on its merits. The mere fact that an innovation is incremental is not a ground for refusing the granting of a patent. In fact, most innovation is incremental by nature since technology normally progresses in incremental steps. In order to distinguish inventions that meet the inventive step/non-obviousness criterion from others that do not meet the criterion, patent law and practice have developed and established patentability criteria that need to be met before a patent can be granted.

Some health policy-makers argue that therapeutic efficacy should be used as an additional criterion to prevent evergreening and that patent protection for incremental innovations should be granted only if the invention provides sufficient additional therapeutic benefits. While the therapeutic value of a product as such is not a patentability criterion in most jurisdictions, therapeutic advantages over what exists in the prior art⁶⁵ may be considered when determining inventive step. Furthermore, any intention behind patent grant – for example, to build a defensive layer of additional patents to be used against competitors – is not a relevant criterion in the granting procedure. Post-grant measures such as exceptions and limitations, and the regulation of licensing practices, can be applied to deal with undesirable effects of validly granted patents. Thus, a patent must be available if the patentability criteria of novelty, inventive step, and industrial applicability are met.

In the context of a patent system, and to the extent that the evergreening debate concerns the grant of patents (rather than how patent rights are exercised by patent holders), the debate can be considered from two angles:

- How are the patentability criteria defined by the relevant national law and interpreted by case law and practice? Many countries have revised their legislation to adopt different types of measures. Section 3(d) of India’s Patent Act 1970 (see Box 3.16) and Section 22 of the Philippines’ Intellectual Property Code are two examples of a narrow definition of patentability criteria. Countries apply different approaches, however, and various definitions and practices exist in the granting of patents to pharmaceutical inventions (e.g. for claimed inventions relating to second medical use, dosage regimes etc.).
- How are the patentability criteria applied by examiners in a consistent manner that is in line with the established definition and interpretation? Some patent offices have set up search and examination guidelines as instruments to support the examiners’ work with a view to ensuring high quality of granted patents. Such guidelines need to be regularly revised and maintained. WIPO has published a collection of links

Box 3.16. How India defines and applies patentability criteria

When revising its patent law to comply with the TRIPS requirement that pharmaceutical products be patentable, India adopted specific patentability criteria for chemical products by introducing Section 3(d) to its Patent Act (Patents Amendment Act of 2005). According to this section, “the mere discovery of a new form of a known substance which does not result in the enhancement of the known efficacy of that substance or the mere discovery of any new property or new use for a known substance or of the mere use of a known process, machine or apparatus unless such known process results in a new product or employs at least one new reactant” is not considered an invention and is thus not patentable.

In 2007, the Indian Patent Office, following an opposition filed by a patient organization, refused to grant a pharmaceutical company a patent for the cancer drug imatinib mesylate based on Section 3(d). The patent office considered the beta crystalline form of imatinib mesylate to be a new form of a known substance without the enhancement in efficacy required under Section 3(d). The company filed two lawsuits. In one lawsuit, it challenged the decision of the Patent Office, claiming that imatinib mesylate fulfils the patentability requirements under the Indian Patent Act as it enhances the efficacy of a known substance. In a second lawsuit, the company claimed that Section 3(d) does not comply with the TRIPS Agreement and violated the Indian Constitution. On 6 August 2007 the High Court in Madras decided that it was not the forum to address questions on compliance with the TRIPS Agreement and rejected the constitutional challenge. On 6 June 2009, the Intellectual Property Appellate Board of Chennai dismissed the lawsuit against the Indian Patent Office. This judgment was appealed by the patent applicant to the Supreme Court and a decision is pending. The decision is expected to have major implications for the supply of generic drugs from India in the future (UNAIDS/WHO/UNDP, 2011).

In two other cases in 2008 and 2009, the Indian Patent Office applied the Madras High Court’s interpretation of “efficacy” to reject patent applications for formulations of two existing HIV/AIDS medicines, one, a paediatric suspension of nevirapine hemihydrate and the second, tenofovir disoproxil.

to a range of patent offices’ guidelines for easy access to this information.⁶⁶ Argentina adopted guidelines for patent examiners along similar lines as the Indian Section 3(d) of India’s Patent Act 1970 in May 2012.⁶⁷ In addition, patent offices need to regularly train examiners, maintain a supportive infrastructure (e.g. prior art databases).

One question that has been raised is whether this task of ascertaining whether incremental innovation that otherwise meets the criteria for patentability offers therapeutic benefits or deters competition should be assigned to patent offices or would better be done by competition or health authorities (Yamane, 2011).

Leaving aside the question of patentability, it must be noted that the granting of a patent on an incremental improvement of a pharmaceutical is independent from the granted patent of the original product. Specifically, it does not extend the patent term of the earlier patent. While the improved form of the medicine will be covered by the new patent, the patent protection of the original version will end with the expiration of the first patent.

(d) Patent filing strategies in the public and private sector and the exercise of patent rights

Apart from the provisions of the national or international law and their interpretation by the courts, the patent filing

strategies of applicants could determine the innovation and imitation landscape for medical technologies. Filing a patent application involves a series of decisions regarding the specific invention(s) for which patents are to be sought, for what practical purpose, in which jurisdictions, in whose name, with whose funds and when.

Factors determining whether or not a patent application is filed may range from whether the technology is a better solution than any currently available options, to the size of the potential market for the technology, or the likelihood of competition. For public-sector researchers, notably in the field of public health, considerations tend to be focused on concerns about how the decision to patent or not the technology would advance the institutional or policy goals of their particular research establishment, and whether a patent would help secure suitable partners for downstream product development. The capital requirements needed to further develop the technology into a medical product must be considered, including the need to license in any other proprietary technology, the cost of satisfying any regulatory requirements, and the prospects of attracting investment or partners to finance or co-develop these requirements if they cannot be met in-house.

From the inventor’s perspective, patent protection may not be the best strategy if secrecy can be maintained and the technology cannot be reverse-engineered. Similarly, patenting would not be the best strategy if competitors were able to easily develop alternatives to the patented

invention (i.e. they could design around it) or it was likely to be difficult to ascertain whether competitors were using it without authorization.

Patent application filing strategies determine the countries or territories in which protection is to be sought. Fees must be paid for the grant and maintenance of each patent in each separate country or territory, which can be expensive, and may not be justified in markets where the patent is unlikely to be used. The Patent Cooperation Treaty (PCT) enables a single patent application to be filed with effect for all PCT contracting states. Since national processing of an application only takes place in the subsequent national phase, patent applicants can use the international phase to decide in which PCT contracting states they will eventually seek patent protection. According to a WIPO survey on Patenting Strategies carried out in 2009 and 2010 (WIPO, 2011b), when asked to compare 2010 with 2009, pharmaceutical industry respondents reported that they expected small increases in the growth rates in both PCT filings and filings in their home country. On the other hand, they expected to see large increases in growth rates for filings abroad.

Patent filing strategies can be offensive or defensive. An offensive strategy aims to leverage exclusive rights over a technology in order to extract economic returns either from exclusive use of the patented technology or from licensing arrangements. A defensive patent strategy is aimed solely at protecting the inventor or patent owner's freedom to operate (FTO) using its own technology by avoiding a situation in which a competitor obtains exclusive rights to it. Equally, patent holders may publicly or formally waive patent rights, or grant a royalty-free licence, or declare that they will not assert certain patents once acquired in certain territories, for certain uses, or in general.⁶⁸

There are differences between private and public patenting strategies. Private-sector entities – mostly publicly traded or privately held companies – aim to generate a return on their shareholders' investment. In contrast, public-sector and public-interest entities generally conduct research and do

not produce commercial products with the aim of serving a general or specific public interest. Instead, they focus on smaller portfolios of fewer patents which typically contain broader claims over key results of upstream research. These patents can be licensed to private-sector entities which have capacity to carry out additional R&D. This in turn may lead to delivery of products to the public, and at the same time, may generate revenue for public-sector entities.

Some countries have adopted policies to encourage research institutions and universities to take out patents based on inventions arising from publicly funded research. The best-known example of such a policy is the US Bayh–Dole Act of 1980. This policy has inspired the adoption of similar measures in other countries, such as South Africa's Intellectual Property Rights from Publicly Financed Research and Development Act of 2008 and the Philippine Technology Transfer Act of 2009 (see Box 3.17). Such policies, and a general trend towards more active management of technologies created through publicly funded research, are leading to the steady accumulation of publicly held patent portfolios, including on key upstream technologies that provide platforms for a range of new medical technologies.

PDPs which focus on R&D for new products aimed at addressing neglected health needs may also have distinct patent filing and IP management strategies (see Chapter III, Section C.4).

4. Post-grant issues: questions related to the use of patents

Once a patent has been granted, certain legal and practical considerations determine how it actually influences and impacts on the development and dissemination of the patented technology. These include options for defining the legal scope of a patent rights, and approaches to licensing the rights granted under a patent. This section outlines several of these considerations most relevant to product development.

Box 3.17. The Philippine Technology Transfer Act of 2009

Recognizing the importance of science, technology and innovation for development and progress, the stated objective of the Act is to “promote and facilitate the transfer, dissemination, and effective use, management and commercialization of intellectual property, technology and knowledge resulting from R&D funded by the government for the benefit of national economy and taxpayers” (Section 3). IPRs resulting from publicly funded research, as well as the revenues from their commercialization belong, as a general rule, to the R&D institute performing the research. However, the Government Funding Agencies may be authorized to use the protected invention in cases of extreme urgency or for reasons of public interest, including health. R&D institutes that avail themselves of public research funds are explicitly requested to identify, protect and manage the IPRs generated from their activities and to pursue the commercial exploitation of the invention concerned, including through the establishment of spin-off companies (Section 8(a) and (k)). R&D institutes concerned are also encouraged to establish their own technology licensing offices (Section 20).⁶⁹

(a) Research tools

Patentable biotechnological inventions are not necessarily end products such as new drugs, but can be “upstream” research tools that are essential for the development of “downstream” pharmaceutical products. Research tools can be an object or a process for laboratory use. Where technologies comprise DNA sequences, genetic researchers often have no way to invent around them. For example, expressed sequence tags are tiny portions of an entire gene that can be used to help identify unknown genes and to map their positions within a genome. Polymerase chain reaction is a well-known research tool or technique used to amplify small segments of DNA. Broad patenting of these types of inventions may disadvantage those wishing to use them to develop other products, while narrower claims may facilitate their downstream use.

It is for these reasons that Switzerland, a country with a substantial research-based pharmaceutical industry, has introduced a right to a non-exclusive licence with regard to the use of research tools, for example, for cell proliferation in the field of biotechnology.⁷⁰

(b) Research exception

A research exception or experimental use exception is one of the most commonly used types of “limited exceptions” to national patent laws pursuant to Article 30 of the TRIPS Agreement. A WTO Dispute Settlement Panel has defined the term as “the exception under which use of the patented product for scientific experimentation, during the term of the patent and without consent, is not an infringement”.⁷¹ Many countries provide varying levels of exceptions for acts carried out for experimental purposes or scientific research. A WIPO Committee on Development and Intellectual Property report identifies 98 instances.⁷² Some countries limit the exception to acts carried out without commercial or gainful intent. This exemption enables researchers to examine the patented inventions and to research on improvements without having to fear that they are infringing the patent. In general, the research exemption applies to research *on* or *into* a patented invention, for example, working on the patented invention in order to explore unknown effects or further develop the invention. Many countries do not apply the research exemption to research made *with* the patented invention, which is what, for instance, downstream researchers do when they conduct genetic research with patented research tools.

For example, under Swiss patent law research for commercial or non-commercial purposes is allowed as long as the research objective is to generate new knowledge about the patented invention (Article 9 G b of the Swiss patent law).⁷³ Brazilian patent legislation exempts acts carried out by third parties without the consent of the patent owner for experimental purposes in connection with scientific or technological studies or research.⁷⁴ The

Bangui Agreement provides that “the rights deriving from the patent shall not extend ... to acts in relation to a patented invention that are carried out for experimental purposes in the course of scientific and technical research”. One study has taken the view that, in the absence of any qualifying language, the provisions of these instruments would provide a safe harbour against patent infringement for virtually all scientific and technology research activities.⁷⁵

Other jurisdictions have recognized research exemptions subject to certain limiting factors. For example, in the United States, acts of research and experimentation are distinguished on the basis of whether they are for commercial or non-commercial purposes. Other states, such as India, Kenya and the Lebanese Republic, have implemented similar provisions. The US Federal Court held in *Madey v. Duke University*⁷⁶ that using a patent without the consent of the patent holder in order to further the “infringer’s legitimate business interests” was to be considered patent infringement.

Replies to a questionnaire from WIPO member states and regional offices provide information on various national practices regarding the experimental use and scientific research exceptions.⁷⁷

Where the general research exception is not wide enough in a particular jurisdiction to allow particular follow-on research, such as use of a patented research tool, the researcher needs to obtain a licence on terms to be mutually agreed. Alternatively, compulsory licensing may allow such downstream research, subject to compliance with the requirements under the applicable national law.⁷⁸

(c) Licensing and assignment with respect to innovation

Frequently, a patent owner lacks the resources to exploit an invention and to scale up from laboratory research stage to bring a product to market. The resources required: to develop a product include the skills, facilities and capital to conduct further research; to carry out tests, trials and production engineering; to obtain regulatory approval; and then to manufacture, to market and to distribute the final product. The ingenuity and competitive edge of an invention alone are not sufficient to assure its successful implementation. In this situation, a public-sector or private-sector patent owner must consider whether it is in its best interests to assign the technology, or to license it to another party who can develop it. Each choice offers different degrees of control over the technology and may yield different levels of return and health benefits.

A patent assignment may include sales, or transfer free of compensation, such as to a PDP. An assignment entails a loss of control over the technology. In general, an assignment at an earlier stage of R&D offers a lower return to the assignor than at a later stage, as the assignee

is typically assuming greater uncertainty and risk. The assignor may assume obligations to provide technical advice for a certain period.

Patent licences vary in scope. An exclusive licence guarantees that the licensee will have no competition in the production and distribution of the given product, not even from the licensor. Licences can be restricted to a particular territory, and can allow or prohibit sub-licences. A non-exclusive licence allows the licensor to grant other licences to other parties in the contractual territory. Licences can also be restricted to particular fields of use. This allows a licensor to grant a licence to the same patent or related patents to different parties in different fields. Patents for medical technologies are often suitable for field-of-use licences because such technologies often have multiple uses. For example, the same technology can be applied to diagnostic and therapeutic uses with respect to the same disease or different diseases. Field-of-use licensing grants the licensor greater freedom to deal with the patent with other parties in other fields of use and extract greater returns. Licences can also include options to commercialize additional compounds or fields of use that could allow the licensee to integrate additional products in its pipeline. The return from a licensee to the licensor depends on the objective of the licensor and the licensee, the degree of exclusivity, size of contractual territory, restrictions on use, options included and the duration of the licence, as well as the value of the technology itself. Alternatively, technology can be voluntarily shared even without a formal licensing arrangement.

A licensing strategy covers an entity's inputs as well as its outputs in the product development process. The strategy determines, in line with the entity's overall objectives, what licensing models are to be pursued, and to what end. Public-interest IP management can promote innovation by granting licences on non-exclusive terms or, where exclusive licensing is necessary to promote further development, it can restrict the licensed field of use to reserve other areas of research that may use the same technology or all non-commercial uses.

(d) Patents in R&D agreements and other forms of collaboration

Medical technologies are developed through a diverse spectrum of forms of collaboration that have implication for access post patent grant. At one end of the spectrum, traditional public-sector research places all results in the public domain, where they are freely available for use by others involved in product development. At the other end of the spectrum is the conventional vertically integrated private-sector business model which involves conducting R&D in-house within a single company group, exercising exclusive rights to prevent its use by others, thus furthering the company's own commercial interests. Increasingly, few pharmaceutical companies have the capacity to operate in a fully integrated and entirely exclusive manner.

In between these two extremes can be found new forms of commercial collaboration which combine different inputs in order to deliver a complex product such as a new drug or vaccine. In the field of biotechnology, there are frequently several different licensors and other right holders by the time the final product is ready for market. Patent rights can also be leveraged in other non-conventional ways, such as to enable access to improvements and developments of licensed technologies through open source or public health patent pools and also through commercial patent pools which enable competitors to develop products based on shared pre-competitive technology platforms (see the discussion of innovation structures in Chapter III, Section B.4(e) above).

(e) Patent thickets

There is no generally agreed definition of the term "patent thicket". One author describes a patent thicket as a "dense web of overlapping intellectual property rights that a company must hack its way through in order to actually commercialize new technology" (Shapiro, 2000). In such a situation, multiple patent rights owned by different parties have to be considered by competitors as well as new entrants into a market within that field of technology. Eventually, they must negotiate multiple licence agreements, and this may present difficulties and impede the implementation of a project.

Patent thickets have been observed for complex technologies, such as information and communications technology (ICT), and for pharmaceuticals. They can arise in technical fields where a number of companies compete at the same level and where patent ownership is fragmented. Key issues that have been highlighted with respect to patent thickets include: the high density of patents potentially impeding R&D; high, possibly excessive, licensing costs; refusal of the patent holder to grant a licence; and difficulties associated with inventing around a patent (IPO, 2011).⁷⁹

Cross-licensing agreements have been proposed as a solution. However, some have argued that this measure could aggravate the issue, as it could induce competing companies to obtain larger numbers of patents in order to improve their bargaining capacity. Patent pools have also been suggested as a way to address transaction costs.⁸⁰

Empirical studies of patent thickets show varied results. One study found that, among academic researchers in the biomedical field, 3 per cent had abandoned a project during the preceding three years due to too many patents covering their particular research field. The study found that access to tangible research input was more problematic, as 20 per cent of academic-to-academic requests were refused.⁸¹ Another study found that 40 per cent – including 76 per cent of those in the biosciences

industry who responded to the survey – considered that their research was affected by difficulties in accessing patented technologies. Of these respondents, 58 per cent reported delays, 50 per cent reported changes in their research plans and 28 per cent had abandoned their research. The most common reason for changing or abandoning the research was overly complex licensing negotiations (58 per cent), followed by high individual royalties (49 per cent).⁸²

In the pharmaceutical field, a European Commission study has also used the term “patent thickets” to refer to a strategy adopted by originator companies to file multiple patents for the same medicine – a strategy that results in delaying or blocking the entry of generic medicines into the market (European Commission, 2009).

(f) Patent landscapes and medical technologies

The term “patent landscape” is used in this study to refer to a report about the search, analysis and illustration of the patent situation or patenting activity in a specific technology field according to predefined criteria and concrete questions. There is no commonly agreed definition of the term patent landscape, or of what such a report should contain. It may refer to a list of all patent applications/patents found, or to a more elaborate report that includes analysis and visualization.

The value of a landscape report is enhanced by visualizing its results and by conclusions derived from the empirical findings. Patent landscapes can therefore be useful for policy discussions, strategic research planning or technology transfer. However, they only provide a snapshot of the patenting situation at the time the search was carried out.

The first step in landscaping is usually a state-of-the-art search for patent applications/patents in the technological field of interest. The next step is normally to identify the relevant patent family members. The results are then analysed, for example to answer specific questions, such as those relating to patterns of patenting (Who files applications? What is filed and where?) or certain patterns of innovation (innovation trends, diversity of solutions for a technical problem, collaborations between researchers). Subsequent analysis of the findings may lead to various conclusions or recommendations.

Some landscape reports go further and look at the legal status of patent applications/patents, for example, whether applications have resulted in granted patents and whether such patents are still in force. However, landscape reports rarely cover legal status since this information is generally not easy to obtain, as it is not systematically collected and maintained in a single database.⁸³ Moreover, legal status is always subject to change. However, determining legal status is critical for a FTO analysis.

WIPO has compiled a list of patent landscape reports in various technical fields that have been published by international organizations, national IP offices, non-governmental organizations and private-sector entities.⁸⁴

(g) Overview of freedom to operate issues

Linked with the scope of patent landscape reports is the analysis of freedom to operate. This sub-section briefly sketches the issues involved in such an analysis.⁸⁵

(i) *Defining freedom to operate*

Assessments of freedom to operate (FTO) are important in deciding whether to initiate, continue with R&D projects, use or market new products. An FTO assessment is based on a legal opinion on whether the making, using, selling, or importing of a specified product is free from potential infringement of third party IP or tangible property rights. Managers use FTO analysis when making risk management decisions in relation to R&D, product launch and commercialization. However, FTO does not mean an absolute freedom from any risk of infringing another party's IP. It is a relative assessment based on analysis and knowledge of IP landscapes for a given product, in a given jurisdiction, at a given point in time.

(ii) *Freedom to operate strategies*

The decision to undertake an FTO analysis, and to commission an FTO opinion from legal counsel or a patent attorney, is based on a preliminary risk assessment. FTO considerations are relevant at all stages of the product development cycle. In practice, however, carrying out a detailed FTO analysis and legal opinion on every product or process early in the pipeline would be impractical. This is because the detailed specifications of the product could not be known to a sufficient degree of detail and certitude. On the other hand, obtaining any needed licences at a late stage in the development process runs the risk that either no licence would be obtained or that the conditions would be unfavourable and thus the bargaining flexibilities would be reduced. In addition, there could be a risk of becoming involved in a lawsuit for IP infringement.

Negotiating a licence is a straightforward way to obtain the consent of the right holder for the intended commercial activity. This approach may have the advantage of focusing on mutual interests in a deal in a way that proves beneficial for all parties. Licences may include additional information, such as know-how, regulatory data, trade secrets and trademarks. Agreements may include upfront payments, milestone payments or royalty rates, or a combination of all three, or they may be in the form of a cross-licence, whereby the licensees and the licensor grant each other certain rights. Licences may also include – and indeed frequently do – grant-backs for improvements, options on new inventions and the mutual sharing of new

data. These options may be particularly relevant if long-term collaboration is sought and if further research has the potential to lead to improvements in the licensed/protected technology.

However, licence negotiations may not always lead to the desired agreement, even if a potential licensee has made reasonable efforts to obtain a licence. In such situations, a compulsory licence is a route that could possibly be explored.⁸⁶

Instead of seeking a licensing agreement or a compulsory licence, another viable strategy could be to aim to have the “blocking” patent invalidated. The blocking patent may have been granted erroneously and could therefore be challenged and invalidated. However, going into litigation can be costly and lengthy, and the outcome is often uncertain.

An additional option would be to seek a nonassertion covenant in which a right holder confirms in a public statement that the rights will not be enforced under certain circumstances or in certain defined fields or geographies. Such agreements may be particularly relevant for “humanitarian” licensing aimed at responding to socio-economic needs. In addition, these agreements deliver the added benefit of ensuring that product liability issues are simplified. (Krattiger, 2007a)

Instead of pursuing available legal options, the company may adapt the project to the IP situation. One such option could be to modify the product in a way that no licence would be required. Such a strategy works if available alternatives exist and if the different options

are analysed at an early R&D stage (i.e. when it may be easier to modify the product). The lack of alternative options may serve to incentivize further research to find a new solution for the project. Inventing around may delay product development but can lead to new inventions – and perhaps even better products – thus resulting in new IP for cross-licensing. On the other hand, inventing around may increase costs.

A review of available legal, research and financial options may lead to a decision to abandon the project. The alternative, electing to overlook existing patents and awaiting a choice by the patent holder whether or not to enforce their rights, could result in additional financial loss – particularly if there is a successful claim for damages based on knowing infringement.

Finally, FTO issues can also be resolved through mergers and acquisitions of competing companies.

The process of developing a sound strategy for securing FTO should consider all options, and decisions should be based on the assessment of the risks of each option in relation to the institutional context, product type, and market dynamics. In practice, several options are typically pursued concurrently.

An FTO opinion provides only a snapshot of the IP related to a product at a given point in time. The patent landscape changes as patent applications are filed, granted, expire or are invalidated. Therefore, strategies need to be regularly revised and tactics need to be adapted in response to changing circumstances.

E. Sharing of influenza viruses and access to vaccines and other benefits

Key points

- The WHO Pandemic Influenza Preparedness (PIP) Framework for the Sharing of Influenza Viruses and Access to Vaccines and other Benefits provides a global approach to the sharing of influenza viruses with pandemic potential. It also enables the sharing of benefits derived from such viruses, including the management of related intellectual property (IP).
- The Standard Material Transfer Agreements (SMTA) agreed under the PIP Framework stipulate that participating laboratories should not seek to obtain intellectual property rights (IPRs) on PIP biological material. In addition, these agreements provide for a range of options for biological material recipients, such as influenza vaccine manufacturers, to enter into benefit sharing agreements.

A highly significant development in itself, given its central role in preparing for a potential pandemic, the PIP Framework also serves to illustrate many of the points made in earlier sections of this chapter relating to the role of public-sector institutions and networks, capacity-building in medical innovation, sharing of benefits of the fruits of innovation, and dealing with IP in a public health context.

1. WHO Global Influenza Surveillance and Response System

The WHO Global Influenza Surveillance and Response System (GISRS) (formerly known as the Global Influenza Surveillance Network) was created in 1952 to advise WHO member states on influenza control measures. This system monitors the evolution of seasonal influenza viruses and other subtypes of influenza viruses that infect humans sporadically. Among its many responsibilities, the GISRS selects and develops candidate influenza viruses for development and production of seasonal and other influenza vaccines, including pandemic vaccines. The GISRS also serves as a global alert mechanism for the emergence of influenza viruses with pandemic potential. Its activities have contributed greatly to the understanding of influenza epidemiology, and have facilitated effective, internationally coordinated responses, to outbreaks of seasonal, H5N1 and other influenza virus subtypes with pandemic potential.

The system comprises different categories of laboratories with National Influenza Centres (NICs) forming the backbone of the GISRS. Under their WHO terms of reference, NICs are requested to regularly ship representative clinical specimens/virus isolates to WHO collaborating centres for in-depth antigenic and genetic analyses. To fulfil its role as a global alert mechanism for the emergence of influenza viruses with pandemic potential, the GISRS relies on its

members to share in a timely manner all influenza viruses with pandemic potential.

The re-emergence of highly pathogenic avian influenza A(H5N1) in 2003 highlighted the risk of an influenza pandemic. The inability of developing countries to secure safe and affordable access to pandemic vaccines was underscored by the global limitation of influenza vaccine production capacity. In early 2007, this situation prompted one country to announce that it would stop sharing its A(H5N1) viruses with the GISRS until it:

- provided greater transparency of its activities
- enabled increased access by developing countries to the benefits derived from the use of such viruses, notably vaccines.

This event led to the adoption by the May 2007 World Health Assembly of a resolution which became the basis for negotiations on a framework for the sharing of influenza viruses and other benefits.⁸⁷ Two issues were central to the discussions:

- improving the transparency of the activities of the GISRS
- improving fairness and equity of access to influenza vaccines and other benefits derived from the work of the laboratories in the WHO system.

2. Intellectual property rights in the context of PIP negotiations

The role of patents, and more specifically the rules regarding the rights of the GISRS laboratories to seek patent protection on inventions developed with viruses contributed to the GISRS, was a core issue throughout the negotiation process. Technical papers prepared by the

Box 3.18. WIPO Patent Search Report on PIP-Related Patents and Patent Applications

In 2010, WHO member states requested information from WIPO on PIP-related patents to support the WHO Open-Ended Working Group of Member States on Pandemic Influenza Preparedness: Sharing of Influenza Viruses and Access to Vaccines and other Benefits (OEWG). WIPO prepared this report, and presented it at the meeting of the OEWG in April 2011.

The patent search report highlights several critical points:

- In the pool of patent information assembled and analysed in this report, no patent documents were identified that included claims having, as a sole and/or single element, either a complete native virion, a native viral strain, a native viral genome in its entirety, or a complete assembled complement of native viral proteins from a specific virus.
- The report discusses in detail certain patent families, represented by patent applications, where the scope of the claims is broad and could potentially be construed as covering known viral sequences, processes and compositions of matter. It is well established that issued patents frequently have narrower claims than the corresponding patent applications. Therefore, the scope of the claims in the patent applications identified and analysed in this search may very well be restricted during the patent application prosecution and grant process.
- While some patent applications from members of the WHO Global Influenza Surveillance Network are identified as falling within the scope of the search, the report does not analyse to what extent collaborations, licences and technology transfer are taking place between these and other entities, including between and among developed and developing countries.
- A number of patent applications were identified from companies based in industrialized countries that are now co-owned by companies of developing countries. This is arguably one form of technology transfer and should be seen in the light of emerging models that facilitate broad access to new technologies, including in health, by developing countries.⁸⁸

WHO in response to a request by member states found that: "There are no significant patent barriers to the manufacture of any of the marketed types of influenza vaccines. Some patents protect specific processes or products, but for each of the types of marketed vaccines, there is sufficient FTO to permit manufacturers in developing and emerging economies to make the vaccine of their choice. For future vaccines based on new technologies, there are potential intellectual property barriers; however it is not known which, if any, of those technologies could make marketable vaccines that could be sustainably produced".⁸⁹

In order to provide further information on patenting activity related to influenza viruses with pandemic potential, the WHO, based on resolution WHA60.28, requested WIPO to prepare a working paper on *Patent Issues Related to Influenza Viruses and Their Genes*.⁹⁰ In 2010, upon request from WHO member states, WIPO presented a patent search report on PIP-related patents to the WHO Open-Ended Working Group of Member States on Pandemic Influenza Preparedness: Sharing of Influenza Viruses and Access to Vaccines and other Benefits (see Box 3.18).

3. The PIP Framework

The PIP Framework was adopted by the 64th World Health Assembly in 2011. The Framework provides a global approach to the sharing of influenza viruses with pandemic potential for risk assessment and response,

and the sharing of benefits derived from such viruses. The scope of the Framework is limited to influenza viruses with pandemic potential. The Framework defines the materials covered under it as "PIP Biological Materials".

The PIP Framework contains a Standard Material Transfer Agreement (SMTA 1) applicable to all GISRS laboratories. SMTA 1 specifies terms and conditions for transferring viruses both within the GISRS and to entities outside the system. Among others, SMTA 1 states that members of the GISRS should not seek to obtain IPRs on PIP biological materials.

Under the PIP Framework, recipients of PIP biological materials, such as influenza vaccine manufacturers, play a critical role in supporting global pandemic preparedness and response. This includes the payment of an annual partnership contribution and the negotiation and signing of benefit sharing agreements with the WHO. A model benefit sharing agreement or "SMTA 2" is contained in Annex 2 of the PIP Framework. It sets out a list of options for benefit sharing from which recipients are required to choose. One such option is the granting of royalty-free licences to manufacturers in developing countries on IPRs for the production of pandemic influenza vaccines, adjuvants, antiviral products or diagnostic materials needed in a pandemic. A similar provision allows the WHO to receive licences that may then be sublicensed to manufacturers in developing countries under appropriate terms. In this manner, the Framework provides opportunities for IP holders to share IP related to pandemic influenza preparedness or response. It does not, however, compel them to do so.

Endnotes

- 1 This section is largely based on Temin (1979).
- 2 Streptomycin was introduced commercially in 1946 under a patent granted in 1948. However, scientists at Rutgers University who were involved in the discovery of streptomycin convinced the originator company to license it on an unrestricted basis at a royalty rate of 2.5 per cent and to assign the patents to the Rutgers Research Foundation. In the United States, competition drove down the price of streptomycin from US\$ 4,000 per pound to US\$ 282 per pound by 1950.
- 3 For more information, see Chapter II, Section A.6(b).
- 4 Source: GE Healthcare (2011) and Immelt et al. (2009).
- 5 Source: www.britannica.com/EBchecked/topic/1357082/pharmaceutical-industry/260283/History; and Newman et al. (2008).
- 6 See <http://pateststate.com/category.htm>.
- 7 See http://ec.europa.eu/competition/sectors/pharmaceuticals/inquiry/communication_en.pdf.
- 8 See www.phrma.org/issues/intellectual-property.
- 9 WHA, *Resolution: WHA61.21: Global strategy and plan of action on public health, innovation and intellectual property*, para. 7.
- 10 For more information, see Chapter III, Section C.
- 11 Ibid.
- 12 See www.ornl.gov/sci/techresources/Human_Genome/home.shtml.
- 13 See <http://hapmap.ncbi.nlm.nih.gov/index.html.en>.
- 14 Source: www.meningvax.org.
- 15 See www.andi-africa.org.
- 16 For more information, see Chapter IV, Box 4.3.
- 17 See www.economist.com/node/18836582.
- 18 See www.seruminstitute.com/content/research.htm; and www.who.int/immunization_delivery/new_vaccines/technologies_aerosol/en/.
- 19 See www.cigb.edu.cu.
- 20 See www.innovax.cn.
- 21 See www.fiocruz.br/bio_eng/cgi/cgilua.exe/sys/start.htm?tpl=home.
- 22 See www.fapesp.br/week/media/pres/kalil.pdf.
- 23 The legal background and the policy issues around the legal protection of pharmaceutical test data are set out in Chapter II, Section B.1(c).
- 24 Source: Ker (2012).
- 25 WHA, *Resolution: WHA58.34: Ministerial Summit on Health Research*. ICTRP website at <http://apps.who.int/trialsearch/>.
- 26 EMA, "European Medicines Agency Policy on Access to Documents (Related to Medicinal Products for Human and Veterinary Use)", Policy/0043, 2010.
- 27 EMA, "Workshop on Access to Clinical-Trial Data and Transparency Kicks Off Process Towards Proactive Publication of Data", Press release, 23 November 2012.
- 28 See WHO (2010g).
- 29 The Synaptic Leap's Synthetic Praziquantel Project at www.thesynapticleap.org/node/286. CSIR India's Open Source Drug Discovery Project at www.osdd.net/. EWG Submission: "Open Source Drug Discovery" at www.who.int/phi/public_hearings/second/contributions/ZakirThomasCouncilofScientificIndustrialResearch.pdf. Sage Bionetworks at <http://sagebase.org/>.
- 30 CEWG Submission: *New Investment Strategy: Innovative Developing Country Research Awards Global Forum for Health Research 2011*, at www.who.int/phi/news/cewg_2011/en/index.html.
- 31 Source: www.osdd.net.
- 32 For the use of AMC in the area of vaccines, see Chapter III, Box 3.5.
- 33 For examples, see: www.mpegla.com; www.vialicensing.com; and www.sisvel.com.
- 34 See Chapter I, Section B.2(a), and Annex I, Sections A.8 and B.9.
- 35 See www.who.int/csr/sars/goarn2003_4_16/en/.
- 36 Simon et al. (2005). See also the presentation at www.who.int/intellectualproperty/events/en/JamesSimon.pdf.
- 37 Correa (2009) and Verbeure et al. (2006).
- 38 GSPA-PHI Element 2.3(c).
- 39 GSPA-PHI Element 7.1(a).
- 40 WHA, *Resolution: WHA63.28: Establishment of a consultative expert working group on research and development: financing and coordination*.
- 41 A detailed presentation and analysis on each of these proposals is set out in Annex 3 of the 2012 CEWG report (WHO, 2012a).
- 42 Source: Röttingen et al. (2012); see also WHO (2012a).
- 43 See http://apps.who.int/gb/ebwha/pdf_files/EB132/B132_21-en.pdf.
- 44 Sources: WHO (2006b); Widdus and White (2004).
- 45 See also Annex I, Section B.4, for more background on objectives and approach to IP.

- 46 Uniting to Combat NTDS, “London Declaration on Neglected Tropical Diseases”, 30 January 2012.
- 47 Source: www.wiporesearch.org.
- 48 The issue of patentable subject matter is addressed in Chapter II, Section B.1(b)(iii).
- 49 See www.globalmedicaltechnologyalliance.org/wp-content/uploads/GMTA_Patents_for_Medical_Devices_and_Pharmaceuticals_Rev_FINAL_19_Mar_2012.pdf.
- 50 Official Journal of the European Communities L 213/13 of 30 July 1998.
- 51 USPTO, “Final Guidelines for Determining Utility of Gene-Related Inventions”, Press release, 4 January 2001.
- 52 WIPO document WIPO/GRTKF/IC/1/6.
- 53 The issue of novelty is addressed in Chapter II, Section B.1(b)(iii).
- 54 See www.comunidadandina.org/ingles/normativa/D486e.htm.
- 55 See www.epo.org/lawpractice/legaltexts/epc.html.
- 56 See www.patentdocs.org/2012/03/supreme-court-remands-myrriad-case.html.
- 57 See www.ca9.uscourts.gov/images/stories/opinions-orders/10-1406.pdf.
- 58 See www.patentdocs.org/2012/11/supreme-court-grants-cert-in-amp-v-myrriad.html.
- 59 See www.supremecourt.gov/opinions/11pdf/10-1150.pdf.
- 60 G 0002/08 (Dosage regime/ABBOTT RESPIRATORY) of 19.2.2010.
- 61 See www.epo.org/law-practice/legal-texts/html/guidelines/e/g_vi_7_1.htm.
- 62 The issue of inventive step/non-obviousness is addressed in Chapter II, Section B.1(b)(iii).
- 63 See <http://ec.europa.eu/competition/sectors/pharmaceuticals/inquiry/>.
- 64 See www.ipmall.info/hosted_resources/crs/R40917_091113.pdf.
- 65 For more information on prior art, see Chapter II, Endnote 67.
- 66 See www.wipo.int/patentlaw/en/guidelines.html.
- 67 Joint Resolution 118/2012, 546/2012 and 107/2012 (Ministry of Industry, Ministry of Health and National Industrial Property Institute) of 5 May 2012, published in Official Gazette of 8 May 2012.
- 68 See Chapter IV, Section C.3(d).
- 69 See www.wipo.int/wipolex/en/details.jsp?id=9605.
- 70 Article 40b Swiss Patent Law, www.admin.ch/ch/d/sr/c232_14.html.
- 71 See *Canada – Patent Protection of Pharmaceutical Products* (DS114).
- 72 WIPO document CDIP/5/4 Annex II.
- 73 See www.admin.ch/ch/d/sr/c232_14.html.
- 74 UNCTAD/ICTSD, “The Research and Experimentation Exceptions in Patent Law: Jurisdictional Variations and the WIPO Development Agenda”, Policy Brief Number 7, 2010.
- 75 *Ibid.*
- 76 *Madey v. Duke University*, 307 F.3d 1351 (Fed.Cir. 2002).
- 77 See www.wipo.int/scp/en/exceptions.
- 78 See Chapter IV, Section C.3(a)(ii) and (iii).
- 79 WIPO document SCP/12/3 Rev.2.
- 80 *Ibid.*
- 81 See www.nationalacademies.org/gateway/pga/3330.html.
- 82 See: WIPO document SCP/12/3 Rev.2; and <http://sipi.aaas.org/survey/>.
- 83 See Chapter II, Section B.1(b)(ix).
- 84 See www.wipo.int/patentscope/en/programs/patent_landscapes/index.html.
- 85 This section is a summary of Chapter 14.1 “Freedom to Operate, Public Sector Research and Product-Development Partnerships: Strategies and Risk-Management Options” of the *IP Handbook of Best Practices* (Krattiger et al. (eds.), 2007), available at www.iphandbook.org/handbook/ch14/p01.
- 86 For further explanations on compulsory licences, see Chapter IV, Section C.3(a)(ii) and (iii).
- 87 WHA, *Resolution: WHA60.28: Pandemic influenza preparedness: sharing of influenza viruses and access to vaccines and other benefits*.
- 88 Source: WIPO (2011c).
- 89 See www.who.int/influenza/resources/technical_studies_under_resolution_wha63_1_en.pdf. See also www.who.int/vaccine_research/diseases/influenza/Mapping_Intellectual_Property_Pandemic_Influenza_Vaccines.pdf.
- 90 See www.who.int/influenza/resources/documents/wipo_ipdoc/en/.

IV. Medical technologies: the access dimension

Chapter III explained the role of intellectual property (IP) and other policy measures in health innovation; this chapter provides a detailed description of the access dimension, the underlying concepts, data and methodological approaches. It also offers an overview of the main determinants of access related to health systems, IP and trade policy.

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A. Access to medical technologies: the context

Key points

- Access to medicines and other medical technologies is part of a broader challenge of ensuring access to health care, which requires a functioning national health care system.
- Improved access to medicines will only provide public health benefits if the medicines accessed are quality products.
- The WHO Essential Medicines Lists provide helpful guidance on the rational selection of medicines.
- Price is a critical determinant of access to medicines, especially in countries where the public health sector is weak and where treatment is purchased on the private market and paid for by people out of their own pockets.
- In general, generic products are cheaper than originator products, but even low-priced generic medicines are often still unaffordable for large sections of the population in many low- and middle-income countries (LMICs).
- Since 2001, a significant increase in international funding for essential medicines, especially for HIV/AIDS, malaria and TB and vaccines has vastly improved access to these products in many LMICs.
- A fundamental prerequisite for a functioning health care system is government commitment to adequately and sustainably fund the national health system and the reliable supply of essential medicines.
- Improved availability of affordable, quality antiretrovirals (ARVs) has been responsible for a dramatic increase in the number of HIV/AIDS patients receiving treatment. While many of the older treatments are available from generic sources, more recent ARVs are still patent protected in many countries.
- With the introduction of the product patent regime in India, generic versions of new patented treatments will only be available from India after patent expiration, unless they can be produced there under voluntary or compulsory licences.
- The UN Political Declaration on HIV/AIDS commits UN member states to remove obstacles limiting the capacity of LMICs to provide affordable and effective HIV prevention and treatment, including among others, through TRIPS flexibilities and the promotion of generic competition as well as through tiered pricing, open-source sharing of patents and patent pools.
- In both public-sector and private-sector facilities in many LMICs, the availability of medicines for chronic diseases remains lower than that of medicines for acute conditions although essential treatments are available at low prices.
- Paediatric formulations for many medicines have yet to be developed. Additional incentives are necessary in order to ensure the development of new paediatric formulations.
- National immunization programmes are a highly effective public health tool for the prevention of illness and the spread of infectious diseases.

This chapter offers an overview of the main determinants of access related to health systems, intellectual property (IP) and trade policy. Many other very important socio-economic factors determine access to medical technologies – factors such as health financing, the importance of a qualified health care workforce, poverty and cultural issues – and lack of access is rarely due entirely to a single determinant but these are not addressed in this study, as they are not part of the interface between health, IP and trade.

Multiple factors must interact in order to create sustainable access to medical technologies. Pneumonia, the single largest cause of death in children worldwide, provides an illustration of the complexity of the access problem. Every year, this disease kills nearly 1.3 million children under the age of five years, accounting for 18 per cent of all

deaths of children of this age worldwide – more than AIDS, malaria and tuberculosis combined (UNICEF, 2012; WHO, 2012c). Children can be protected from pneumonia – it can be prevented by simple interventions, and it can be treated with low-cost, low-tech medication and care.¹ This example of basic and inexpensive medicines that are still inaccessible clearly indicates that barriers to access are more complex than affordability alone.

Lack of access is generally understood to mean the absence of available treatment options for the patient. Appropriate treatment has to be physically available and needs to be affordable for the patient.

In high-income countries a high percentage of expenditures on medical technologies is publicly financed or reimbursed

by health insurance schemes, in LMICs, most health care expenditure is paid by patients out of their own pockets.

Medical technologies are complex products that can only be effective in conjunction with expert advice and other health services. The issue of access to medicines is one aspect of a broader problem of access to health care. Delivering access requires a functioning national health care system. Providing needed medications to patients is just one component of that system.

The WHO has defined “access” to medicines as the equitable availability and affordability of essential medicines during the process of medicine acquisition (WHO, 2003b; 2004c). To describe the required conditions for ensuring access to medicines, the WHO has developed an access framework for essential medicines.

1. The WHO access framework for essential medicines

The WHO access framework for essential medicines consists of four determinants that need to be fulfilled simultaneously in order to provide access to medicines (WHO, 2004c):

- rational selection and use of medicines
- affordable prices
- sustainable financing
- reliable health and supply systems.

Improved access to medicines will only provide public health benefits if it also involves improved access to quality products. The necessary stringent quality assurance and regulation of quality of health products is the responsibility of manufacturers, suppliers and national regulatory authorities. The WHO framework on access assumes quality and regulation of medicines as an integral part of access to medicines.

Other frameworks for access to medicines have been formulated over time. In addition to the WHO framework, health policy experts have proposed a framework revolving around the so-called “5As” of availability, accessibility, affordability, adequacy and acceptability (Obrist et al., 2007).² The most recently developed framework pays more attention to the international aspects of partnerships for access to medicines (Frost and Reich, 2010).

The following sections briefly summarize the four determinants of access outlined in the WHO framework for access to essential medicines.

(a) Rational selection and use of medicines

Rational selection of medicines requires a country to decide, according to well-defined criteria, which medicines

are most important in order to address the national burden of disease. Through its work on the WHO Model Lists of Essential Medicines (EML), the WHO has provided guidance to countries on the development of their own national essential medicine lists (see Box 4.1).

A list of essential medicines can help countries prioritize the purchasing and distribution of medicines, thereby reducing costs to the health system by focusing on the essential products needed. The addition of a medicine to the WHO EML directly encourages individual countries to add the drug to their national EML and to internal drug registries. Some countries restrict drug importations to medicines based on their national EML. Similarly, several foundations and major charities base their medicine supply on the WHO EML. In 2003, 156 countries had developed national essential medicines lists and in 2009 WHO reported that 79 per cent countries had updated their national EMLs in the last five years.³

Equally important as rational selection of medicines is their rational use. Irrational use – the inappropriate, improper, incorrect use of medicines – is a major problem worldwide. Irrational use can cause harm through adverse reactions and increase antimicrobial resistance (Holloway and van Dijk, 2011) and can waste scarce resources. One example is the use of antibiotics in Europe where some countries use three times as many antibiotics per capita as do other countries with similar disease profiles (Holloway and van Dijk, 2011). Examples of irrational use include:

- the use of too many medicines per patient (poly-pharmacy)
- the use of unnecessary medicines
- the use of the incorrect medicine for a condition
- the failure to prescribe a necessary medicine.

In addition, problems with irrational use arise over issues of formulation (such as oral or paediatric formulations), inappropriate self-medication, and non-adherence to dosing regimens by both prescribers and patients. Worldwide patient adherence to treatment has been estimated to be about 50 per cent (Holloway and van Dijk, 2011), and in many cases where medicines are dispensed, the instructions given to the patient and the labelling of the dispensed medicines are inadequate.

The development of evidence-based clinical guidelines is an important tool to promote rational selection and use of medicines. Such development, however, is challenging, especially with regard to NCDs. The pharmaceutical industry is heavily engaged in this disease area because of the long-term market potential of treatments for chronic diseases which requires a careful analysis and management of potential conflicts of interest between the industry, patient organizations, professional associations, health insurance and public-sector organizations.⁴

Box 4.1. The WHO Model List of Essential Medicines

Essential medicines are “those that satisfy the priority health care needs of the population Essential medicines are intended to be available within the context of functioning health systems at all times in adequate amounts, in the appropriate dosage forms, with assured quality and adequate information, and at a price the individual and the community can afford. The implementation of the concept of essential medicines is intended to be flexible and adaptable to many different situations; exactly which medicines are regarded as essential remains a national responsibility” (WHO, 2002a).

The first EML was published in 1977. Selection criteria were developed relating to safety, quality, efficacy and total cost (Mirza, 2008; Greene, 2010). The 17th EML contains 445 medicines and 358 molecules excluding duplicates (van den Ham et al., 2011), and includes treatment options for malaria, HIV/AIDS, TB, reproductive health and non-communicable diseases (NCDs), such as cardiovascular disease, cancer, chronic respiratory disease and diabetes, based on the best available evidence (WHO, 2011d). In 2007, the first EML for children was developed and published (WHO, 2011f).

The EML provides guidance about the medicines recommended to treat common health problems. It typically includes all of the medicines recommended in standard treatment guidelines, as well as other medicines needed to address most of the clinical problems at a given level of care.

The EML lists medicines by their international nonproprietary name (INN), also known as the generic name, without specifying a manufacturer. The list is updated every two years by the WHO Expert Committee for the Selection and Use of Essential Medicines, using a transparent, evidence-based process.

Before 2002, expensive medicines were often not included on the EML as the selection criteria emphasized the need for low-priced medicines. The main criterion for selection today is effectiveness. In the evaluation process, information on comparative cost and cost-effectiveness must be presented, for example, as cost per case prevented or cost per quality-adjusted life year gained. Cost still can be relevant for the selection within a therapeutic class to identify the best value for money if efficacy is comparable (van den Ham et al., 2011). If an expensive but cost-effective medicine is placed on the EML, this implies that it must become available and affordable. First-line antiretrovirals (ARVs) were the first notable example of this new approach and they were added to the EML in 2002. At that time, they cost over US\$ 10,000 per patient per year. Since then, prices have decreased dramatically.

With the exception of a number of mainly HIV/AIDS medicines, the vast majority of medicines on the EML are off patent and generic versions are widely available, including medicines for the main NCDs (Attaran, 2004; Mackey and Liang, 2012).

(b) Affordable prices

Another important determinant for access to medicines is price and affordability. Affordability depends on a number of factors, including the question of reimbursement, or whether the expense is one-time or recurring. To assess affordability, the price of the medicines must first be established and then compared with available resources.

Prices of medicines are a critical determinant of access to medicines, especially in countries where the public health sector is weak and poor people have to purchase their treatment on the private market and pay for it out of their meagre resources. In some developing countries, up to 80 per cent to 90 per cent of medicines are purchased out-of-pocket as opposed to being paid for by national health insurance schemes or private insurance schemes (WHO, 2004c). Poor patients are willing to pay more for medicines than they would for other consumer goods, but, nonetheless, may face unaffordable prices. For this important reason, many governments regulate medicine prices (see later in this chapter).

Data on the availability of medicines and consumer prices are poor in most developing countries, but surveys of medicines prices and availability have been conducted in the past years by HAI and the WHO (WHO/HAI, 2008). Prices are typically reported as median prices in the local currency and also as median price ratios (MPRs), which compare local prices with a set of international reference prices (IRPs) reported by Management Sciences for Health.⁵ MPRs allow for simple expression of the difference between median local medicine prices and the IRP. An IRP represents actual procurement prices for medicines offered to LMICs by non-profit suppliers, and usually does not include freight costs (Cameron et al., 2009). An MPR of 2, for example, means that the local medicine price is twice the IRP, whereas an MPR of less than 1 means that the local price is less than the IRP.

“Affordability” is calculated by the WHO as the number of days' wages of the lowest-paid, unskilled government worker required to purchase selected courses of treatment for common acute and chronic conditions (WHO/HAI, 2008).

Total health care expenditures can be considered “catastrophic” if they exceed 10 per cent of a household's total resources or 40 per cent of non-food expenditure (Wagner et al., 2011).

Another measure of affordability requires assessing the proportion of the population that would be pushed below the international poverty lines of US\$ 1.25 or US\$ 2 a day because medicines or medical care were purchased. One study of 16 LMICs finds that substantial proportions of these countries' populations would be pushed below the poverty line as a result of purchasing four common medicines, and an even greater proportion would be in this situation if they used originator products (Niëns et al., 2010). For further discussion of generic availability and pricing, see Section B.1 of this chapter.

IP protection plays a role in determining the affordability of medical technologies. Generic medicines are, on average, cheaper than originator products, in part due to price competition between producers. The WHO analysed availability and affordability of essential medicines in the public and private sectors in 46 LMICs between 2001 and 2009. “Availability” was defined as the percentage of outlets where an individual medicine product could be physically located on the day of the survey (WHO/HAI, 2008). These surveys of selected generic medicines indicate that the global average median availability of such medicines in the public sector is less than 42 per cent (WHO, 2012c). Generally, availability of generics is higher in the private sector – almost 72 per cent in the same studies – although in many parts of the world, the private sector prefers to stock originator products. Even for generic products, prices in the private sector tend to be higher. Prices for even the lowest-priced generic products in the private sector, adjusted for purchasing power parity, were at least nine to 25 times the IRP in most WHO regions. For originator products, private-sector prices were at least 20 times higher than the IRP in all WHO regions (Cameron et al., 2009). For unadjusted country data on generic prices and availability, see WHO (2012c) (see also data in UN, 2011b; 2012).

It is estimated that costs to patients could be 60 per cent lower in the private sector if generics were stocked preferentially over originator products (Cameron and Laing, 2010). However, the poorest populations may not be able to afford even the lowest-priced generic products, especially when they are only available through the higher-priced private system (Niëns et al., 2010). It is estimated that each year up to 10 per cent of the population in the 89 countries for which data are available suffers financial catastrophe and impoverishment associated with direct out-of-pocket payments for health (WHO, 2012c). Ensuring availability of medicines at little or no cost through the public health system is thus critical for universal access and a primary responsibility of governments.

(c) Sustainable financing

Sustainable financing of health systems is a prerequisite for a steady supply of medicines and other medical technologies. Per capita expenditure on health care tends to be low in low-income countries, although a large proportion usually goes to medicine purchases – between 20 per cent and 60 per cent of the recurrent health budget.⁶ The Commission on Macroeconomics and Health (CMH) recommended that developing countries raise domestic budgetary spending on health to 2 per cent of their gross national product by 2015, with the goal of achieving universal access to essential health services. The CMH also recommended that donor countries commit significant financing and investment to health research and development (R&D) by coordinating with and drawing additional resources from international and intergovernmental organizations (WHO, 2001a). Policy-makers should have as objectives, among others: to increase public funding for health, including for essential medicines; to reduce out-of-pocket spending by patients, especially by the poor; and to expand health insurance coverage (WHO, 2004c).

In 2009, in 36 out of 89 countries for which data are available out-of-pocket expenditures for health accounted for more than 50 per cent of total health spending (WHO, 2012c).

Since 2001, the world has seen a significant increase in international funding for essential medicines in certain disease areas, vaccines and other medical products such as antimalarial bed nets, for distribution to poorer countries, including through mechanisms such as the Global Fund to Fight AIDS, Tuberculosis and Malaria (Global Fund), UNITAID, the GAVI Alliance, the US President's Emergency Plan for AIDS Relief (PEPFAR), the Clinton Health Access Initiative (CHAI) and other international initiatives. This has vastly improved access to these products in many countries. Such donor assistance and development loans can help fund health-sector financing, but it must also be provided on sustainable terms.

A commitment of the government to adequately and sustainably fund the national health system is the key condition for reaching universal (health) coverage, meaning that all people in a country have access to adequate health services.

(d) Reliable health and supply systems

Another precondition for providing access to medicines is a reliable, functioning health system that is able to supply patients with needed medical technologies of adequate quality in a timely manner. These systems include the ability to forecast needs, as well as to procure, store, transport and inventory medicines and medical devices and distribute them appropriately. Supply systems remain

weak and fragmented in many developing countries as can be seen from Figure 4.1, which captures Tanzania's complex pharmaceutical supply chain. The first row of boxes in the map corresponds to categories of products designated by a specific colour. The next row represent various partners supporting the different categories of products identified by a specific colour under the four main groups of donors (government, bilateral, multilateral and NGO or private). The third row of boxes stands for the agents, which procure products on behalf of financing partners. The last three but one row of boxes represent the various levels of warehousing before the products reach the patient.

The mapped medical products are funded by 22 donors, procured in various ways through 19 actors, warehoused in two stages involving 14 different entities, and finally reach patients through six divergent points of distribution. The map illustrates the challenges of managing and coordinating a supply chain flowing through five levels adding new actors at each stage, and shows that some products such as ARVs are supported by more donors than others, for example, contraceptives and TB have only two donors each (Ministry of Health and Social Welfare, 2008). Similar fragmentations of the supply chain can be found in many other countries.

Without improvement, access to medicines and other needed medical technologies will remain a formidable challenge. Adequate regulatory capacity is also required to ensure access to safe and effective medicines for both imported and domestically manufactured medicines.

Another key component of a reliable health system necessary to ensure access to medicines is a strong health workforce. Current data on health workforce can be found in WHO global atlas of the health workforce.⁷

For policy-makers the key issues are: to integrate medicines more directly into health-sector development;

to create more efficient mixes of public-private-NGO approaches in medicines supply; to have regulatory control systems that provide assured quality medicines; to explore creative purchasing schemes; and to include traditional medicines in the provision of health care (WHO, 2004c). More research is needed in this area. The Alliance for Health Policy and Systems Research adopts a health systems perspective on access to medicines (see Box 4.2).

2. Access to medicines in specific areas

While access to medicines remains a problem in all disease areas, this section focuses on a number of particular areas – HIV/AIDS, NCDs, paediatric medicines and vaccines – because of their specificity and importance.

(a) HIV/AIDS

Access to antiretroviral (ARV) therapy in LMICs has grown dramatically in recent years, with coverage increasing from only 400,000 people living with HIV in 2003 to more than 8 million by the end of 2011. AIDS-related deaths dropped by 24 per cent globally over the period 2005 to 2011 alone (UNAIDS, 2012).

The main drivers of this increased coverage are donor commitment and decreasing prices of ARVs. Substantial price reductions for commonly used first-line ARVs have been achieved since 2000. The annual cost of first-line regimens in low-income countries decreased from over US\$ 692 per person in 2000 to a weighted median price of US\$ 121 per person for the ten most widely used first-line regimens in 2010, representing a reduction of more than 98 per cent (WHO/UNAIDS/UNICEF, 2011). Prices for second-line regimens are much higher, ranging between US\$ 554 for the most common regimen in low-income countries and US\$ 692

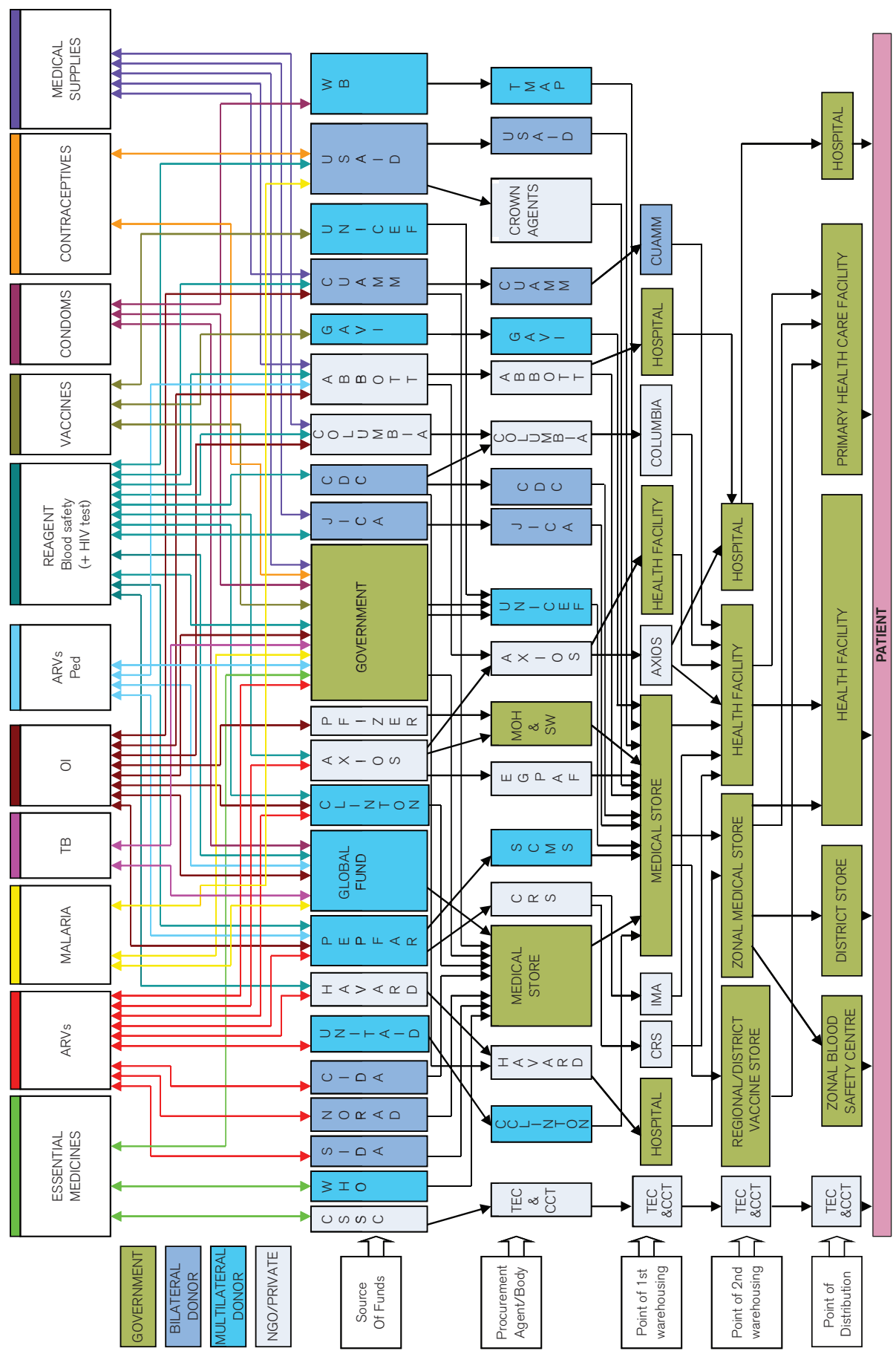
Box 4.2. Alliance for Health Policy and Systems Research: access to medicines

Since 2010, the Alliance for Health Policy and Systems Research has been leading the Access to Medicines Policy Research project, which adopts a health systems perspective on access to medicines. It acknowledges that vertical, fragmented approaches, usually focusing on medicines supply and unrelated to the wider issue of access to health services and interventions, may not be effective in addressing the need for populations' access to medicines.

This project led to a call for proposals formulated around the following three questions:

- In risk protection schemes, which innovations and policies improve equitable access to and appropriate use of medicines, sustainability of the health insurance system and financial impact on insurance members?
- How do policies and other interventions into private markets (such as information, subsidies, price controls, donations, regulatory mechanisms, promotion practices, etc.) impact on access to and appropriate use of medicines?
- How can stakeholders use the information available in the system (e.g. price, availability, quality, utilization, registration and procurement) in a transparent way so as to improve access and use of medicines?⁸

Figure 4.1. Medicines supply systems in Tanzania, 2007



Source: Ministry of Health and Social Welfare (2008).

in middle-income countries.⁹ These reductions are due to many factors, including:

- increased funding for ARV therapy and emergence of a generic ARV market creating economies of scale
- political will at national and international levels to provide treatment due to pressure from HIV/AIDS activists
- creation and use of the WHO standard treatment guidelines
- use of compulsory licences and government use
- the rejection of patent applications in key producing countries, thus enabling generic companies to compete
- price decrease of originator products and voluntary licence agreements and non-assert declarations
- price negotiations, including by bulk purchasers
- enhanced price transparency through ARV price publications and databases.¹⁰

The need for affordable ARVs further increased following two developments:

- The adoption of updated WHO HIV treatment guidelines, which recommended starting treatment earlier in the disease course in order to reduce HIV-related mortality and prevent opportunistic infections such as TB.
- Strengthened evidence on the HIV prevention benefits of ARV therapy, resulting in the adoption of new WHO

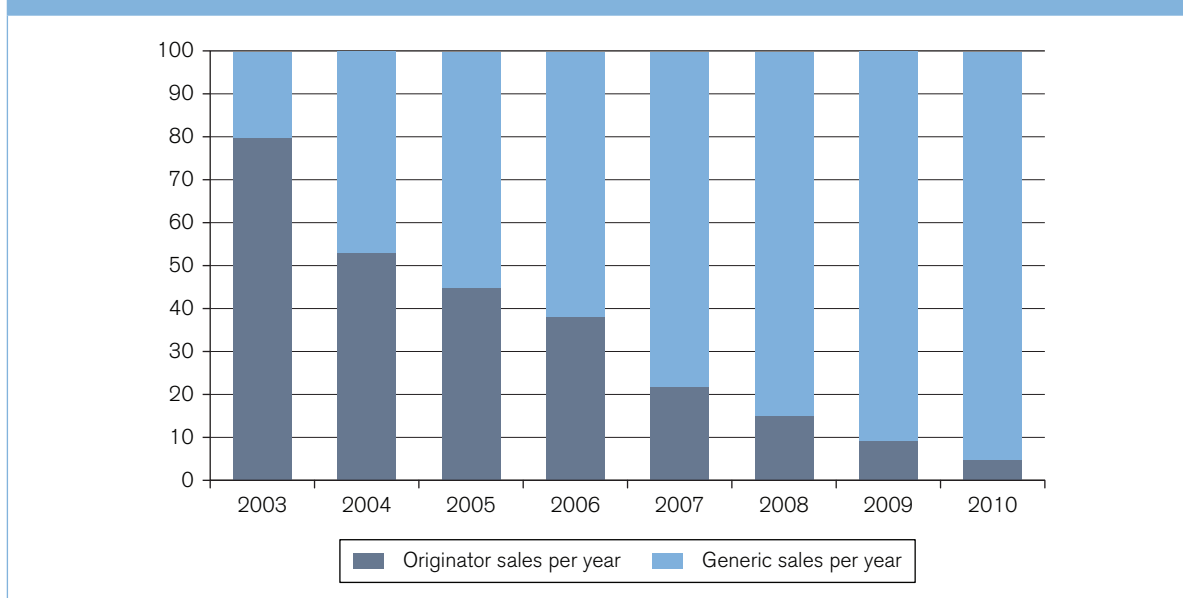
guidelines on the use of ARVs for HIV prevention in HIV discordant couples. Consideration should also be given to the use of ARVs for HIV prevention in other populations (WHO, 2012b).

Lower prices for ARVs are essential if governments and donor agencies are to meet the target of having 15 million people with HIV receiving ARV treatment by 2015, as set out in the 2011 UN Political Declaration on HIV/AIDS. They are also essential if governments and donor agencies are to meet their commitments to keep patients on lifelong ARV therapy (UN, 2011a).

The impact of patents on access to medicines has often been illustrated using the example of HIV/AIDS. Access to ARVs has presented a unique challenge because the earliest effective treatments became available only in the late 1980s. Thus, while today older HIV/AIDS treatments are available from generic sources, more recently developed ARVs are still patent protected in many countries.¹¹

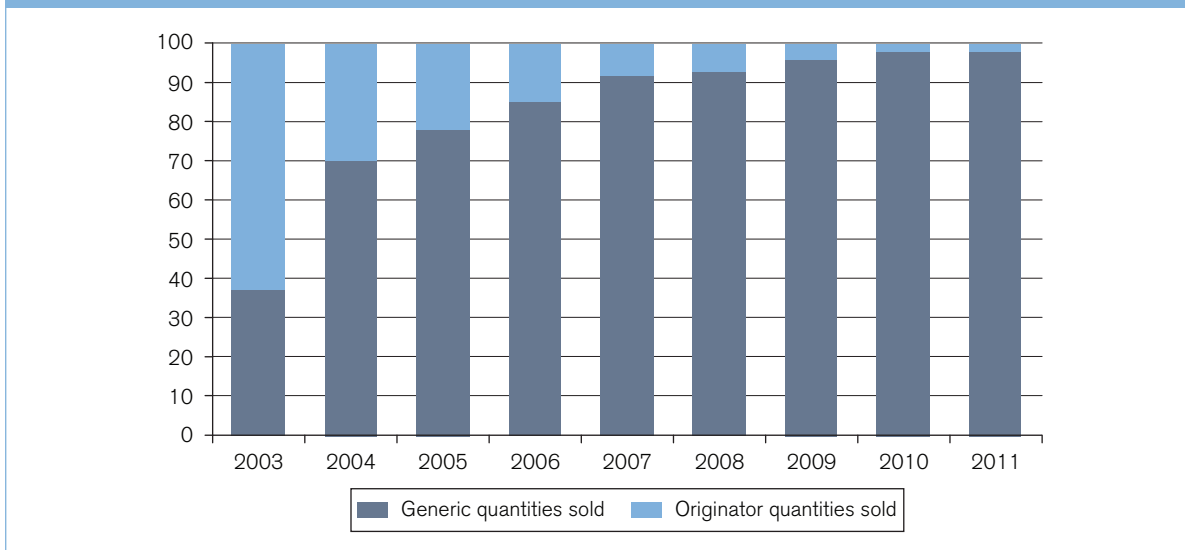
Figure 4.2 shows the increases in generic ARVs in terms of sales between 2003 and 2011. The data are sourced from the WHO Global Price Reporting Mechanism for HIV, TB and malaria. This reporting mechanism is a database which records international transactions of HIV, TB and malaria commodities purchased by national programmes in LMICs. Figure 4.3 shows the increases in the quantities of generic ARVs sold between 2003 and 2011.

Figure 4.2. Sales per year of ARVs: generic and originator, in %



Source: Global Price Reporting Mechanism for HIV, tuberculosis and malaria at www.who.int/hiv/amds/gprm/en/ and Transaction Prices for Antiretroviral Medicines and HIV Diagnostics from 2008 to July 2011 at www.who.int/hiv/pub/amds/gprm_report_oct11/en/index.html.

Figure 4.3. Quantities per year of ARVs: generic and originator, in %



Source: Global Price Reporting Mechanism for HIV, tuberculosis and malaria at www.who.int/hiv/amds/gprm/en/ and Transaction Prices for Antiretroviral Medicines and HIV Diagnostics from 2008 to July 2011 at www.who.int/hiv/pub/amds/gprm_report_oct11/en/index.html.

Indian companies provide most of the generic ARVs in the world, far exceeding those produced by non-Indian generic companies or originator companies. Since 2006, generic ARVs from India have accounted for more than 80 per cent of the donor-funded, developing-country market (Waning et al., 2010). India's important role in the generic ARV market is due to a number of factors, including the fact that a pharmaceutical patent regime did not exist in India until 2005, thus allowing Indian-based companies to produce generic versions of ARVs which were still under patent in other jurisdictions. As a result of the introduction of the product patent regime in India in 2005, pharmaceutical product patents will be granted in India and, consequently, generic versions of new treatments will only be available after patent expiration. Already, certain ARVs newly recommended by the WHO are much more expensive than older regimens, and are also patented more widely, including in India and other major generics-producing countries.¹²

The 2011 Political Declaration on HIV/AIDS commits UN member states to remove, where feasible, obstacles limiting the capacity of LMICs to provide affordable and effective HIV prevention and treatment by 2015, including reducing costs associated with lifelong chronic care through the use of the flexibilities contained in the Agreement on Trade-Related Aspects of Intellectual Property Rights (TRIPS Agreement)¹³ and the promotion of generic competition. The Declaration also encourages the voluntary use of other mechanisms to promote access – for example, tiered pricing, open-source sharing of patents and patent pools, including through entities such as the Medicines Patent Pool – in order to help reduce treatment costs and encourage development of new HIV treatment formulations (UN, 2011a).

(b) Non-communicable diseases

Until recently, the emphasis on “access” to medicines has primarily been directed towards infectious, communicable diseases. Now, however, demographic and epidemiological transitions demand that additional focus should be placed on access to the medical technologies that are needed to treat NCDs. According to the WHO Global Status Report on Non-Communicable Diseases, 36 million of the 57 million (63.2 per cent) global deaths in 2008 were due to NCDs, principally cardiovascular diseases, diabetes, cancers and chronic respiratory diseases (WHO, 2010b). Almost 80 per cent of these deaths occur in LMICs and 85 per cent of the world's population lives in LMICs.¹⁴ NCDs thus are the most common causes of death in most countries, with the exception of Africa.¹⁵ While prevention of NCDs is a key objective, access to essential medicines to treat cardiovascular diseases, diabetes, chronic obstructive pulmonary disease (COPD) including asthma, many cancers (including palliative pain treatment) and depression must be ensured. However, providing treatment for chronic diseases puts an enormous and continuous financial strain on household budgets, often necessitating catastrophic health expenditures and thus pushing families below the poverty line (Niëns et al., 2010).

In considering how to meet the challenge of NCDs, certain parallels can be drawn with HIV/AIDS, which is now generally managed as a chronic disease. There is, nevertheless, a major difference with regard to the role of IP: while HIV/AIDS treatment has been developed relatively recently, and thus is still more widely patented, virtually all of the treatments for NCDs that are on the WHO EML are now off patent and the majority of essential medicines

to treat NCDs are low-cost medicines (NCD Alliance, 2011; Mackey and Liang, 2012). Patents play a role with regard to prices of more recent medicines. It is, however, important to carefully assess the public health benefits of new treatments. Many of the higher-priced treatments for NCDs are not superior, or are only marginally better than older, existing treatments.¹⁶

Currently, major gaps in access to both originator and generic medicines for chronic diseases persist (Mendis et al., 2007). A study comparing the mean availability of 30 medicines for chronic and acute conditions in 40 developing countries found that availability of medicines for chronic diseases was lower than for acute conditions in both public and private-sector facilities (Cameron et al., 2011). Low public-sector availability of essential medicines is often caused by a lack of public resources or under-budgeting, inaccurate demand forecasting, and inefficient procurement and distribution.¹⁷

New strategies for the provision of affordable quality medicines for chronic disease will require a level of effort not unlike the efforts that have been made for treating HIV/AIDS patients. The 2011 UN Political Declaration of the High-level Meeting of the General Assembly on the Prevention and Control of Non-communicable Diseases¹⁸ commits UN member states to improve accessibility to safe, affordable, effective and quality medicines and technologies to diagnose and to treat NCDs. The Global NCD Action Plan 2013-2020, which is under development, will seek to facilitate the implementation of this commitment through the strengthening of health systems and the monitoring of progress to achieve the global voluntary targets which include access to basic technologies and essential NCD medicines.

(c) Paediatric medicines

In 2006, a joint report produced by the WHO and the United Nations Children's Fund (UNICEF) highlighted the need for the creation of an essential medicines list for children (WHO/UNICEF, 2006). The first WHO Model List of Essential Medicines List for Children was published in October 2007 (WHO, 2011f).¹⁹

Availability of paediatric medicines is low in many LMICs. One study found that in 14 African countries a given paediatric formulation was available in between 28 per cent and 48 per cent of primary health care clinics. Availability at retail or private pharmacies tended to be higher, ranging between 38 per cent and 63 per cent (Robertson et al., 2009).

For many medicines, paediatric formulations have not yet been developed.²⁰ The WHO has identified products for the prevention and treatment of TB – particularly in HIV-infected children – and products for new born care as among the most urgent priorities pharmaceutical research for children's medicines.²¹

There are a number of reasons for the lack of research in paediatric medicines. Markets for paediatric medicines tend to be more fragmented than those for adult formulations. The reasons for such fragmentation include the fact that, of necessity, doses of medicines for children are determined by body weight. In addition, paediatric medicines must be available in flexible dosage forms, they must be pleasant tasting and they must be easy for children to swallow.²² Furthermore, it is more expensive to conduct clinical trials in children.²³ In order to provide more incentives to pharmaceutical companies to develop new paediatric formulations, some geographical regions, including Europe and the United States, have introduced paediatric patent term extensions or market exclusivity periods that provide for an additional period of market exclusivity for the product if a paediatric formulation is developed.

Because paediatric formulations are a niche and potentially economically unattractive market, improving access requires extensive collaboration between the public and private sectors. One international effort to improve access to paediatric medicines is UNITAID's work in the area of paediatric ARVs. In cooperation with the Clinton Foundation, UNITAID has provided predictable funding for the large-scale purchase of paediatric ARVs, creating incentives for producers of paediatric ARVs.²⁴ These efforts have resulted in an increase of the number of suppliers and a decrease in the price of quality AIDS medicines for children (UNITAID, 2009; UNITAID, 2011).

(d) Vaccines

National immunization programmes are a highly effective public health tool for the prevention of illness and the spread of infectious diseases, and they are almost always cost-effective in terms of public health outcomes (WHO, 2011c).

The WHO, UNICEF and the World Bank estimate that the cost of immunizing a child in developing countries is about US\$ 18 per live birth (WHO/UNICEF/World Bank, 2009). Protecting more children through vaccination with existing vaccines and introducing new vaccines in immunization programmes will represent an important contribution towards reaching the Millennium Development Goals (MDGs), including Goal 4, "Target 4A: Reduce by two thirds, between 1990 and 2015, the under-five mortality rate". The inclusion of new vaccines in immunization programmes, including pneumococcal and rotavirus vaccines, will help countries to reach the MDGs, but will lead to an increase in costs to about US\$ 30 per live birth (WHO/UNICEF/World Bank, 2009). The arrival of new manufacturers on the market in the next three to seven years could contribute to lower prices in the future.

The degree of access to vaccines varies according to disease area. Global immunization coverage for children

Box 4.3. GAVI Alliance

The GAVI Alliance (formerly known as the Global Alliance for Vaccines and Immunization), a public private partnership, funds new and under-used vaccines for children living in the 70 poorest countries in the world. By the end of 2011, the GAVI Alliance had contributed to the immunization of about 326 million children worldwide, averting more than five and a half million deaths.

Since its launch in 2000, the GAVI Alliance has committed US\$ 7.2 billion, 80 per cent of which has been committed to the purchase of vaccines. It also provides support to strengthen national health systems and civil society organizations to improve vaccine delivery to developing countries (57 eligible countries as of 2011 that have a per capita gross national income equal to or less than US\$ 1,520) for GAVI funding.²⁵

is almost 80 per cent for the six vaccines covered in the Expanded Programme on Immunization (i.e. vaccines against diphtheria, pertussis, tetanus, polio, measles and TB) (WHO, 2011c). The work of the GAVI Alliance has contributed significantly to the immunization of children in developing countries (see Box 4.3). If countries raised the global vaccine coverage against childhood diseases to 90 per cent by 2015, an additional two million childhood deaths per year could be averted. This could significantly impact MDG 4 (WHO/UNICEF/World Bank, 2009). The main challenge in this regard is not the price of the vaccines, but the difficulty in reaching populations in remote regions, weak health and logistical support systems, a lack of understanding about the importance of vaccines and, in certain cases, misconceptions about the safety of vaccines, especially in poorer populations (WHO/UNICEF/World Bank, 2009).

In terms of access to newer vaccines (such as those against human papillomavirus (HPV), rotavirus and pneumococcal disease), huge inequalities exist between developed and developing countries. Two of the greatest sources of child mortality in developing countries (pneumonia and diarrhoeal diseases) are often preventable with the newer vaccines, but these vaccines are not generally available in developing countries (WHO, 2011c). By 2008, only 31 countries (primarily in the developed world) had introduced the pneumococcal vaccine (WHO/UNICEF/World Bank, 2009). Currently, the vaccines remain relatively expensive due to the limited number of producers (Oxfam/MSF, 2010). Several Indian, Brazilian and Chinese manufacturers have plans to produce HPV, pneumococcal and rotavirus vaccines in the near future, and this may, in turn, result in lower prices and improved access.

While in the area of medicines, new and innovative products are often protected by product patents, in the area of vaccines, a lack of technical skills and expertise (know-how) has frequently been the barrier to increasing the number of producers. Setting up a vaccine manufacturing plant requires a highly skilled workforce and broad technical experience and knowledge which may be specific to only one particular vaccine. For example, the reason for the limited number of manufacturers of pandemic influenza vaccines (an issue which posed challenges during 2009/2010 H1N1

pandemic influenza) was the lack of the necessary know-how and the limited market for seasonal influenza vaccines in developing countries.²⁶

3. Access to medical devices

Medical devices play a crucial role in the prevention, diagnosis, treatment and management of medical conditions. Obtaining the benefits of medical devices is dependent to a large extent on a functioning health system, including necessary human resources capable of handling more complicated devices. It is also dependent on financing systems for reimbursement and the available infrastructure. For example, an infusion pump used to infuse medication or nutrients into a patient's circulatory system alone will not solve the patient's problem; it will only benefit the patient if the health system also provides the needed medication or fluid nutrition as well as complementary services to screen, diagnose, treat and rehabilitate. Thus, there is a need for integrated health care delivery models in which medical devices are one part of the overall health system.

The maturation of the concept of "essential" medicines has led to discussions about the application of the framework to other medical technologies. These discussions regarding "essential" medical devices are still at an early stage. While it is clear that some devices are indispensable in order to provide adequate treatment, no consensus has been reached on the issue of what could be considered essential medical devices. This is because the effectiveness of such devices might be dependent on the level of care, the infrastructure and the epidemiology in a specific region.

The issue of access to medical devices has barely been researched. It is necessary to carry out operational research to assess the current situation, develop reference documents, guidelines, standards and legislation (WHO, 2010a). There is a need to determine whether the current medical devices on the global market adequately meet the needs of health care providers and patients throughout the world and, if not, to propose remedial action. In 2010, the WHO Priority Medical Devices report identified gaps in the availability of medical devices and

highlighted obstacles that hinder the full use of medical devices as public health tools (WHO, 2010a). Based on these findings, the WHO developed an approach to identify the most important health problems on a global level – a process that involved using the WHO global burden of disease framework and disease risk factor estimates. Clinical guidelines were used to identify how best to manage the most important health problems, with a particular emphasis on devices. Unfortunately, however, the clinical guidelines do not specify which devices are required to perform certain procedures and thus their

implementation becomes quite complicated if the decision makers do not know which devices to select, procure and use. The third and final step linked the first two steps together to produce a list of key medical devices in the form of an availability matrix needed for the management of the identified high-burden conditions, at a given health care level and in a given context (WHO, 2010a). Overall, the need to have appropriate, affordable, accessible and safe medical devices remains a major challenge in many parts of the world, both for health systems and for the medical device industry.

B. Health systems-related determinants of access

Key points

- Many developed countries use a variety of measures to increase the market share of affordable generics in order to control health budgets. Low- and middle-income countries (LMIC) could generate additional savings by implementing the same types of measures.
- While differential pricing can be used as a complementary tool to increase access, government commitment to provide access to medicines to those who cannot afford them remains essential.
- In many countries, medicines are still subject to indirect taxes such as a purchase tax, sales tax or value added tax (VAT) increasing the price of medicines.
- Mark-ups can significantly increase the price of medicines and thus have an impact on access to medicines.
- Procurement systems should be designed to obtain selected medicines and other medical products of good quality, at the right time, in the required quantities and at favourable costs. Pooled procurement can contribute to cost savings in the procurement process.
- Patent information about specific products in specific markets can facilitate the procurement of generic medicines.
- Trends show that local production is growing and diversifying in some LMICs through national efforts and numerous regional and international initiatives. From a public health point of view, it is important that the incentives provided are not just aimed at industrial development per se.
- Regulation should promote access to medical technologies and should not unnecessarily delay the market entry of products.
- The WHO Prequalification Programme has greatly facilitated access to quality essential medicines in LMICs.
- In the medical device sector, the lack of regulatory authorities, regulations and lack of enforcement of existing regulations has a negative impact on access to quality products.
- The steady increase in the use of substandard and spurious/falsely-labelled/falsified/counterfeit (SFFC) medical products poses serious public health problems, especially in regions where the regulatory and enforcement systems are weak.
- Other challenges for regulatory systems that impact access include lack of political support and adequate resources, lack of effective collaboration among regulators and duplicative inspections, a focus on regulating products without effective oversight of the supply chain, poorly developed systems for post-marketing surveillance, and double standards for locally produced and imported products.

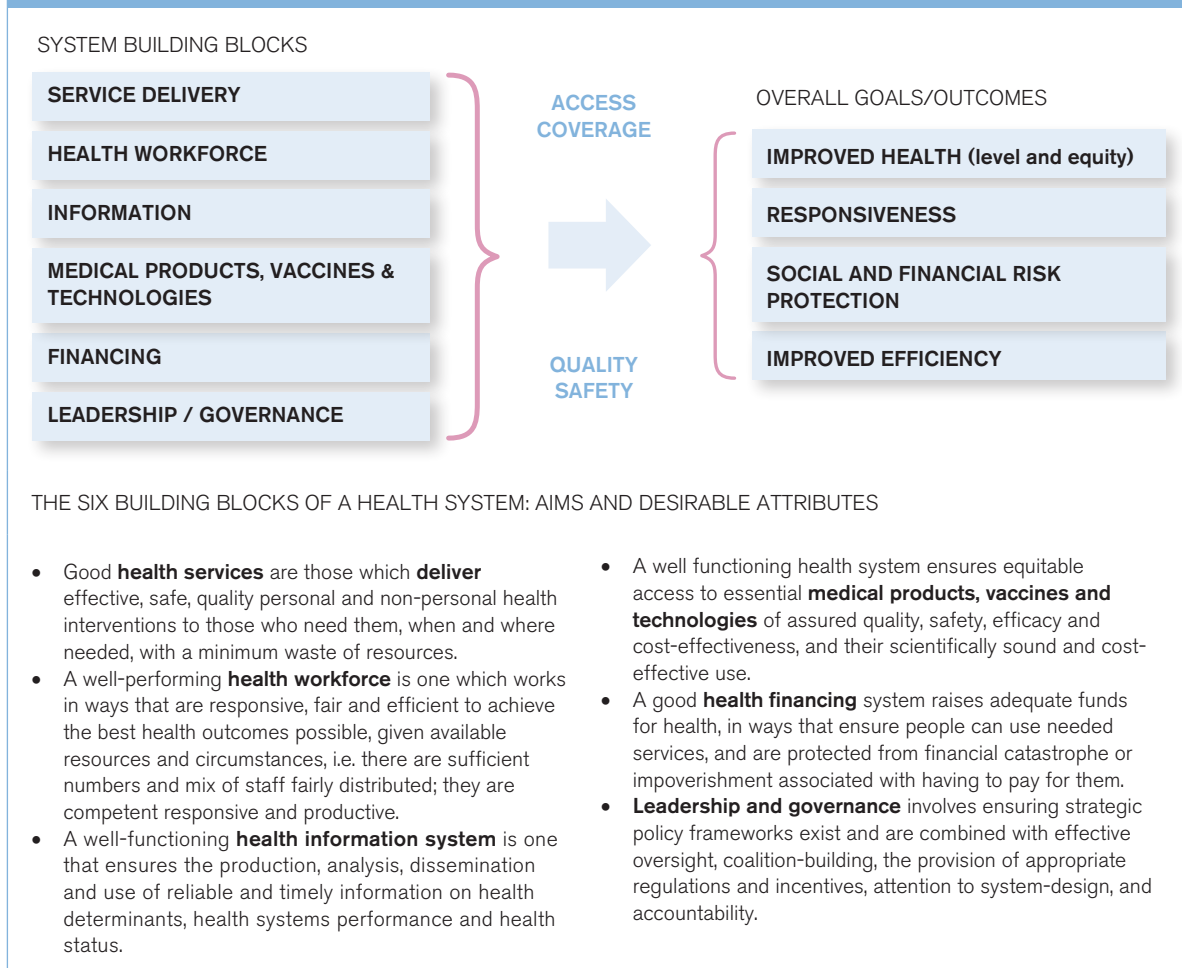
There are different determinants of access and any lack of access to medicines or other medical technologies is rarely due entirely to a single determinant. The following sections discuss the main determinants of access that are linked to health, IP and trade.

One overarching determinant for access to medical technologies is a well-functioning health system. A health system consists of all organizations, people and actions whose primary intent is to promote, restore or maintain health (WHO, 2000a). The WHO conceptualizes health systems in terms of six building blocks whose interplay helps in achieving desired health outcomes through ensuring universal coverage and equitable access to quality assured and safe health care (see Figure 4.4).

One important building block of any health system is equitable access to essential medical products of assured quality, safety, efficacy and cost-effectiveness, and their scientifically sound and cost-effective use (WHO, 2007). All six building blocks of the health system are interdependent (see Figure 4.4).

This section describes some of the main health systems-related determinants of access to medicines and medical technologies. It explains the importance of measures to control medicine prices, in determining access and it demonstrates how taxes, duties and high mark-ups, when imposed on manufacturers' prices, can further result in unaffordability. Efficient public procurement can also ease access, as can, under certain conditions,

Figure 4.4. The WHO Health System Framework



Source: WHO (2007).

local production and associated transfer of technology. The final segment in this section looks at regulation of medicines and medical technologies, and it explains why these are important aspects to ensure access to quality products.

1. Generic medicines policies, price controls and reference pricing

Generic medicines policies which aim to increase the market share of cheaper generic medicines, control prices of medicines and regulate the level of medical expenses reimbursement are key policy interventions to control health budgets, and make medicines and other health products and services more affordable.

(a) Generic medicines policies

The use of generic medicines has been steadily rising not only in developing countries but also in developed countries as a result of economic pressure on health budgets. Many countries are using different measures to

increase the market share of cheaper generics to control health budgets. Many of the current “blockbuster” drugs are nearing the end of their patent term and, over the next few years, it is to be expected that the market share of generics will continue to rise further.

Generic medicines policies can be divided into so-called supply-side and demand-side policies (King and Kanavos, 2002).

(i) Supply-side measures

Supply-side measures are primarily directed towards the specific health care system stakeholders that are responsible for medicine regulation, registration, competition (antitrust) policy, intellectual property rights (IPRs), pricing and reimbursement. Through such measures, policy-makers can impact the:

- speed with which a generic product is reviewed by the regulatory authority
- decision when to grant a patent through application of an appropriate definition of patentability criteria

- relationship between market authorization of medicines and patent protection (Bolar-exception and patent linkage)
- way clinical test data are protected from unfair competition
- ability of the originator to extend IP protection, for example through patent term extensions
- level of competition among manufacturers, and monitoring of agreements between originators and generic companies
- price(s) of generic product(s)
- reimbursement to the purchasers of medicine(s).

(ii) *Demand-side measures*

Generally, demand-side measures are directed at stakeholders such as health care professionals who prescribe medicines (usually physicians), people who dispense and/or sell medicines, and patients/consumers who ask for generic medicines. These measures usually relate to activities that occur after an originator loses market exclusivity and generic medicines have entered the market.

Through the use of appropriate demand-side measures policy-makers can impact the:

- prescribing of generic version(s) by physicians using the international nonproprietary name (INN)/generic name instead of the trade name
- dispensing of the generic version(s) by people who dispense and/or sell medicines
- confidence of prescribers, dispensers and consumers in the quality of generic medicines
- overall consumption pattern of the generic medicine(s) in the health care system
- demand by the consumer for generic products through higher co-payments for originator products
- perception of generic medicines (often patients agree that generics can help reduce costs, but many still prefer to take originator products).

Most of the policies in high-income countries work through a health insurance system, which has reimbursement procedures or requires higher co-payments, so as to incentivize consumers to choose generic medicines. The differences in contextual factors between high-income countries and LMICs that influence pro-generic medicines policies make it difficult to predict which policies can be successfully translated from high-income countries to LMICs.

Two enabling conditions may be needed before an LMIC can effectively implement pro-generic medicines policies:

- A mechanism to provide certainty that the generic medicines are of assured quality. This involves having

an effective regulatory system, and possibly, a well-functioning trademark system.

- A robust supply of generic medicines to ensure the availability of assured quality, low-cost medicines.

The characteristics of the health care systems in many LMICs suggest that demand-side policies driven by consumers may be more important, as medicines are largely financed out-of-pocket and the selection of products purchased is made directly by consumers or patients without prescribers acting as intermediaries.

(b) Price control

There is potential for manufacturers to exploit market exclusivity when facing demand for medicines that remains relatively constant irrespective of changes in price (so-called “inelastic demand”). This has led many countries to regulate prices for at least some portion of the pharmaceutical market, most often patented products. Canada and Mexico, for example, have established price review regulation for on-patent pharmaceuticals, a move that is aimed at ensuring that prices paid by any section of the population, insured or not, are not excessive. In most other high-income countries, insurance coverage schemes require manufacturers to accept price limits in exchange for financing through reimbursement schemes.²⁷

Various price control strategies have been used. These include, among others, controlling profits of manufacturers, direct price controls, comparing prices to internal or external references, constraining spending by physicians, enforcing prescription guidelines, tying marketing approval to prices, and placing limits on the promotion of medicines. Price control measures have also been subject to disputes in domestic jurisdictions.

Price controls can be applied either at the manufacturer, wholesaler or retailer level (see Box 4.4 for reference prices and price controls in Colombia). The most direct control method is when a government sets the sale price and prevents sales at any other price. Governments that enjoy some monopsonistic (i.e. where there is only one buyer) power may also directly negotiate favourable prices with manufacturers. The former method could be based on estimates of costs, which could be inaccurate, while the latter method may be more successful, depending on the degree of monopsony enjoyed by the government. Canada’s Patented Medicines Prices Review Board protects interests of Canadian consumers by ensuring that the prices of patented medicines are not excessive. It reviews the prices that patentees charge for patented products in Canadian markets. If the Board considers a price excessive, it can order price reductions and/or the offset of excess revenues (see www.pmprb-cepmb.gc.ca/).

Another method used by governments is to set an artificially low reimbursement price for a new drug, so that any price above must be borne by the patient. The reimbursement

Box 4.4. Reference prices and price controls in Colombia

Colombia's National Medicines Pricing Commission fixes reference prices for all medicines commercialized in the country's public sector at least once a year. To do so, it takes into account the average price in the domestic market for a group of homogenous pharmaceutical products, i.e. products with identical composition, doses and formulas. If the price applied for such a medicine is above the reference price for homogenous products, direct price controls are applied and a maximum retail price is fixed by the Commission.

Direct price controls are also applied if there are less than three homogenous products on the market. In such cases, the Commission establishes an international reference price (IRP) by comparing the price applied for the same product in at least three of eight selected countries from the region (Argentina, Brazil, Chile, Ecuador, Mexico, Panama, Peru and Uruguay) and in Organisation for Economic Co-operation and Development (OECD) countries. The lowest price found in any of these countries is fixed as the maximum retail price for Colombia.

The application of price controls has played a prominent role in the case of lopinavir and ritonavir provided to HIV/AIDS patients in Colombia. In 2009, the Colombian Ministry of Health rejected a 2008 application for a compulsory licence on the grounds of lack of public interest. As this medicine was listed on the national EML, its supply by insurers to patients was mandatory, and therefore the price applied by the right holder would not block access. At the same time, the Commission decided to regulate the price of the medicine concerned. The prices were fixed at US\$ 1,067 for the public sector and US\$ 1,591 for the private sector, representing an average reduction of between 54 per cent and 68 per cent per person per year (Brazilian Interdisciplinary AIDS Association, 2009). The right holder's appeal against the decision was rejected. In 2010, the originator company agreed to sell the medicine at the price fixed by the Commission.

price then functions as the *de facto* market price. Finally, governments may regularly cut the reimbursement price of already existing marketed drugs. These types of price controls are market interventions, and controlled prices should allow for reasonable profits so as to avoid forcing needed suppliers out of the market.

(c) Reference pricing

Reference pricing can determine, or be used for, negotiating the nationally regulated price or reimbursement level of a product based on the price(s) of a pharmaceutical product in other countries ("external") or relative to existing therapies in the same country ("internal"). Reference pricing typically controls the reimbursement level and thus is mainly useful in countries with insurance-based systems. This is seen as less restrictive than direct price controls.

(i) External reference pricing

International or external reference pricing is the practice of comparing the price(s) of a pharmaceutical product with the prices in a set of reference countries (Espin et al., 2011). Various methods can be used for selecting reference countries in the "basket" and for calculating external reference prices. There are also many ways to apply external reference pricing in practice. Box 4.4 describes how external reference pricing and price controls work in Colombia.

(ii) Internal reference pricing

By contrast, internal reference pricing compares the same or similar medicines in the same country. Medicines to be compared are classified according to the Anatomical

Therapeutic Chemical (ATC) system, which compares medicines at five levels, from the organ or system on which the drug works through to the chemical structure (ATC 5 level).²⁸ Internal reference pricing is "the practice of using the price(s) of identical medicines (ATC 5 level) or similar products (ATC 4 level) or even with therapeutic equivalent treatment (not necessarily a medicine) in a country" to determine a price.²⁹ Internal reference pricing is particularly effective when considering the pricing of originator products, which contain the same active pharmaceutical ingredient (API) as generic versions, but are typically more expensive.

(d) Health technology assessments

In the past years, an increasing number of countries have started to introduce pay-for-performance schemes based on health technology assessments that evaluate the medical benefits and the cost-effectiveness of a treatment as a tool to contain costs and to direct expenditure to improved health outcomes (Kanavos et al., 2010).

Assessing health technologies is a multidisciplinary process: information about the medical, social, economic and ethical issues relating to the use of a health technology is gathered in a systematic, transparent and unbiased manner, so as to inform the formulation of safe, effective health policies that are patient-focused and that seek to achieve best value.³⁰ A health technology assessment of a medicine, or of a medical device or a clinical or surgical procedure, therefore not only examines its safety, efficacy or effectiveness, but also undertakes a cost-benefit analysis and evaluates various other aspects of the use of a medical product or technology. While health

technology assessments can differ widely, cost-benefit analyses focus on clinical effectiveness – a comparison of health outcomes of alternative technologies with available alternatives – and on cost-effectiveness – comparing improvements in health outcomes with the additional costs of the technology. The latter comparison enables a determination as to whether the costs are proportionate to the health outcomes, and thus whether the medical product should be provided to the patient (for more information, see Garrido et al., 2008). To what extent such health technology assessments will contribute to control health expenditures in the long term cannot be fully assessed yet.

(e) Volume limitations

Governments may also impose volume limitations to control the quantity of a new drug that may be sold. France imposes price-volume agreements on manufacturers of new medicines (OECD, 2008). A “price-volume” agreement links the reimbursement price of a new drug to a volume sales threshold. If the threshold is exceeded, the manufacturer must provide compensation through price reduction or cash payments to the government (depending on the country) or remove the product from the market. Through such volume limitations the payer can control the maximum cost implications of the introduction of new, expensive treatments and limit the incentive for companies to promote a wide use of new expensive treatments.

2. Differential pricing strategies

Differential pricing (also known as “tiered pricing” or “price discrimination”) occurs when companies charge different prices for the same product depending on the different classes of purchasers, and where such price differences cannot be explained by differences in the cost of production. Price differentials may exist across different geographical areas or according to differences in purchasing power and socio-economic segments. Because differential pricing involves the division of markets into different tiers or groups, the practice is also known as tiered pricing. Such price discrimination is only feasible to the extent that markets can be effectively segmented, in order to prevent

arbitrage (the purchase of products in the lower-price market and subsequent sale in the higher-price market).

Tiered pricing can be practised in different ways. Private companies can negotiate individual agreements with other companies. They can also negotiate price discounts with governments or through regional or global bulk purchasing arrangements and the licensing of production for specified markets. Creating market segmentation can be achieved through various marketing strategies (e.g. using different trademarks, license agreements, dosage forms or presentation of products), by having more stringent supply chain management by purchasers, and by having import controls in high-income countries and export controls in poorer countries (see Box 4.5 for differential packaging as another example to support differential pricing strategies). Differential pricing can, in principle, make medicines more affordable to larger segments of the population and could also lead to increased sales, thus benefiting pharmaceutical manufacturers (Yadav, 2010).

However, it reaches its limits where the affordability level of patients is less than the marginal cost of manufacturing. Differential pricing can thus only be a complementary policy, whereas continuing government commitment to provide access to medicines to the poor is essential (Yadav, 2010).

Companies are sometimes reluctant to follow tiered pricing strategies. A possible reason is fear of price erosion in high-income markets as a result of arbitrage. Companies may also be reluctant to provide differential prices to middle-income countries, as it may be difficult for them to preserve higher prices in neighbouring markets or in countries with a similar income level.

The ability to differentiate within countries according to socio-economic segments of the population, and also to differentiate between the public and private sectors, might serve to overcome these difficulties. Preventing lower priced products from flowing back to high-income private markets will remain a challenge, but the trend may be changing. Box 4.5 presents an example on how differential packaging can be used to separate markets. Recently, a number of research-based companies have run pilot programmes extending differential pricing, including

Box 4.5. Differential packaging

In 2001, as part of the Memorandum of Understanding between the WHO and Novartis to make available artemether-lumefantrine at cost price for use in the public sector of malaria-endemic countries, Novartis developed differential packaging for artemether-lumefantrine destined for the public sector. This differed from the existing packaging for products destined for the private sector. The WHO collaborated with the company to develop four different course-of-therapy packs (for four separate age groups), each containing pictorial diagrams on how to take the medicines and all aimed at improving adherence to treatment among illiterate population groups. Initially, packs were made available to WHO procurement services. They were subsequently made available to UNICEF and, progressively, to additional procurement services supplying the public sector only. The leakage of such packs from the public sector into the private sector is not significant. The use of a distinctive “Green Leaf” logo on the packs facilitates the process of tracking and monitoring of availability and market share at point of sale.

intra-country differential pricing, to emerging economies. They have also expanded these programmes to encompass a broader range of medicines, including cancer medicines and biologicals.³¹ This shows that companies are working to adapt their current single global price model to the socio-economic reality in emerging economies, thus basing their business model on a different volume to price equation.

One example of differential pricing is the Accelerating Access Initiative, a partnership established in May 2000. Among five UN organizations (UNAIDS, UNICEF, the United Nations Population Fund (UNFPA), the World Bank and the WHO) and five pharmaceutical companies. The objective was to address the lack of affordable HIV medicines and of HIV/AIDS care in selected developing countries (WHO/UNAIDS, 2002). The pharmaceutical companies involved agreed to either donate medicines and/or provide significant cost reductions.

Differential pricing is already well established in the vaccine market. A three-tiered pricing structure is used for most vaccines sold in both developed and developing countries. Companies charge the highest prices in high-income countries, low prices in countries prioritised by the GAVI Alliance, and intermediate prices in middle-income countries. Vaccines are also the sector where differential pricing is more widespread within a country: for example, one company offers its hepatitis B vaccine at two different prices within India, with the public sector only paying about half the price paid by the private sector.

3. Taxes

While medicines are often subject to indirect taxes such as a purchase tax, sales tax or VAT, entities producing

and selling medicines may also be subject to direct taxes on the revenue generated (e.g. corporate income tax). Taxes add up to the end-price paid by the consumer and is, therefore, a factor that affects access to medicines.

In 2010, the VAT rate on medicines in high-income countries was between zero and 25 per cent, with Australia, Japan and the Republic of Korea having a tax exemption policy. Similarly, countries such as Colombia, Ethiopia, the State of Kuwait, Malaysia, Nicaragua, Oman, Pakistan, Uganda and Ukraine reported zero VAT and sales tax on medicines. In LMICs that charged taxes on medicines, the tax rate ranged from 5 per cent to about 34 per cent. In some LMICs, the situation in relation to taxation of medicines is even more complex and variable, sometimes with multiple federal and state taxes being applied. Furthermore, imported and locally made medicines are sometimes taxed differently. The study concludes that domestic taxes such as VAT or sales tax are often the third largest component in the final price of a medicine (Creese, 2011).

Certain practical tax measures can be used to reduce the price of medicines (the Peruvian experience with tax exemption measures is set out in Box 4.6). One such measure is to remove taxes on medicines that have relatively inelastic demand patterns (i.e. people will buy these medicines regardless of their price). For example, Mongolia removed taxes on imported omeprazole sold in private pharmacies, a move that led to a price fall of between US\$ 5.91 and US\$ 4.85 for a 30-capsule pack, while the Philippines removed 12-per-cent VAT thus reducing the price of a pack of ten generic co-trimoxazole tablets (480 mg) from 14.90 pesos to 13.30 pesos (Creese, 2011).

Another measure that may improve access to medicines is alterations in tax rates. It should be possible to evaluate the

Box 4.6. Peru: tax exemption measures for cancer/diabetes treatment drugs

In 2010 and 2011, Peru carried out two studies on the impact of tax exemption measures on the price of certain cancer and diabetes medicines. In 75 per cent of the 40 diabetes medicines in the retail sector examined as part of the studies, companies had not passed on possible price reductions resulting from the introduction of tax exemption measures. In the public sector, prices for 44 per cent of the medicines examined did not reflect the potential benefits accruing from tax exemption measures, whereas 56 per cent partially reflected such measures in the form of price reductions. For medicines not subject to competition, prices either did not vary, or were subject to large variations (up to 248 per cent), depending on the volume purchased.

Of the five cancer treatments examined which were marketed in the retail sector before and after the introduction of tax exemption measures, prices decreased in two cases, but did not change in the case of three other retail prices (i.e. the benefit due as a result of the introduction of tax exemption measures was not passed on).

In the public sector, prices were evaluated for eight medicines before and after tax exemption measures. In the case of four medicines, companies had not passed on the tax exemption in the form of reduced prices. By contrast, prices decreased for the other four medicines examined. Following the introduction of tax exemption measures, prices remained stable for the six drugs for which there was no competition. Prices decreased in the case of the two drugs for which there were alternatives on the market. In one of these cases, the price reduction was up to 38 per cent.³²

consequences of defined changes in tax rates that either improve or reduce access to medicines, and then propose tax policy changes accordingly. In 2004, Kyrgyzstan reduced VAT and regional sales tax on medicines, while in Pakistan, following a successful consumer advocacy challenge, the 15-per-cent sales tax on medicines was removed altogether. Although alterations in tax rates may not occur until there is a change in national tax regimes, the impact of this measure may be substantial (Creese, 2011). Removing customs duties discussed later in this chapter is a similar measure that can have a direct bearing on prices and access. In both cases, however, it is important to ensure that savings due to reduced taxes or custom duties are passed on to the consumer, since this is not always the case, as can be seen from the example of Peru (see Box 4.6).

The reduction or elimination of taxes on medicines may also be coupled with the increase in, or introduction of, taxes on public health “bads” (i.e. tobacco, alcohol and unhealthy food). Advocates of this approach often argue that the funds raised from taxes on unhealthy consumption patterns and behaviours can easily balance out, or sometimes surpass, revenue losses due to the reduction or elimination of taxes on medicines, leaving both government and individuals better off (Creese, 2011). In their view, this approach would therefore offer the potential of linking significant revenue gains with improved access to medicines.

4. Mark-ups

A mark-up represents the add-on charges and costs applied by different stakeholders in the supply chain in order to recover overhead costs and distribution charges, and make a profit. The price of a medicine includes mark-ups that have been added along its supply chain distribution. Medicine mark-ups can be added by manufacturers, wholesalers, retailers, pharmacists and many others who play a role in the supply chain distribution (Ball, 2011). Like taxes, a mark-up also contributes to the price of medicines and thus has a direct bearing on access to medicines.

Mark-ups, including those charged by wholesalers and retailers, are common in medicine supply chain distributions in both the public and private sectors. For example, a secondary analysis of WHO/Health Action International (HAI) surveys of developing countries indicates that wholesale mark-ups ranged from 2 per cent in one country to a combined mark-up by importers, distributors, and wholesalers of 380 per cent in another country (Cameron et al., 2009). In addition, a secondary analysis of WHO/HAI surveys indicates that there is huge variability in the cumulative percentage mark-ups (i.e. all mark-ups added from manufacturer’s selling price to final patient price) between the public and private sectors (Cameron et al., 2009). Mark-ups on medicines can also vary depending on the type of medicine (i.e. originator versus generic). Without

appropriate regulation of mark-ups, there can be significant elevation of the consumer price, and, consequently, a substantial impact on access to medicines.

In high-income countries, mark-up regulation in medicine supply chain distributions is usually part of a comprehensive pricing strategy that also addresses medicine reimbursement (Ball, 2011). There is little data on mark-up regulation in the pharmaceutical supply chain in LMICs. WHO pharmaceutical indicator survey data show that around 60 per cent of low-income countries report regulating wholesale or retail mark-ups. In middle-income countries, regulation in the public sector is at a comparable level (Ball, 2011).

Mark-up regulation can positively impact access to medicines, but may also have some adverse effects (Ball, 2011). Because mark-up regulation reduces margins for businesses, some medicines may no longer be offered, or may be offered in reduced quantities, thus adversely affecting product availability and price competition.

5. Effective and efficient procurement mechanisms

Effective procurement of medical products requires the systematic coordination of business operations, information technology, quality assurance, safety and risk management, and legal systems. Furthermore, it is important to be able to contain costs through regular review of procurement models and approaches, monitoring of prices, and record-keeping, in order to make informed decisions (Ombaka, 2009).

(a) Principles for effective procurement

Procurement systems are designed to obtain the selected medicines and products of good quality, at the right time, in the required quantities, and at favourable costs. The WHO has developed a series of operational principles in procurement systems, the purpose of which is to increase access through lower prices and uninterrupted supply (WHO, 2001c). These principles are:

- Divide different procurement functions and responsibilities (selection, quantification, product specification, pre-selection of suppliers and adjudication of tenders) among multiple parties and give each one of them the necessary expertise and resources to do their particular job.
- Ensure transparency of procurement and tender procedures, follow written procedures throughout, and use explicit criteria to award contracts.
- Provide for a reliable management information system that functions to plan, and monitor procurement on a regular basis, including through the execution of an annual external audit.

- Limit public-sector procurement to an essential drugs list or national/local formulary list so as to ensure that the necessary products are procured.
- List drugs by their INN/generic name, on procurement and tender documents.
- Quantify procurement orders based on past consumption, provided that such data have been proven to be accurate. Consumption data must be updated continually, in order to take into account changes in morbidity, and factors such as seasonality and prescribing patterns.
- Finance procurement using reliable mechanisms, such as decentralized drug purchasing accounts or revolving drug funds. In each case, the mechanism itself must also be adequately funded.
- Purchase the largest appropriate quantity in order to achieve economies of scale.
- Obtain favourable prices without compromising quality when procuring for the public sector.
- Monitor this process of procurement where prices are negotiated centrally but ordering done by individual health facilities in the periphery.
- Pre-qualification of possible suppliers is essential, and criteria such as product quality, reliability of service, time for delivery and financial sustainability should be considered.
- Assured quality of purchased medicines, according to international standards.

Parties to the WTO Agreement on Government Procurement are also bound to provide for competitive, non-discriminatory and transparent tendering for a range of public procurement in the health sector. Further guidance on how to organize efficient procurement of medical technologies can be obtained from different sources. The World Health Organization Good Governance for Medicines programme offers a technical support package for tackling unethical issues in the public pharmaceutical sector (WHO, 2010d). The WHO has developed a model quality assurance system for procurement agencies (WHO, 2006a). The World Bank has prepared guidelines containing standard bidding documents and a technical note for use by implementing agencies procuring health-sector goods through international competitive bidding.³³ For the purpose of combating HIV/AIDS, these guidelines have been adapted in a separate decision maker's guide.³⁴

(b) Procurement and patent information

Procurement systems should be designed to obtain selected medicines and other medical products of good quality, at the right time, in the required quantities, and at favourable costs. While generally the supplier is responsible for ensuring that all necessary rights to products, including IPRs, have been secured in accordance with the specifications in tender documents and procurement contracts, procurement agencies also have to consider the patent status of products early in

the procurement process. Checking the validity of patents, price or licence negotiations with the patent holder and the possible use of compulsory licences or government use by the respective government takes time. Therefore, if this information is only gathered at a late stage of the procurement process, delays in the procurement can lead to stock outs. The content and sources of patent information is further explained in Chapter II, Section B.1(b)(viii). This was also the subject of a WHO/WIPO/WTO joint technical symposium entitled "Access to Medicines, Patent Information and Freedom to Operate", held in February 2011.³⁵

(c) Pooled procurement

Pooled procurement, also known as "group purchasing" or "bulk purchasing" has been defined as "purchasing done by one procurement office on behalf of a group of facilities, health systems or countries" (MSH, 2012). Pooled procurement is a strategy that can make medicines more affordable and that can help resolving challenges such as poor quality, and other bottlenecks generally associated with procurement and supply chains of essential medicines.

Economies of scale and long-term prospects of supply, which are prevalent in most public-sector procurement systems, enable suppliers to lower their prices. Pooled procurement in the health sector occurs in one form or another in both developed and developing countries. Both the public sector and private sector (e.g. a group of private hospitals sharing a joint procurement system) use those mechanisms at various levels of scale. In high-income countries, large insurance and reimbursement systems support the purchase of medicines and other medical technologies that are acquired through pooled procurement. LMICs now increasingly adopt joint purchasing practices. Current programmes in India and China to expand health care to their large populations are examples of this phenomenon. In public-sector procurement, most countries benefit from the advantages of central bulk procurement. Many low-income countries have established central procurement agencies to manage the pooled needs of the health care system. With the leverage of larger orders, they can achieve economies of scale and negotiate best prices. Fully functioning pooled procurement systems contribute to the development of quality control systems, promote the improvement of storage and delivery infrastructure to accommodate large quantities of medicines and other health technologies.

Successful pooled procurement schemes have reported substantial reductions in the unit price of medicines. Some well-known examples include the Organisation of Eastern Caribbean States (OECS), the Pan American Health Organization (PAHO) Strategic Fund for Essential Public Health Supplies, the PAHO Strategic Fund for Vaccines, the African Association of Central Medical Stores, and

the Group Purchasing Program of the Gulf Cooperation Council (GPP/GCC). The OECS, a self-financing public-sector monopsony, has consistently reported substantial reductions in the unit price of medicines. In 2001–2002, an annual survey of 20 popular drugs available in the OECS region, found that prices under the pooled procurement scheme of the OECS were 44 per cent lower than individual country prices (OECS, 2001). The GPP/GCC also experienced that improved procurement can reduce costs and enhance the efficiency of health service. The PAHO Strategic Fund is another example of pooled procurement. The Fund was developed by the PAHO Secretariat at the request of member states. Currently, 23 PAHO member states participate in this strategic fund, which was created to promote access to quality, essential public health supplies in the Americas. The Global Fund employs the Voluntary Pooled Procurement as a cost-effective way of ensuring efficient procurement of ARVs, rapid diagnostic kits for HIV and malaria, Artemisinin-based combination therapies and long-lasting insecticidal nets (Global Fund, 2010a; 2010b).

6. Local production and technology transfer

Most countries import medicines, diagnostics, vaccines and other medical products from the global market. Nevertheless, a number of LMICs aspire to build and strengthen their domestic medical products industry. Trends show that local production is growing and diversifying in some of these countries.³⁶ However, the evidence that local production results in increased access to medical products is inconclusive (WHO, 2011g).

In order to become economically viable, local producers, particularly those based in low-income countries, have to address a number of challenges. These challenges may include:

- weak physical infrastructure
- scarcity of appropriately trained technical staff
- dependence on imported raw materials, including active pharmaceutical ingredients (APIs)
- weak and uncertain markets
- lack of economies of scale
- high import duties and taxes
- lack of a conducive policy environment and policy coherence across sectors
- weak quality control and regulation measures
- existence of patents on key products or technologies
- later regulatory clearance due to data exclusivity rules, where recognized.

Overcoming these challenges can add to the cost of production, thus making the product relatively

uncompetitive in comparison with cheaper imports. According to Kaplan and Laing (2005), “local production of medicines at higher cost than equivalent imports may have no impact whatsoever on patient access to needed medicines”.

The framework diagram depicted in Figure 4.5 outlines the main relevant factors from both an industrial policy (Box A) and a public health policy (Box B) perspective. It indicates that common or shared goals exist between these two perspectives, such that the objectives of industrial policy can also help to meet those of public health (Box C). The government’s role is to provide a range of direct and indirect financial incentives and to help ensure coherence across the entire policy arena (Box D).

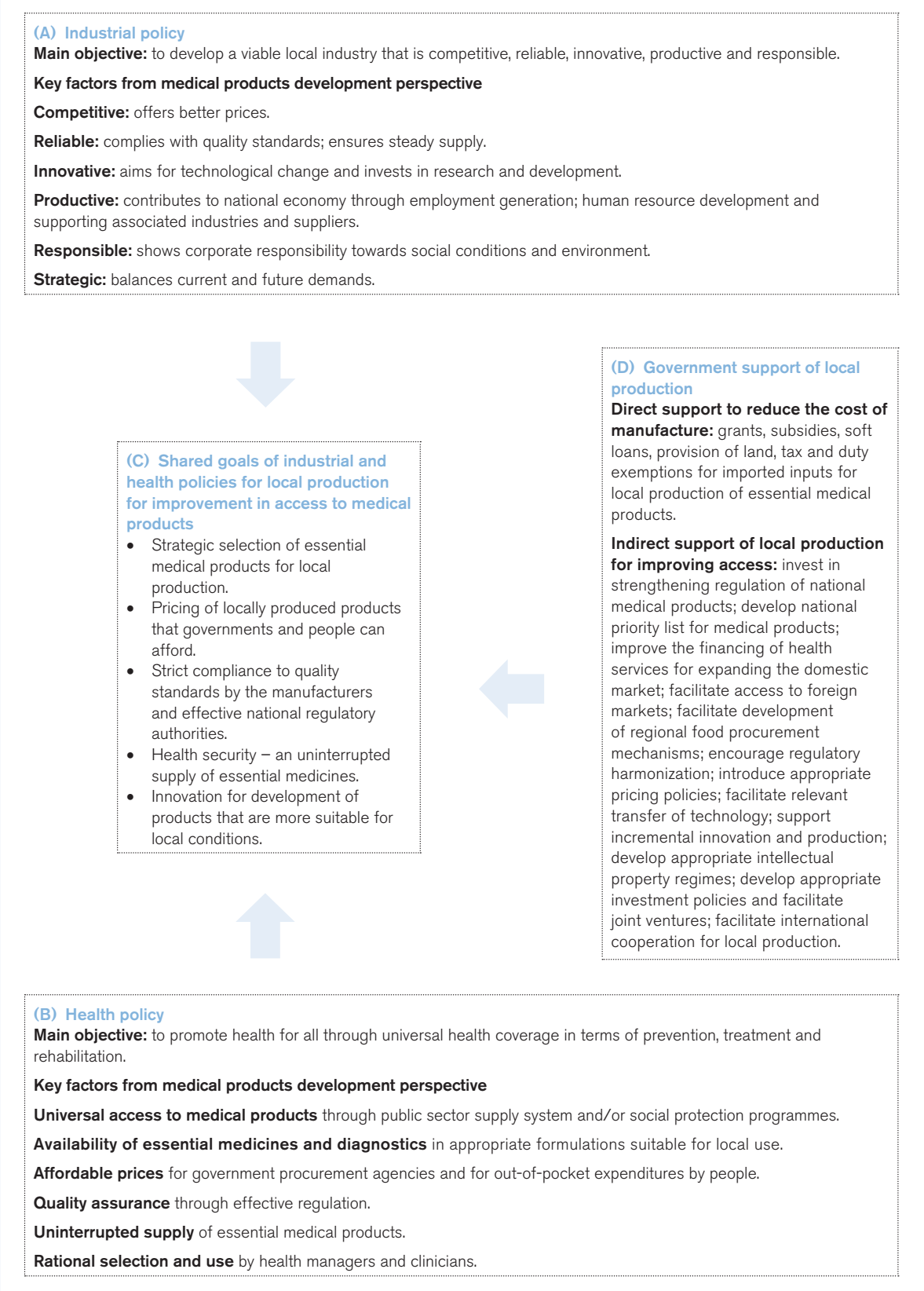
It is important that any incentives for local production are not just aimed at increasing industrial development per se. A good example is the WHO technology transfer for pandemic influenza vaccines and enabling technologies described in Box 4.7. They should also explicitly aim to improve people’s access to locally produced medical products. To achieve this, it is important that government incentives are designed to support the shared goals of industrial policies and health policies, for example, by strengthening an effective national regulatory authority. The WHO guidelines on transfer of technology in pharmaceutical manufacturing provide useful guidance in this area.³⁷

Currently, the TRIPS Agreement transitional period, within which least-developed countries (LDCs) are not required to grant and enforce pharmaceutical patents up to 2016, could provide opportunities to set up local production in LDCs for products that are still under patent protection in other countries.³⁸

Some existing technology transfer projects designed to involve LDCs in local and regional manufacturing initiatives through collaborations with private companies and national governments. One such initiative is a joint venture between an Indian generic manufacturer and a Ugandan company. Under this programme, Indian experts provide training to local staff. This partnership resulted in the establishment of a manufacturing plant near Kampala to produce ARV medicines and antimalarials. The plant has been certified by the WHO as compliant with good manufacturing practices (GMPs) and has obtained WHO pre-qualification for two products.

The Brazilian government is cooperating with the Mozambique Ministry of Health to establish Mozambique’s first manufacturing facility for the production of first-line ARV medicines, based on the portfolio of drugs produced by the Oswaldo Cruz Foundation. 2011 saw the signing of an agreement to construct the facility. As part of this agreement, Brazil will supply equipment and training for local technicians working in the facility.

Figure 4.5. Local production and access to essential medical products: a framework for improving public health



Source: WHO (2011g).

Box 4.7. WHO technology transfer for pandemic influenza vaccines and enabling technologies

The WHO Global Pandemic Influenza Action Plan, published in 2006, identified the construction of new influenza vaccine production plants in developing countries as a priority, so as to increase global capacity and pandemic preparedness.³⁹ The WHO has provided seed funding to 14 vaccine manufacturers in Brazil, China, Egypt, India, Indonesia, Iran, Kazakhstan, the Republic of Korea, Mexico, Romania, Serbia, South Africa, Thailand and Viet Nam to enable domestic production.

The classical methods of manufacturing influenza vaccine, such as the 1940s vintage hen egg-derived technology that still accounts for the bulk of influenza vaccine production, are not protected by IPRs. A central technology transfer hub was established in the Netherlands, thereby concentrating expertise in a single location from which technology transfer to multiple recipients could be carried out efficiently. Personnel from the majority of the countries who provided funding for the project, as well as personnel from national regulatory agencies, have received training at this technology transfer hub (Hendriks et al., 2011).

Enabling technologies

Live attenuated influenza vaccine technology: Several of the manufacturers opted to use the live attenuated influenza vaccine technology, which produces a high-yield, low-cost vaccine that is easy to administer. In order to facilitate access to the know-how, clinical data and seed strains required for this technology, the WHO, on behalf of developing country vaccine manufacturers, negotiated and acquired a transferable non-exclusive licence. Sub-licences were granted to three developing country vaccine manufacturers.

Adjuvant technology: Adjuvants have been shown to permit dose-sparing for pandemic influenza vaccines, and thus multiply capacity, enabling a larger number of people to be immunized. However, the know-how on these adjuvants has been predominantly in the hands of a few multinational vaccine manufacturers. The WHO determined that the IPRs on one of the lead adjuvants had limited geographical scope, and therefore could be produced in developing countries. To transfer the necessary know-how on how to produce the adjuvant, the WHO facilitated the establishment of an adjuvant technology transfer hub at the University of Lausanne. The hub established production processes for the adjuvant, and has already successfully transferred the technology to Indonesia and Viet Nam.

In 2012, the South African government, through a South African company, entered into a joint venture with a Swiss company to establish the first pharmaceutical plant to manufacture APIs for ARV medicines in South Africa. This will involve the construction of a new facility in South Africa designed to develop locally mined fluorspar into higher value fluorochemical products. The project is aimed at reducing South Africa's dependence on imported drugs and enabling the manufacture of ARV medicines from locally sourced and produced APIs.

Regulation of medical technologies plays a key role in determining access to quality-assured medical products. While certain positive developments have taken place in recent years, regulatory control for medicines and medical technologies in LMICs needs to improve further. The WHO works with its member states in assessing national regulatory systems to identify gaps, develop strategies for improvement and support countries in their commitment to build national regulatory capacity. WHO (2010c) provides an overview of the regulatory situation in Africa (see Box 4.8).

7. Regulatory mechanisms and access to medical technologies

This section builds on Chapter II, Section A.6, and focuses on the WHO Prequalification Programme, the role of global donors in regulatory standards harmonization, complex supply and management systems, and the problem of substandard and spurious/falsely-labelled/falsified/counterfeit (SFFC) products.

(a) The Prequalification Programme

The Prequalification Programme, a UN initiative managed by the WHO, has contributed substantially to improving access to quality medicines in developing countries through ensuring compliance with quality standards (see Box 4.8). The programme aims to facilitate access to medical technologies that meet international standards of quality, safety and efficacy. It extends to medicines used for HIV/AIDS, TB, malaria, reproductive health and influenza as well as vaccines and diagnostics.⁴⁰

Box 4.8. WHO assessment of medicines regulatory systems in sub-Saharan African countries

A recent WHO report synthesizes the findings of assessments carried out on national medicines regulatory authorities in 26 African countries over an eight-year period and provides an overview of the regulatory situation in Africa (WHO, 2010c).

The report concluded that while structures for medicines regulation existed, and while the main regulatory functions were being addressed, in practice, the measures were often inadequate. Common weaknesses included fragmented laws in need of consolidation, weak management structures and processes, and a severe lack of staff and resources. On the whole, countries did not have the capacity to control the quality, safety and efficacy of the medicines circulating in their markets or passing through their territories.

The WHO recommends that regulatory capacity in African countries be strengthened, using the following approaches:

- Encourage and assist countries to assess their own regulatory systems in a systematic way in order to identify and address gaps.
- Work towards consistent implementation of all essential regulatory functions in African countries, based on the key provisions in the existing legal frameworks.
- Develop and improve management structures, specific technical regulatory expertise and physical resources (both human and financial) available to national medicines regulatory authorities in Africa.
- Consider mechanisms for sharing the outcomes of regulatory assessments.

The Prequalification Programme does not replace national regulatory authorities or national authorization systems for the importation of medical technologies. If a product meets the specified requirements, and if the manufacturing site complies with current GMP, both the product linked to a specific manufacturing site and details of the product manufacturer are added to a list of pre-qualified medicinal products. This list is published by the WHO on a publicly accessible website.⁴¹

WHO pre-qualification is a recognized quality standard that is used and referred to by many international donors and procurement agencies.

(b) Regulation of medical devices

Medical devices include a wide range of tools – from the simple wooden tongue depressor and stethoscope to the most sophisticated implants and medical imaging apparatus. As is the case with vaccines and medicines, governments need to put in place policies that ensure access to quality, affordable medical devices, and also ensure their

safe and appropriate use and disposal. Therefore, strong regulatory systems are needed so as to ensure the safety, effectiveness and performance of medical devices. A recent example for this need is the use of non-medical grade silicone in breast implants manufactured by a company based in France (see Box 4.9). In general, medical devices are submitted to regulatory controls and, consequently, most countries have an authority that is responsible for implementing and enforcing specific product regulations for medical devices.⁴² This also holds true for LMICs where more than 70 regulatory control authorities are in place (WHO, 2010a). Conversely, many other LMICs still do not have an authority responsible for implementing and enforcing medical device regulations. Implementation and enforcement are complicated, due to shortages of professional biomedical engineers, lack of harmonization in medical devices procedures and limited information. National guidelines, policies or recommendations on the procurement of medical devices are not used in a majority of countries, either because they are not available or because there is no recognized authority in place to implement them. This creates challenges to establish priorities in the selection of medical devices on the basis of their impact on

Box 4.9. Europe: tightening the control to guarantee the safety of medical devices

The EU legal framework relating to the safety and performance of medical devices was harmonized in the 1990s.⁴³ Under this legislation, medical devices are subject to strict pre-market controls by independent assessment bodies (notified bodies), which review the manufacturer's design and safety data for the product. Despite such control mechanisms, non-medical grade silicone was used in breast implants manufactured by a company based in France, thereby resulting in an unusually high short-term rupture rate of these breast implants. Incidents such as this highlight the need to modernize and strengthen the EU legislation that applies to medical devices. In February 2012, the European Commissioner for Health and Consumer Policy announced the imminent completion of the revision of the relevant legislation, based on the identification of shortcomings in the current laws. The Commissioner has also called on EU member states to immediately tighten controls and increase surveillance (European Commission, 2012).

the burden of disease. The lack of regulatory authorities, regulations and lack of enforcement of existing regulations has a negative impact on access to quality products. The WHO has published a global overview and guiding principles on medical device regulations to assist countries in establishing appropriate regulatory systems for medical devices (WHO, 2003a).

(c) Role of global donors in regulatory standards harmonization

Increasingly, major donors and donor programmes such as the Global Fund to Fight AIDS, Tuberculosis and Malaria (Global Fund), the US President's Emergency Plan for AIDS Relief (PEPFAR) and UNITAID are financing major procurement programmes to increase access to medicines, with a specific focus on the major infectious diseases HIV/AIDS, malaria and TB. Donors demand compliance with certain quality standards, often by way of reference to the Prequalification Programme and WHO quality standards. The donor community and the NGO community use WHO pre-qualified quality control laboratories for quality control analysis of the procured products, and such laboratories are becoming increasingly available in all WHO regions. Donors have also started to commit funds aimed at ensuring that national quality assurance systems are put in place, and several donors have directed funding towards regulatory capacity-building in the receiving countries. Although significant progress has been made, the quality assurance policies of programmes such as the Global Fund, PEPFAR, UNITAID, UNFPA, the Global Drug Facility and UNICEF are not yet fully aligned. Given the extent of these programmes and the dominant role they play in the procurement of HIV/AIDS, malaria and TB medicines, diverging requirements for quality and safety can lead to market distortions, as different conditions need to be fulfilled for different purchasers. The creation of a single competitive market would represent an important contribution to the process of enabling access to good quality, affordable medicines.

(d) Complex supply and management systems

One of the main regulatory determinants that are also linked to international trade is the increasing fragmentation of global supply chains. In order to lower costs, many manufacturers have in the past outsourced basic research and production of, for example, APIs and medical device components to countries such as China, India and the Republic of Korea. As a result, growing trade in the products between continents creates a more complex supply chain, challenging the regulatory agencies that need to survey the complete supply chain, so as to ensure that end products meet the required quality standards.

A finished pharmaceutical dosage form or medical device may have been assembled using materials

sourced or outsourced from many different parts of the world. In the case of the United States, for example, 80 per cent of APIs and 40 per cent of finished product medicines are imported from other countries (Institute of Medicine, 2012).

One of the hazards of purchasing ingredients for medicines or parts for a medical device from abroad is that it is more difficult to inspect the various elements of the long and complex supply chain. For example, a company that has received GMP certification to supply APIs from a stringent regulatory authority may also purchase APIs from other manufacturers who have not been certified. Furthermore, the large number of parties who may be involved in API production can result in a situation where manufacturing sites change, thus creating risks for process and method transfer-related issues.

(e) Substandard and spurious/falsely-labelled/falsified/counterfeit medical products: a global concern

The steady increase in the production, sale and use of substandard and SFFC medical products poses serious public health problems. Medical products that do not meet quality standards, and contain either none or the wrong doses of active ingredients or different substances, result in therapeutic failure, exacerbation of disease, resistance to medicines and even death. Although the number of reported cases of substandard and SFFC medical products continues to rise, the exact magnitude of the problem is unknown, as the diversity of information sources makes compiling statistics a challenge.⁴⁴

(i) What are we talking about?

While the terms “spurious, falsely-labelled, falsified and counterfeit” are used in public health debates to describe the same problem of deliberately mislabelled medicines with respect to their identity and/or source, substandard medicines are medicines that do not meet the required quality standards. A brief summary of the main terms used to describe substandard and counterfeit medical products is provided in Box 4.10. While both phenomena constitute a threat to public health, it is important to distinguish between the two, as to different measures are needed and different actors need to be involved to effectively fight against them.

(ii) What is the problem?

All types of medicines, including both originator and generic products, are subject to counterfeiting – from medicines for the treatment of life-threatening conditions to inexpensive generic versions of painkillers and antihistamines. The ingredients found in such products may range from random mixtures of harmful toxic substances to inactive, ineffective preparations. Some products contain a declared,

Box 4.10. Terminology: substandard medicines and counterfeits

A multitude of terms is used in the debate on substandard and counterfeit medical products, sometimes giving different meanings to the same term. How these terms are used and defined is of particular relevance for the adoption and application of sound and acceptable measures to combat the proliferation of substandard and counterfeit medical products (Clift, 2010). In 2010, the WHO carried out a survey in 60 member states which was aimed at ascertaining information about the various terms and definitions used in these countries' respective national laws.⁴⁵ The findings showed that the legal definition of counterfeit differs widely in various national contexts.

Substandard medicines: "Substandard medicines are pharmaceutical products that fail to meet either their quality standards or their specifications, or both. Each pharmaceutical product that a manufacturer produces has to comply with quality assurance standards and specifications, at release and throughout its shelf-life, according to the requirements of the territory of use. Normally, these standards and specifications are reviewed, assessed and approved by the applicable national or regional medicines regulatory authority before the product is authorized for marketing".⁴⁶

SFFC medicines are deliberately and fraudulently mislabelled with respect to identity and/or source. The source of SFFC medicines is therefore usually unknown and their content unreliable. SFFC medicines may include products with the correct ingredients or with the wrong ingredients, without active ingredients, with insufficient or too much active ingredient, or with fake packaging.⁴⁷

The **TRIPS Agreement** defines "counterfeit" in relation to trademarks in a general manner, not specific to the public health sector. According to footnote 14(a) to Article 51 of the TRIPS Agreement: "Counterfeit trademark goods" shall mean any goods, including packaging, bearing without authorization a trademark which is identical to the trademark validly registered in respect of such goods, or which cannot be distinguished in its essential aspects from such a trademark, and which thereby infringes the rights of the owner of the trademark in question under the law of the country of importation". Counterfeiting is thus limited to goods using identical or similar trademarks without authorization of the trademark owner. It generally entails slavish copying of the protected trademark. Given the intended confusion between the genuine product and the copy, fraud is usually involved. However, the use of the term "counterfeit" in practice seems to have diverged from this narrow meaning in a number of WTO members, where it encompasses other forms and categories of IPR infringement.

active ingredient and look so similar to the genuine product that they deceive health professionals as well as patients. Substandard and SFFC products are always illegal.⁴⁸

The nature of the problem of substandard and SFFC products is different in different settings. In some countries, especially in developed countries, expensive hormones, steroids, anticancer medicines and lifestyle drugs account for the majority of products sold – often by way of Internet-based transactions. In other countries, SFFC products often relate to inexpensive medicines, including generic medicines.

In developing countries, the most disturbing trend is the prevalence of substandard and SFFC medical products for the treatment of life-threatening conditions such as malaria, TB and HIV/AIDS (see Box 4.11 for the quality of antimalarials in sub-Saharan African countries). Experience has shown that vulnerable patient groups who pay for medicines out of their own pockets are often the most affected by the negative impacts of substandard and SFFC products (WHO, 2011h).

Substandard and SFFC medicines are found everywhere in the world, but are typically a much greater problem in regions where regulatory and enforcement systems for medicines are weakest. In industrialized countries with

effective regulatory systems and market control, the incidence of these medicines is very low – less than one per cent of market value, according to the estimates of the countries concerned.⁴⁹

The prime motivation for the production and distribution of substandard and SFFC medical products is the potentially huge profits. A number of factors favour their production and circulation, including:

- a lack of equitable access to and affordability of essential medicines
- the presence of outlets for unregulated medicines
- a lack of appropriate legislation
- absence or weakness of national medicines regulatory authorities
- inadequate enforcement of existing legislation
- complex supply chains
- weak criminal sanctions (WHO, 2011h).

(iii) *How to combat substandard and SFFC medical products?*

Combating substandard and SFFC medical products forms part of the work of regulatory agencies, but other law enforcement agencies are also involved in this area (see

Box 4.11. WHO survey of the quality of selected antimalarials in six countries in sub-Saharan Africa

The six countries involved in this WHO survey (Cameroon, Ethiopia, Ghana, Kenya, Nigeria and Tanzania) have been supported in the past by the WHO with specific measures designed to strengthen their regulatory controls over antimalarial products. Of the 267 samples fully tested, 28.5 per cent failed to comply with specifications. This is a high failure rate, and it suggests a problem in the quality of antimalarials present in distribution channels. The complexity of markets – and the number of products from different manufacturers available in these markets – seems to be one of the factors contributing to making medicines regulation more difficult and increasing the possibility of consumers obtaining access to substandard medicines on the market.

When failure rates in imported products and locally manufactured products were compared, higher failure rates were found among locally manufactured products. This may be due to different regulatory standards for locally manufactured medicines and imported medicines. The total failure rate of samples of WHO-pre-qualified medicines collected from all six countries involved in the survey was very low – below 4 per cent, emphasizing the importance of the normative role of the WHO in medicines regulation and the importance of its pre-qualification mechanism for quality assurance of procured medicines (WHO, 2011b).

Chapter II, Section B.1(f)). In most countries, regulatory authorities can take measures against substandard and SFFC medicines and their manufacturers. In the case of substandard medicines, the identity of the producer is known and the problem lies in non-compliance with GMP standards. Counterfeiters, on the other hand, usually work in unauthorized settings with the intention of hiding their identity. This means that enforcement measures taken by national and regional regulatory procedures may be only partially successful. Thus, the standard regulatory approach for legally manufactured but substandard medicines cannot be successful on its own. To effectively combat SFFC medicines, other measures such as border controls and criminal prosecution need to play a greater role. In addition, measures need to be adapted to the situation in each individual country. Border controls may be effective if products are imported. They are particularly relevant because, increasingly, substandard and SFFC medicines are imported. In countries where SFFC products are manufactured locally, the emphasis needs to be placed on identifying and prosecuting the local manufacturers of these products. There is, therefore, a need for collaboration both at national and international level between various government institutions, including legislative bodies, relevant enforcement agencies and the courts (WHO, 2011h).

At the international level, the problem of SFFC medicines was first addressed in 1985 at the Conference of Experts on the Rational Use of Drugs in Nairobi. The meeting recommended that the WHO, together with other international organizations and NGOs, study the feasibility of setting up a clearing house to collect data and inform governments about the nature and extent of counterfeiting. In 1988, WHO member states requested the WHO to initiate programmes for the prevention and detection of the export, import and smuggling of SFFC pharmaceutical preparations.⁵⁰ The rapid spread of SFFC medicines in many national distribution channels, coupled with increasing trade and sales via the Internet, finally led

to the establishment of the International Medical Products Anti-Counterfeiting Taskforce (IMPACT) in 2006. IMPACT was established to raise awareness, exchange information, encourage cooperation and provide assistance on issues related to counterfeit medicines and involved international organizations, NGOs, enforcement agencies, drug regulatory authorities and pharmaceutical manufacturers. The set of draft principles and elements for national legislation against counterfeit medical products produced by IMPACT was further developed in 2007 and addressed definitional issues, responsibilities of public-sector and private-sector stakeholders, and sanctions.⁵¹

The detention of in-transit generic medicines by European custom authorities (see Section C later in this chapter) and criticism regarding the involvement of the pharmaceutical industry and other stakeholders such as INTERPOL with IMPACT triggered an intense debate. This focused on the relationship between combating substandard and SFFC medical products from a public health perspective, the enforcement of IPRs and the role that the WHO should play, or not play, including its role in IMPACT. To respond to concerns raised, the World Health Assembly (WHA) in 2010 convened a working group comprising representatives of member states. The working group was, among others, mandated to examine: the role of the WHO in ensuring the availability of good-quality, safe, efficacious and affordable medicines, and to examine its relationship with IMPACT and its role in the prevention and control of substandard and SFFC medical products. The mandate stipulated that these issues should be examined from a public health perspective, explicitly excluding trade and IP considerations.⁵² In May 2012, the WHA established a new voluntary member state-driven mechanism aimed at preventing and controlling substandard and SFFC medical products and associated activities from a public health perspective, excluding trade and IP considerations.⁵³ The mechanism will regularly report to the WHA on its progress and on any recommendations arising out of its work.

(f) Other regulatory determinants that impact access

Besides the fragmentation of the supply chain and the globalization of the pharmaceutical manufacturing processes and substandard and SFFC products, many other challenges have an impact on the functioning of the regulatory systems, including:

- lack of political support coupled with regulatory authorities' inadequate human and financial resources
- lack of effective collaboration and lack of trust in other regulatory authorities' decisions, including a trend

towards duplicative inspections of production facilities and assessments, which create limited added value

- focus on regulating products without effective oversight of the supply chain
- poorly developed systems for monitoring products safety after marketing authorization
- double standards whereby, for example, locally manufactured products are not required to meet the same standards as imported products (see Box 4.1.1).

All these challenges put regulatory systems under strain and impact the steady supply of quality medicines and other regulated medical products.

C. IP-related determinants of access

Key points

- The mere existence of intellectual property rights (IPRs) on a product is not a barrier to, nor its absence a guarantee of, access to that product. The impact of IPRs on access to medical technologies depends on how they are regulated nationally, and how they are managed by the right holder.
- WTO members have the flexibility to design their national intellectual property (IP) systems within the minimum standards set by the TRIPS Agreement, in cognizance of a country's economic, developmental and other objectives, including public health.
- Defining patentability criteria and their application in practice may have a considerable impact on access to medical technologies.
- Substantive examination and opposition procedures can help to address the problem of erroneously granted patents. This has implications for market entry by generic producers.
- The regulatory review exception allows potential competitors to complete the marketing approval process during the patent term, in order to enable early market entry of generic medicines upon expiry of the patent.
- WTO members are free to determine the grounds for granting compulsory licences. Such grounds can include public interest in general and are not limited to public health emergencies.
- Compulsory licences and government-use authorizations have been used to import cheaper generic medicines or to produce them locally.
- In 2003, WTO members agreed to introduce a new flexibility into the TRIPS Agreement. The flexibility, known as the Paragraph 6 System, is designed to enhance access to medicines by removing a potential barrier for countries that need to import medicines.
- While the reasons for the limited use of the Paragraph 6 System are still under consideration, it could be more widely used in the future, for example, following the introduction of the product patent regime in key potential exporting countries, or in the case of a pandemic or some other health security event where effective treatments may be patented in all major supplier countries.
- Under the TRIPS Agreement, WTO members are free to determine their exhaustion regime. An international exhaustion regime allows the parallel importation of patented medical products.
- Some countries allow the patent term to be extended, upon request of the patent holder to compensate for regulatory and other delays. Different views have been expressed about the impact of such extensions on public health.
- Companies increasingly use voluntary licences as part of their corporate social responsibility programmes, especially in the area of HIV/AIDS. This trend has been reinforced by the creation of the Medicines Patent Pool.
- The most common provisions in free trade agreements (FTA) that affect the pharmaceutical sector are definition of patentability criteria, patent term extensions, test data protection, linkage of regulatory approval with patents and enforcement of IPRs, including border measures. Such provisions can delay market entry of generics and increase prices of medicines.

This section focuses on the IP-related determinants for improving access. It builds on the overview of the IP system and policy discussed in Chapter II, Section B.1, and focuses on its impact on access to medical technologies. In contrast, Chapter III, section D, considers the IP system from the perspective of innovation.

IP law and its practical implementation interact with access to technologies in a complex manner. For example, a finished medical product typically combines numerous inputs and innovations, some of which may be

protected by IPRs, potentially held by different parties. The mere existence of an IPR cannot create a barrier to a protected product or technology, but neither does its absence serve as a guarantee of access to the protected product or technology. Much depends on: how the acquisition, maintenance and enforcement of IPRs are regulated under the applicable national law; how such law is applied in practice; where IPRs are applied for; for how long the IPRs are exercised; who holds the IPR; and how the IPR holders choose to exercise – or not to exercise – their rights.

The current international IP regime – as defined by the TRIPS Agreement, the respective WIPO treaties and a number of regional agreements – sets minimum standards of IP protection. However, it gives countries responsibility for designing their national IP systems within the confines of these international laws while also taking into account different considerations such as the stage of their social, economic and cultural development, as well as specific interests and needs, including in the area of public health. The public policy options and other options afforded to members under the TRIPS Agreement are commonly referred to as “flexibilities”. This chapter categorizes and sets out these flexibilities and other IP-related determinants of access in pre-grant and post-grant stages.

1. Determinants of access prior to patent grant

Pre-grant patent issues essentially relate to questions such as what is considered patentable subject matter, what subject matter is specifically excluded, and how specific criteria for patentability are defined and applied by patent offices. Both the rules regarding patentability, and how they are applied in practice, ultimately determine the boundaries of a right to exclude others from using protected inventions and thus can have considerable (but not always decisive) impact on access to that technology. Erroneously granted patents potentially impede access and possibly impede further research, and are not in the public interest. Detailed explanations on patentability criteria (patentable subject matter, novelty, inventive step/obviousness, industrial applicability/usefulness and disclosure) are provided in Chapter II, Section B.1(b)(iii). The following, while not exhaustive, describes a number of particular issues which are relevant for access to medical technologies. Issues relating to the patenting of first and second medical indications of known products are discussed in Chapter III, Section D.3(b).

(a) Diagnostic, surgical or therapeutic methods for the treatment of humans or animals

Diagnostic, surgical or therapeutic methods for the treatment of humans or animals are often excluded from patentability (consistent with the optional exclusion provided for in Article 27.3(a) of the TRIPS Agreement). Where such exclusion occurs, it typically derives from concerns that a doctor should be free to apply the method of treatment that best suits a patient, without having to secure approval from a patent holder. A judgment in the United Kingdom explains the reason for the exclusion as “merely to keep patent law from interfering directly with what the doctor actually does to the patient”.⁵⁴ Some laws expressly clarify that this exclusion does not apply to any apparatus or product (such as medical devices) that may be used for the purpose of diagnosis, surgery or therapy. In some countries, inventions concerning diagnostic, surgical or therapeutic methods for the treatment of humans or animals are not patentable because they are not regarded as inventions that meet the requirement of industrial applicability.⁵⁵ In some other countries, patents on such methods of medical treatment are not enforceable.

(b) Patent examination and patent registration

From the perspective of access to medical technologies, it is important to be aware of the changes that are typically made during the patent examination and grant procedure and, therefore, clearly differentiate patent claims made in the published patent application from claims contained in the patent as granted. There is no guarantee that an application will mature into a patent, and any claims in an issued patent may be much narrower than what was originally sought. Only the claims as granted determine the legal scope of the right (for guidelines for the examination of pharmaceutical patents see Box 4.12).

Box 4.12. Guidelines for the examination of pharmaceutical patents: developing a public health perspective

In order to support the examiners' work, and also ensure that all patentability criteria are met, many patent authorities have established search and examination guidelines which describe in detail the application of patent law to particular circumstances. WIPO has published a collection of links to the guidelines produced by a range of patent offices.⁵⁶ In addition, the International Bureau of WIPO, following consultations with the International Searching and Preliminary Examining Authorities under the Patent Cooperation Treaty (PCT), published the PCT International Search and Preliminary Examination Guidelines.⁵⁷

The International Centre for Trade and Sustainable Development (ICTSD), the WHO and the United Nations Conference on Trade and Development (UNCTAD) have published guidelines for the examination of pharmaceutical patents. The guidelines are intended to be a contribution towards the improvement of transparency and efficiency of patentability examination for pharmaceutical inventions, particularly in developing countries (ICTSD/UNCTAD/WHO, 2007).

To obtain information about the grant, the validity of the patent, as well as the eventual scope of patent protection, it is necessary to review the patent itself and its legal status, including whether a patent has been amended or corrected, or whether a patent has lapsed due to non-payment of maintenance fees. This needs to be done for every jurisdiction, since considerable variation may exist. Further, some claims may have been rejected by one patent office, but may have been granted by another. Such variations in the scope of patents within a patent family are especially likely to occur between jurisdictions that provide for substantive examination as jurisdictions that only provide for registration to later judicial proceedings, if any, the question of patent scope or validity.

(c) Patent quality

Errors can occur in patent grant and administration. Such errors can be burdensome for rights holders, third parties and the patent administration. To ensure that patent procedures meet the required standards and deliver high-quality results, many patent offices around the world have introduced quality management measures. Such systems measure outputs aimed at promoting higher quality standards and continued patent system improvements.

Quality management measures comprise certain general principles: a patent office should be clear about its functions and provide the necessary resources (staff, premises, equipment and training) to deliver its functions effectively; procedures should be properly documented and feedback mechanisms (internal and external customer communication) should be provided to identify problems and opportunities so that procedures could be improved to avoid recurrence of problems; staff responsibilities should be clear and, to the extent possible, objectives should be measurable; regular and comprehensive quality reviews should be carried out.⁵⁸ For example, at the international level, the PCT Common Quality Framework for International Search and Preliminary Examination, which is set out in Chapter 21 of the PCT International Search and Preliminary Guidelines, requires International Authorities under the PCT to establish quality management systems containing certain features which are important for ensuring effective search and examination according to the requirements of the PCT. The quality reports are published on a dedicated website.⁵⁹ In the WIPO Standing Committee on the Law of Patents, member states are currently discussing the issue of quality of patents.⁶⁰

2. Pre-grant and post-grant review procedures

Depending on national rules, third parties often have the option of filing oppositions against a patent either before or after the grant, or of filing observations during the

patent examination process. India, for example, provides both a pre-grant and a post-grant opposition system. The character of both examination and opposition procedures have an impact on what types of inventions are ultimately patented, and thus can be decisive in relation to short-term market entry by generic producers.

Opposition proceedings are designed to ensure that patents are not granted on claimed inventions that do not satisfy the patentability requirements. For example, an opponent might submit prior art documents showing that the key features of the claimed invention had already been publicly disclosed.⁶¹ Opposition procedures are thus a tool that can contribute to higher quality of patents and legal certainty. However, few patents are opposed, and oppositions tend to involve commercially more significant patents. For example, in 2009 the European Patent Office (EPO) reported a rate of opposition proceedings of 5.2 per cent.⁶²

Some countries provide a re-examination mechanism which allows a patent application or a patent to be re-examined in the light of new prior art. In countries where a patent application is published before a patent grant, third parties can analyse the claimed invention before the patent office makes a decision. In some of these countries, third parties may submit prior art relevant to the patentability of the claimed invention without participating in the subsequent procedure.

Similarly, many patent laws allow decisions of a patent office to grant a patent to be challenged by a third party, within a certain period of time, before an administrative review body, such as an appeal board in a patent office.

Erroneously granted patents can lead to delayed entry of generic versions, thus negatively impacting access to medicines. They can also become problematic with regard to patent linkage, for instance, when the grant of marketing approval for medicines is linked with patent status. The regulatory agency may refuse to register generic products based on the existence of patents that should not have been granted in the first place.

The European Commission Pharmaceutical Sector Inquiry report highlighted the importance of opposition procedures in the pharmaceutical area. Before the EPO, the opposition rate was much higher for the pharmaceutical sector than for organic chemistry. While generic companies almost exclusively opposed secondary patents (i.e. patents on improvements or on related aspects of a drug as opposed to the basic molecule itself), they prevailed in approximately 60 per cent of final decisions rendered by the EPO, including the Boards of Appeal, between 2000 and 2007. In an additional 15 per cent of cases, the scope of the patent opposed was restricted. On average, these procedures took more than two years. The report stated that litigation could be seen as an efficient means of creating obstacles for generic companies.⁶³ Any revocation or restriction of secondary patents may considerably affect the legal certainty regarding the validity of the patents.

The majority of interested parties in an opposition proceeding are rival companies, but they may also include patient organizations, public health groups and individuals, among others. As an instance of a challenge by a commercial rival in 2009, the Indian Patent Office upheld a pre-grant opposition filed by a generic drug manufacturer concerning a patent application for crystalline adefovirdipivovil, a treatment for hepatitis B. It was decided that the claimed invention lacked an inventive step and the patent application was rejected.⁶⁴

3. Post-grant determinants of access

A number of important determinants of access to medical technologies relate to the management of patent rights post grant. They include the regulatory review exception, compulsory licensing and government use, parallel imports, and IPR enforcement. In relation to the issue of management of patent rights by rights holders, this section also analyses recent licence agreements in the area of HIV/AIDS.

(a) Exceptions and limitations to patent rights

This section describes certain exceptions and limitations to patent rights that provide safeguards for access to medical technologies. While exceptions for regulatory review purposes, compulsory licences and government use have a direct bearing on access to medical products and are discussed below, research exceptions relate to innovation and are therefore discussed in Chapter III, Section D.4(b).

(i) *Regulatory review (“Bolar”) exception*

During the process of obtaining marketing authorization, the applicant has to produce a first batch of the product, which may be considered an infringement of a related patent. Because regulatory approval may take several years, the inability to use the patented invention during the approval process, prior to patent expiration, would delay market entry of generic versions.

The regulatory review exception mitigates this situation by, in general, entitling anyone to use a patented invention during the patent term without the consent of the patent holder for the purposes of developing information to obtain marketing approval.⁶⁵ This exception thus favours market entry by competitors immediately after the end of the patent term, and is, therefore, an instrument that is specifically designed to ensure early access to generic medicines.

The panel in the WTO case of *Canada – Pharmaceutical patents* of 2000 found that Canada’s regulatory review exception was permitted by Article 30 of the TRIPS

Agreement, which allows limited exceptions to patent rights, subject to certain conditions.⁶⁶ A 2010 WIPO report identified that 48 countries provide for such an exception.⁶⁷ The report maps the different approaches taken by countries in the national implementation of this important policy tool within patent laws. Developed and developing countries alike have tended to follow the Canadian form of an exception that was confirmed as being permitted under WTO rules. This exception extends to activities seeking product approvals under foreign as well as domestic regulatory procedures. Other countries consider that their general research exception is broad enough to cover use of a patent for the purposes of regulatory review, and some laws expressly state this.

The scope of the regulatory review exception varies among countries. In some countries, it applies to any patented product that requires regulatory review; in others, it applies only to pharmaceuticals or medicinal products. In some countries, it applies to all applications for marketing approval; in others, it applies only to certain types of applications, such as those based on bioequivalence data. In some countries, it applies only to regulatory review in the country where the competitor will use the patented invention to prepare its submission; in others, it applies to regulatory review in any country. The range of covered activities can vary, for example, with respect to experimental use other than for purposes of regulatory review.

(ii) *Compulsory licensing and government use*

Compulsory licensing allows the exploitation of a patent during the patent term without the consent of the patent holder, but with the authorization of competent national authorities. This authorization may be given to a third party, or, in the case of government use, to a government agency or to a third party authorized to act on the government’s behalf. The term “compulsory licensing” is often used to refer to both forms of authorization, although they can have important operational distinctions.

Compulsory licences

Some possible grounds for compulsory licensing are suggested in Article 5A of the Paris Convention (e.g. abuse of patent rights, including failure of the patent holder to work the invention) and in Article 31 of the TRIPS Agreement (e.g. national emergency and public non-commercial use). However, this list is not exhaustive. The Doha Declaration on the TRIPS Agreement and Public Health (discussed below) confirmed what was already implicit in the TRIPS Agreement – that WTO members have the freedom to determine the grounds upon which compulsory licences are granted. They are thus not limited to emergencies or other urgent situations, as is sometimes mistakenly believed. A range of grounds have been set out in national laws. Most of these grounds can be grouped as follows:

- **Non-working or insufficient working:** Many countries provide that where a patentee fails to work a patent in its jurisdiction, or where such working by the patentee is insufficient, a compulsory licence may be granted, provided that all other requirements are met. Some national laws simply state that if a patentee is not working the invention, or is not sufficiently working the invention without any legitimate justification, a third party may request a compulsory licence. In some countries, the laws provide detailed provisions clarifying the circumstances that may be applicable. Such clarifications include the types of activities by the patentee that are considered as “working”, in particular, whether importation of the patented invention is considered as “working” in the country or not,⁶⁸ and the situations under which working by the patentee is not considered “sufficient”.
- **Anti-competitive practices:** Some countries provide specific provisions under the patent law that allow the granting of a compulsory licence, in order to remedy an anti-competitive practice engaged in by the patentee. In certain countries, such as the United States, such a remedy is regulated in the competition (antitrust) law, under which compulsory licences may be granted by a competition authority (e.g. the US Federal Trade Commission) where it finds that it is an appropriate remedial action against an adjudicated anti-competitive practice.
- **Public interest:** Many countries allow the granting of compulsory licences on grounds of public interest, without further defining the term. Others mention specific grounds, in particular, national emergencies and circumstances of extreme urgency, national security and public health in general. However, a national emergency or extreme urgency is not a pre-requisite requirement for a compulsory licence under the TRIPS Agreement. Public interest could also include the non-availability of the patented product, such that reasonable needs of the public are not being met. In some cases, the laws refer to more specific health-related situations, such as a compulsory licence on a patent relating to diagnostics, or on a patent concerning a biotechnological research tool. Health-specific grounds can, for example, be found in France and Morocco. Under provisions on the *licence d’office dans l’intérêt de la santé publique*, the health minister can seek the grant of a compulsory licence if the product or method is made available by the right holder in insufficient quantity or unsatisfactory quality, or if the prices charged are abnormally high.⁶⁹
- **Dependent and blocking patents:** Many countries provide for the possibility of requesting a compulsory licence where a patent (second or “dependent” patent) cannot be exploited without infringing another patent (first or “blocking” patent). Article 31(l) of the TRIPS Agreement provides that such compulsory licences can only be granted if the second invention is an important technical advance of considerable economic

significance and that, where a compulsory licence is granted to the holder of a second (dependent) patent to use a first (blocking) patent, the holder of the first patent shall also have a right to a cross-licence to use the second patent.

Government use

A number of national laws explicitly entitles the government, or a third party authorized by the government, to use a patented invention without authorization of the patent holder. The grounds may vary but typically relate to public policy objectives such as national security or health. A specific authorization may be needed to use a patented technology, or the legal system may limit the scope of remedies that are available when a patent is infringed in the performance of a task authorized by the government.⁷⁰

TRIPS requirements for compulsory licences and government use

The requirement that prior efforts be made to negotiate a voluntary licence for a reasonable period of time has been interpreted in different ways in national laws. The requirement to negotiate may be waived in situations of national emergency, in other circumstances of extreme urgency, or in cases of public non-commercial use (Article 31(b)). In cases where the use of the patent is authorized without the consent of the patent holder to remedy adjudicated cases of anti-competitive practices, WTO members are not obliged to apply these conditions. In such cases, the licence need not be predominantly for the supply of the domestic market (thus allowing exports of unlimited quantities) and the amount of remuneration can be different (i.e. it would generally be a lesser amount or even none at all).

The limitation of compulsory licences and government use to predominantly supply the domestic market, found in Article 31(f) of the TRIPS Agreement, was revised following the Doha Declaration to allow production under a compulsory licence exclusively for export under certain terms and conditions. In effect, Article 31(f) limits the quantity that could normally be exported under a standard compulsory licence, which was identified as a potential problem for countries that had insufficient manufacturing capacity or no domestic manufacturing capacity, and therefore wished to import such products. The response to this problem is discussed in Section 3(a)(iii) below on the Paragraph 6 System.

Country experiences and practices

Compulsory licences have not been limited in practice to address infectious diseases or public health emergencies. In early 2012, based on a request under Section 84 of the Indian Patents Act, an Indian generic company obtained a compulsory licence for sorafenib, a treatment for liver and kidney cancer because the Indian Controller of Patents

considered, among others, that it was not available at an affordable price.⁷¹ Between 2006 and 2008, Thailand declared government use for a number of pharmaceutical products, including for clopidogrel (a drug used to treat heart disease), letrozole (a breast cancer drug), docetaxel (a breast and lung cancer drug) and erlotinib (a drug used for treating lung, pancreatic and ovarian cancer).

In 2007, after protracted negotiations with the patent owning companies, the Brazilian government issued a compulsory licence for efavirenz, an important ARV drug used by a third of Brazilians receiving treatment through a national programme. Less than two months after the compulsory licence was issued, the first shipment of generic efavirenz was received from India, where there was no patent on this product. Brazil reported to the TRIPS Council that it had taken two years to locally produce the medicine, partly because the patent law does not require applicants to disclose all information necessary for the commercialization of an end product.⁷² After the licence was issued, the price dropped from US\$ 1.59 per dose for the originator product to US\$ 0.43 per dose for the imported generic version of the drug.⁷³ It is estimated that the Brazilian government's policies, including the use

of TRIPS flexibilities, saved approximately US\$ 1.2 billion on ARV drug purchasing costs between 2001 and 2005 (Nunn et al., 2007).

Several other developing countries have granted government-use authorisations to make available patented ARVs where the originator's price was considered too high or where only limited amounts of the drug were accessible to the population – for example, Malaysia in 2002 and Thailand in 2006-2008 (see Box 4.13). Since 2010, Ecuador has issued two compulsory licences for public non-commercial use with respect to medicines used to treat HIV/AIDS (Box 4.14).

After earlier compulsory licences granted in 2004 and 2007 by the government of Indonesia, the presidential decree of 3 September 2012 subjected seven HIV/AIDS and hepatitis B medicines on the Indonesian market to a government use order until expiry of the relevant patents. Under this order, the pharmaceutical industry has been appointed as the patent exploiter for and on behalf of the government. The decision is based on the urgent need to control HIV/AIDS and hepatitis B in Indonesia.⁷⁴

Box 4.13. Government use of patents: the Thai example

Thailand has authorized government use of patents on several pharmaceutical products used to treat HIV/AIDS, heart attacks, strokes and cancer. The first case concerned efavirenz. In 2005, more than half a million Thai citizens were HIV positive. Although the Thai government had made a commitment in 2003 to provide free ARV treatment to all who needed it, the cost of doing so rose significantly when newer, better and more expensive treatments became available. In November 2006, the Thai Ministry of Public Health issued a decree that it would use the patent rights relating to efavirenz and it authorized the state-owned Government Pharmaceutical Organization (GPO) to import or produce efavirenz under which the patent holder was entitled to receive a royalty of US\$ 0.5 per cent of GPO's total sales value.

Following the declaration of government use for the ARV treatment lopinavir/ritonavir in 2008, the number of patients in Thailand using lopinavir/ritonavir has reportedly increased from 39 to 6,246.⁷⁵ In February 2007, the patent holder announced a global price reduction on efavirenz, benefiting HIV/AIDS patients around the world.

Box 4.14. Public non-commercial use: the example of Ecuador

Ecuador's IP authority granted a compulsory licence to a pharmaceutical distributor with operations in Ecuador. The compulsory licence, granted in April 2010, covers a patent relating to the active ingredient ritonavir, which is a retroviral protease inhibiting compound used for the treatment of HIV/AIDS. The licence covered all the patent rights, including importation, and was limited to use in Ecuador. The licence was reportedly intended for public non-commercial use (Article 31b of the TRIPS Agreement). The Ecuadorian authorities informed the patent owner before they granted the compulsory licence. The licence is valid until the date on which the patent expires in 2014. The licensee is required to pay the patent owner adequate remuneration calculated according to the Tiered Royalty Method, which was based on a royalty of five per cent of the price of the patent owner's product in the United States, adjusted for the difference in gross domestic product per capita between the United States and Ecuador per cent, yielding a royalty rate of US\$ 0.42 per cent of the United States price. The procedure for the grant of the compulsory licence took six months to complete.⁷⁶ In November 2012, Ecuador's Institute of Intellectual Property granted a second compulsory licence for public non-commercial use on another HIV/AIDS medicine (abacavir/lamivudine) to a local manufacturer, expecting thus to achieve a price reduction of 75 per cent.⁷⁷

Government use declarations are also often used in the context of international procurement by UNICEF or other international bodies to enable the import of generic medicines, especially ARV medicines.⁷⁸

Practical experiences show that the bargaining power created by just the legal possibility of a compulsory licence can benefit developing countries even where a compulsory licence is not actually granted (Cornish, 2003). For example, the Brazilian government has demonstrated that legislation which provides for the effective and expeditious use of compulsory licences can be a useful asset in negotiating lower prices for ARV drugs (Abbott and Reichman, 2007). Using the threat of compulsory licensing, the Brazilian government negotiated significant price reductions on efavirenz and nelfinavir in 2001, lopinavir in 2003, the combination of lopinavir and ritonavir in 2005, and tenofovir in 2006.

That said, the use of compulsory licences in the field of medical technical technologies is not limited to developing countries. In developed countries, compulsory licences have been granted, among other reasons, in order to remedy anti-competitive practices that are having an impact on access and innovation in the field of medical technology. In 2002, for example, the US Federal Trade Commission (FTC) ordered a compulsory cross-licence of a patent on tumour necrosis factor to a Swiss company. This gave the licensee freedom to practice the invention in the research, development, manufacture, use, import, export, distribution and sale of the patented product. The licence permitted the Swiss company to compete with a US patent owner. In 2005 and 2007, the Italian Competition Authority investigated abuses of dominant position by two large pharmaceutical companies which refused to license rights to their pharmaceutical products. The result was that royalty-free compulsory licences were issued, with the expectation that the resulting generics would be exported to other European countries where the patents concerned had already expired.⁷⁹ On the other hand, in September 2012, the Italian Administrative Court granted the appeal against a January 2012 decision by the Competition Authority which had fined a pharmaceutical company for exclusionary abuse of dominant position. The Court highlighted that the simple enforcement of exclusive IPRs was not sufficient to support Competition Authority's finding of an abuse of a dominant position.⁸⁰

(iii) *The Paragraph 6 System: an additional flexibility aimed at enhancing access to medicines*

A new pathway for access to medicines ...

Paragraph 6 of the Doha Declaration mandated the TRIPS Council to find a solution to the difficulties faced by countries with insufficient or no manufacturing capacities in the pharmaceutical sector in making effective use of compulsory licensing. This resulted in the 2003 WTO

General Council decision to establish the framework for special compulsory licences, which is an additional flexibility aimed at enabling exports of medicines to these countries. The System – informally dubbed the “Paragraph 6 System” – initially took the form of a waiver of certain conditions regarding compulsory licences. In 2005 WTO members adopted it by consensus as the Protocol Amending the TRIPS Agreement. This outcome, providing an additional legal pathway for access to medicines, has special significance as the sole amendment proposed to any of the WTO multilateral trade agreements since their adoption in 1994. The System has already been available for use since the 2003 waiver decision and will become a permanent feature of the TRIPS Agreement once two thirds of WTO members formally notify their acceptance. A wide cross-section of the WTO membership has already taken this step, with many notices of acceptance received from developing countries, including several LDCs, and virtually all developed countries.⁸¹ Accepting the Protocol is distinct from incorporating the System into national law or choosing to make use of the System. It expresses legal consent that all WTO members should be permitted to use this additional flexibility if they so choose.

Intended by WTO members to contribute to global efforts to strengthen the legal framework for access to medicines, the new System has been endorsed in a number of multilateral forums:

- The 2008 WHO Global Strategy and Plan of Action on Public Health, Innovation and Intellectual Property (GSPA-PHI) identified the use of the System as a specific action.
- The Ministerial Declaration – 2009 High-Level Segment of the Economic and Social Council of the United Nations reaffirmed the right to use the Paragraph 6 System, encouraging the provision of assistance to developing countries in this regard. It expressly called for a broad and timely acceptance of the TRIPS amendment.
- Similarly, the 2011 UN Political Declaration on HIV/AIDS: Intensifying our Efforts to Eliminate HIV/AIDS called for early acceptance of the TRIPS amendment.
- The 2012 Declaration “The future we want”, an outcome document from the United Nations Conference on Sustainable Development (“Rio+20”), reaffirmed the right to use the System along with other TRIPS provisions.

... that addresses a particular procurement scenario.

The System applies in a particular access scenario where an importing country needs medicines to deal with a public health problem, but a potential exporting country faces a legal impediment because Article 31(f) of the TRIPS Agreement limits supply under a compulsory licence predominantly to the domestic market. The special

export licence under the System is free of this constraint, enabling and indeed requiring the full production under a compulsory licence to be exported. Accordingly, the situation addressed by the System would arise only when a country wishes to obtain a particular pharmaceutical product, and:

- The product cannot be produced domestically at all, or in sufficient quantities, due to lack of capacity.
- The preferred producer of the particular product (normally, the cheapest supply that best meets regulatory and quality requirements) is located in a country where a patent is in force on that product and needs a compulsory licence in that country to produce for export.

The System does not apply to most procurement scenarios: for example, when affordable supplies are already available from countries where no patent is in force (this has been the experience with older ARV treatments for HIV/AIDS, the bulk of which have been imported at highly competitive prices by countries from generic producers in India (see Chapter IV, Section A.2(a), on HIV/AIDS); and when prices for the originator product can be reduced

through negotiation to an affordable level without recourse to a compulsory licence, or when the originator company agrees to grant a voluntary licence to a generic producer.

How has it been used in practice ...

By 2012, one special export licence under the System has been exercised. In that instance, the licence was used by a Canadian company to ship medicines to Rwanda (see Box 4.15). Ghana reportedly considered using the System in 2005 when it declared an emergency situation with regard to HIV/AIDS and granted a government use authorization order to import generic HIV/AIDS medicines (although a declaration of emergency is not a requirement for using the System).⁸² Imports were initially intended to be sourced from Canada, where the products were patented, but Ghana later chose to import the products from generic manufacturers in India, where no patent applied. Another potential use⁸³ concerned an Indian company's applications, filed in September 2007 with the Indian patent office, to manufacture and export to Nepal several anti-cancer pharmaceuticals patented in India, including erlotinib. Reportedly, the applicant later withdrew the applications. As an LDC, Nepal was automatically entitled to use the System, but it had not

Box 4.15. Case study on supply of ARVs to Rwanda

In 2004, Médecins Sans Frontières (MSF) approached a Canadian company to produce a triple-combination ARV (zidovudine, lamivudine and nevirapine). MSF initiated this move in the absence of any specific request from an importing country. The company obtained marketing approval in Canada in 2006, less than six months after the date of its application. Canada's Access to Medicines Regime (CAMR), which implements the Paragraph 6 System, had to be amended to cover the product because Canada limits the scope of its law to a specified list of products. The three medicines combined in the product were each covered by a separate patent owned by a separate company. In July 2007, the company sought, without success, voluntary licences from the three patent holders.

In July 2007, Rwanda sent the WTO a brief notification of its intention to import 260,000 packs of the triple-combination ARV, reserving the right to modify the estimated quantity. It said it would not allow patent holders to enforce any patents on the product that may have been granted in its territory. As an LDC, Rwanda was not obliged to state anything else, nor did it need to notify its intention to use the System.⁸⁴ In September 2007, the company applied for a compulsory licence in Canada which, under the System, would allow it to export 15,600,000 tablets (the equivalent of 260,000 packs) over a two-year period. The compulsory licence was granted two weeks later. The Canadian government notified the WTO in October that it was using the System as an exporting country.⁸⁵

Canada reported that in October 2007 the Rwandan government issued a public tender for this triple-combination ARV.⁸⁶ The Canadian company had originally offered its ARV at the no-profit price of US\$ 0.39 per tablet. There were indications that at least four Indian generic manufacturers could supply the product at a lower price. Canada reported that if Rwanda had procured the ARVs from these manufacturers, it would not have needed to use the System at all, since the products were not patented in India. However, during the tender process, the Canadian company halved its price to US\$ 0.195 per tablet. In May 2008, the company announced that it had won the tender.

In line with the terms of the CAMR and the System itself, the tablets shipped to Rwanda were distinguished from the version manufactured for the domestic market by the mark "XCL" and white colouring, instead of the standard blue. The packaging bore an export tracking number issued by the Canadian government. Details of the product and its distinguishing characteristics, as well as details of the shipment, were posted on the web.⁸⁷ A royalty was payable by the Canadian company for the right to use the patent, but the patent holders waived payment. A total of 6,785,000 tablets were shipped to Rwanda in September 2008, and an additional 7,628,000 tablets were shipped in September 2009, i.e. within the two-year validity period of the compulsory licence.⁸⁸

notified the WTO that it wished to import these medicines which is a prerequisite for the use of the System.

... and is it really working as expected?

The TRIPS Council reviews the System each year and reports to the WTO General Council on how the System has been implemented and used, its operational context, and the status of the TRIPS amendment. The discussions have become more detailed since 2010, after Canada and Rwanda used the System, and they now also cover a wider range of issues such as the operational requirements of the System and alternatives to ensure access to medicines. While no firm conclusions have been reached as a result of these discussions, various WTO members have voiced a range of views (WTO, 2010; WTO, 2011), including the following diverse observations on whether the System is fulfilling its intended function:

- By 2012, the System was only used once, and it took three years before the shipments in question proceeded. The System is too complex and administratively unwieldy for further use, and a multi-stakeholder workshop is needed in order to discuss the operation of the System. It is essential to clarify whether constraints on its use were built into the System, thus necessitating its reform, or whether such constraints were a consequence of how individual countries chose to implement it.
- Potential users of the System may be deterred by concerns about political or trade ramifications associated with the use of compulsory licensing.
- The CAMR was successfully utilized, and only a very small portion of the three-year time period was taken up with procedures associated with the System. Much of the time that elapsed between the regulatory review of the medicine in question and the actual shipments was attributable to other factors.
- The limited use of the System is not an appropriate measure of its success, as no delegation demonstrated evidence of obstacles to its use when such use was required. A single case demonstrated that the System could work when necessary, and that it could play a supportive role in the wider effort to improve access to essential medicines, given that alternative ways of procuring the needed medicines are often available.
- The System is not a panacea to solve all public health-related problems. Rather, it is part of a broader picture which includes other important aspects that have an impact on innovation and access, such as infrastructure, tariffs, innovative financing mechanisms, partnerships and cooperation (including at the regional level), and regulatory frameworks.
- Implementation of full patent protection for pharmaceutical products in India, coupled with the approaching expiry of transition periods in LDCs, could make it more difficult in the future to procure generic versions of new medicines. Under such circumstances,

the Paragraph 6 System might assume a greater significance.

... while its full operational context is still being mapped ...

While the System provides an avenue to respond to demand for medicines in a specific procurement scenario, there has been negligible notification of demand from potential beneficiaries who are faced with this particular scenario. This is against a backdrop of widespread expressions of concern about affordable access to medicines. No developing country has notified the WTO that it has a general intention to use the System, although LDCs need not take this step and other countries could also do so at the same time they notify details of the needed product. Countries are entitled to notify their expected needs for medicines at an early stage in the procurement planning process, without having to give a commitment to adhere to the quantities notified or commit to proceed with imports under the System should preferable alternatives arise even at a late stage in the procurement process. In cases where the product needed is patented in the preferred supplying country(ies) – for example, where generic companies have the ability to copy the product, and where importing countries' combined effective demand is sufficient – such early notification may increase the practical likelihood of potential exporters responding to the opportunity to use the System.

One key question is whether, and, if so, in what circumstances, the particular "Paragraph 6" scenario has so far arisen in practice. A further question concerns the extent to which affordable medicines are already available without the need for compulsory licences for export. Reported procurement experiences suggest that many medicines were already available as generic exports from countries where no patent was in force. For example, Brazil, Ecuador and Thailand reportedly issued compulsory licences for the importation of products outside the System from countries where the products were not patented and were already in production as generics. Rwanda's use of the System also took place against a background of lower generic prices being available from other sources. Where generic medicines are available from non-patented sources, the System does not need to be used. This situation may change in future as the progressive impact of changes to pharmaceutical patentability in key export countries such as India makes it less likely that newer generations of medicines will be so readily available in generic versions for export (see Chapter IV, Section A.2(a)). In the future – for example, in response to a pandemic or some other health security event – effective treatments are more likely to be patented in established major supplier countries. In such a scenario, the System could well assume greater importance and be used more extensively. The availability of the System provides a more credible basis for effective use of compulsory licensing for countries with either no production capacity or limited

capacity, thus strengthening their hand in negotiations on price. Past experience with procurement processes (such as Brazil's threat to use compulsory licensing for the ARV drug nelfinavir in 2001) shows how effective use of compulsory licensing can succeed in inducing lower prices without the actual final grant of a licence. The limited role of the System thus far may also partly be due to the fact that many countries procure needed medicines through international procurement programmes which may have other means of leveraging lower prices. Examples of such programmes include those run by PEPFAR, the CHAI, the Global Fund, UNICEF and UNITAID.

One area of current debate centres on the necessity to establish an adequate commercial basis for potential suppliers under the System, in order to respond to needs that have been signalled in notifications to the WTO. The System expressly recognizes the need for economies of scale in the context of its provisions on regional trade agreements, also referring to the possibility for parties to such agreements to make joint notifications.

The special export licence is one legal pathway that can be followed when it represents the optimal route to effective procurement, but, as for any compulsory licence, it does not in itself make the production of a medicine economically viable. Sufficient scale and predictability of demand are prerequisites for making it practically and commercially viable for companies to undertake the regulatory, industrial and commercial steps required to produce and export a medicine under such a licence. Regional approaches to procurement and joint notifications by countries with similar needs for accessible medicines may offer pathways to aggregating demand under the System, thus enabling an effective response to the needs identified.

The System includes measures to ensure that products reach their intended beneficiaries and are not diverted elsewhere. Such measures may include specific labelling or marking, special packaging and/or special colouring/shaping of the products, but these ways of distinguishing products should be feasible and should not have a significant impact on price. Recent industry experience with other forms of labelling and packaging for specific markets, for example in cases of tiered pricing, donation and philanthropic procurement schemes,⁸⁹ may provide practical examples for how to distinguish products without incurring significant costs. Annex II provides more detailed information on the operation and use of the System.

(b) Voluntary and socially responsible licences

An owner of a patent can share IP voluntarily with third parties through licensing agreements. A licence is a contract in which the patent holder allows another party to use the IP, either in return for a payment of royalties (or some other consideration) or free of charge, for a

certain field of use, in a certain territory (which may be for the life of the patent). In the framework of their corporate responsibility programmes, research-based pharmaceutical companies have in the years since the adoption of the Doha Declaration increasingly used licence agreements to allow generic producers to manufacture and distribute generic versions of their products within a defined geographical area.

(i) *Voluntary licence agreements in the area of HIV/AIDS*

Today, most companies that own IPRs covering products for the treatment of HIV/AIDS have signed licence or immunity-from-suit agreements with various generic producers, or have issued non-assert declarations on their HIV/AIDS products. Often, these agreements are referred to as "voluntary" licence agreements, as opposed to compulsory licences (for an overview of current agreements, see the list by Beyer, 2012).

Companies began to use this type of voluntary licence agreements to a greater extent after the adoption of the Doha Declaration. Initially, the scope and territory were rather limited, and some of the agreements were triggered by interventions from third parties.

The trend to license HIV/AIDS products to generic companies has further increased with the creation of the Medicines Patent Pool in 2010. The Pool has so far entered into two licence agreements. The first is with the National Institutes of Health in the United States and covers a patent on darunavir. The second is with Gilead, a US-based biopharmaceutical company and covers patents on another ARV, tenofovir, the co-formulation with emtricitabine, as well as on elvitegravir, cobicistat and their combination with tenofovir and emtricitabine. By 2012, the Pool had signed sub-licence agreements with four Indian generic companies for the manufacturing of all or some of these products. Some of these companies did not sign the agreement for tenofovir, given that in 2009 a patent application for tenofovir was rejected in India.⁹⁰

Companies have further extended licensing programmes to include newer products and pipeline products. While initial agreements had a very limited scope and were predominantly focused on sub-Saharan Africa and LDCs, countries in which patents are often not granted or, if granted, not enforced, some companies have now expanded the geographical coverage to include more middle-income countries, and covering up to 112 countries (Beyer, 2012).⁹¹

Licensing practices have also come under scrutiny. One of the issues highlighted is that the geographical scope is limited and excludes most middle-income countries. The licence agreement signed by the Medicines Patent Pool with Gilead has led to a vigorous debate among public health groups about the added value of this agreement

and role and mandate of the Medicines Patent Pool in that regard.⁹²

Overall, it is very difficult to assess these licensing agreements, given that the terms and conditions are not disclosed, with the notable exception of agreements signed by the Medicines Patent Pool. Basically, with these licence agreements, the licensors allow others to serve the high-volume, low-profit markets in poor countries with a high disease burden of HIV/AIDS (LDCs, sub-Saharan Africa and low-income countries).

Licence agreements could potentially become a more important factor in HIV/AIDS medicines production in the near future. Agreements, if they are signed with multiple companies, can contribute to improved access to medicines through increased competition, which, in turn, leads to lower prices and increased availability of ARV treatments in developing countries. License agreements are also one of the main indicators in used by the Access to Medicines Foundation in their ranking of pharmaceutical companies, see Box 4.16. In discussions about supporting the use of voluntary licences in the future, it has been suggested that guidance should be made available to developing countries. Such guidance would set out what needs to be covered in voluntary licensing agreements and it could also possible include model contracts.⁹³

(ii) *Socially responsible licensing*

Research institutions in the United States have been allowed to patent and license these patents that arise from research funded by federal grants since the passing of the Bayh–Doyle Act in 1980. This legislation has spurred discussions about how licensing policies of universities should recognize public health goals. For example, a debate arose concerning patents held by Yale University over stavudine, a substance that had been synthesized in 1966 and discovered to have reverse transcriptase inhibitor properties by researchers at Yale in the early 1990s. This research was supported by federal grants. The university had exclusively licensed

production, marketing and distribution to a company which sponsored Phase III clinical trials of the drug.⁹⁴ Although the university had not applied for patents in most developing countries, stavudine was patented in South Africa (Patent ZA8707171).⁹⁵ When Médecins Sans Frontières (MSF) began providing antiretroviral treatment in South Africa, the drug was being sold at prices that were 34 times higher than generic versions available in other countries.⁹⁶ In December 2000, MSF approached the South African division of the licensee company for permission to import generic stavudine, but were advised to approach the patent holder, Yale University. Under pressure from civil society, the student body, research communities and the inventor of stavudine in March 2001, the license agreement was revised and the company reached an immunity-from-suit agreement with a generic drugs company in South Africa allowing the marketing of stavudine in South Africa and other African countries (t Hoen, 2009; Beyer, 2012).

Against the background of this debate, a new model of so-called “socially responsible licensing” has arisen, by which new IP-protected technologies can be used and accessed at affordable prices in underserved communities. For instance, in 2002, Eva Harris of the University of California, Berkeley, sought a licensing agreement for a portable diagnostic tool for dengue fever. She proposed a licensing agreement to the university, whereby it would license production and distribution rights to a non-profit organization, which in turn would provide the tool free or at cost, while preserving the university’s right to earn royalties from “derivative technologies distributed in developed countries” (Mohiuddin and Imtiazuddin, 2007). Socially responsible licensing is thus another tool that can contribute to enhancing access to medical technologies in developing countries.

(c) Exhaustion of rights and parallel imports

Parallel imports refer to genuine products first put on the market in another country and imported through a channel parallel to the one authorized by the right holder. Parallel

Box 4.16. Access to Medicine Index

The Access to Medicine Foundation (AMF) is an international non-profit organization dedicated to improving access to medicine. The AMF publishes the Access to Medicine Index, which ranks pharmaceutical companies according to their strategic and technical efforts to enhance global access to medicine. The aim is to develop a transparent means by which pharmaceutical companies can assess, monitor and improve their own performance and their public and investment profiles while building a platform on which all stakeholders can share best practices in the area of global access to medicine.

The Index ranks 20 pharmaceutical companies on their efforts to provide access to medicines, vaccines and diagnostic tests to people living in 103 countries. The Index for 2012 covered 33 priority diseases, including neglected tropical diseases, the ten most important communicable diseases and the ten most important non-communicable diseases in terms of their health burden on the countries included in the Index as well as maternal health and neonatal infections. Rankings are based on a large number of indicators that measure activities across areas, such as R&D, patent policy, pricing and philanthropy. It provides reports on each company’s leading practices and the changes the company has made since publication of the previous Index report. The reports also suggest areas for improvement.⁹⁷

imports are not counterfeit, and the right holder has had the opportunity to receive payment for the first sale. They are sometimes referred to as “grey market goods” – in other words, they are not black market goods, but neither have they been imported through a channel authorized by the right holder.

“Exhaustion” is a legal doctrine according to which the IP right holder cannot prevent the further distribution or resale of goods after consenting to the first sale. In such a situation, the right holder is considered to have “exhausted” its rights over these goods (the exhaustion doctrine is also known as the “first sale doctrine”). The exhaustion doctrine plays a role in enabling access to medicines, as the decision by a country to adopt international, regional or national exhaustion is an important factor in determining whether medical products can be imported (or re-imported) from other countries where prices are lower. Other important factors impacting parallel importation are the rules regarding the regulatory approval regime and private law governing the contract between the manufacturer and its distributors. In case of abuse of IPRs, competition law can also serve as a useful corrective tool.

Countries have employed several options in regulating the exhaustion regime so as best to serve their domestic policy objectives.

(i) International exhaustion

Some countries apply a regime of “international exhaustion”, meaning that IPRs over goods are exhausted after the first sale by or with the consent of a right holder located anywhere in the world. As of 2010, 20 countries have adopted a regime of international exhaustion of patent rights in their domestic laws: these include Argentina, China, Costa Rica, Egypt, India, Kenya and South Africa, as well as the parties to the Cartagena Agreement (the Plurinational State of Bolivia, Colombia, Ecuador and Peru).⁹⁸ In 2002, the UK Commission on Intellectual Property Rights report recommended the adoption of an international exhaustion regime in order to facilitate access to medicines for developing countries and LDCs. The report also noted, however, that establishing a differential pricing system with low prices in developing countries and higher prices in developed countries required that markets with different price levels had to be segmented so that low-priced medicines could not enter higher priced markets.⁹⁹

Later, in 2006, a report by the WHO Commission on Public Health, Innovation and Intellectual Property Rights (CPIH) also called for a differentiation between developed countries and developing countries, recommending that developing countries should maintain their ability to parallel import from other developing countries (WHO, 2006b).

Many countries do not specify rules on exhaustion in their IP laws, rather, they leave it to the courts and administrative

practice. In many cases, different exhaustion regimes apply to patents, trademarks and copyright.

(ii) National exhaustion

Other countries apply the exhaustion doctrine with respect to IPRs, but only to the extent that the first sale takes place within their own territory. This is called “national exhaustion”. Under this regime, the rights of the IP owner are exhausted, but only with respect to goods that have been put on the market in the country with the right holder’s consent, thus enabling the right holder to prevent parallel importation. A total of 40 countries have opted for this type of exhaustion for patents. Such countries include Brazil, Ghana, Madagascar, Malaysia, Mexico, Morocco, Mozambique, Namibia, Thailand, Tunisia, Turkey and Uganda.¹⁰⁰

(iii) Regional exhaustion

A third option is “regional exhaustion”. The first sale of goods in the region by the right holder (or a sale made with his consent) exhausts any IPRs over those products – not only domestically, but within the entire region – and therefore parallel imports within the region cannot be opposed, based on IPRs.¹⁰¹ This is the case, for example, in EU member states and those of the EEA, in African Intellectual Property Organization member states and in Eurasian Patent Organization member states.¹⁰² At the same time, the right holder can still use his IPRs in order to prevent goods from being imported from outside the region in question.

(iv) Policy options for exhaustion regimes

Article 6 of the TRIPS Agreement provides that “nothing in this Agreement shall be used to address the issue of exhaustion of intellectual property rights” for the purposes of WTO dispute settlement, as long as the doctrine is applied in a way that does not discriminate according to the nationality of the right holder. The Doha Declaration clarified that the effect of this provision is to leave each WTO member free to establish its own regime for exhaustion without challenge, subject to the non-discrimination provisions aforementioned. This clarification is reflected in the different choices that members throughout the world have made with respect to exhaustion.

Some countries have adopted specific exhaustion regimes. For example, Rwanda adopted the Law on the Protection of Intellectual Property in 2009 (Law No. 31/2009) which provides for a system of national exhaustion of patent rights with the possibility of international exhaustion for specific products. Article 40 empowers the Minister to declare patent rights exhausted on the advice of a government agency or upon request of an interested party. The law lists several grounds on which such an authorization can be given and provides that the authorization can be revoked if

Box 4.17. Patent term extension: the example of Atorvastatin calcium

Atorvastatin calcium is a medication for the treatment of high cholesterol. The product was approved by the US Food and Drug Administration in December 1996 and was first marketed in 1997. It became one of the best-selling drugs in history. One of the United States patents on this medicine (No. 4,681,893), granted in 1987, had originally been set to expire in May 2006 but was extended by more than three years to September 2009 under a patent term extension provision (35 U.S.C. § 156). The exclusivity period of the basic patent was extended for an additional six months, to March 2010, under a paediatric exclusivity provision.

the parallel importer fails to fulfil the purpose of the Minister's declaration, or if the conditions that gave rise to the declaration cease to exist.

The choice of the exhaustion regime is, of course, only one of the factors determining whether parallel imports can take place. Another important aspect is the contract concluded between the right holder and the distributor. For example, if such a contract prohibits the distributor from re-exporting the goods concerned, the right holder could argue that engaging in parallel importing constitutes an act violating the distributor's contractual obligations, independently of whether his IPRs are exhausted or not. Some FTAs explicitly preserve for the patent owner the right to contractually limit parallel imports. In such situations, competition law can play an important role as a potential correcting factor. For example, Switzerland applies international exhaustion in the field of trademarks. In a recent competition law case in that country, a Swiss company was shown to have continuously applied a contractual clause until 2006 as part of a licence to an Austrian-based firm. This clause prohibited the licensee from exporting to Switzerland the products it had manufactured in Austria under licence. In 2009, the Swiss Competition Commission imposed a fine on the company, as it considered that such a clause constituted a vertical agreement which would significantly affect competition on the Swiss market and, therefore, struck down the clause, thus permitting parallel imports.¹⁰³

Another important factor that determines whether parallel imports can take place is the set of health regulations for market approval of medicines. Any country may prohibit parallel imports of different versions of the same pharmaceutical product if those versions lack marketing approval in the country of importation – even if the country embraces an international exhaustion regime.

(d) Patent term extension

National laws set out the period of time during which the patent can remain in force (the "patent term"). The term of protection available must not end before the expiration of a period of 20 years, counted from the filing date of the patent application. This rule is set out in Article 33 of the TRIPS Agreement and was applied in the WTO case of *Canada – Term of Patent Protection* in 2000.¹⁰⁴

A patent will lose effect before the end of the available term, for example, if it is invalidated, or if the patent holder ceases payment of required maintenance fees. However, patents relating to commercially successful pharmaceutical products are likely to be maintained for the full available term.

A number of WTO members, such as Australia, the European Union, Israel, Japan, the Republic of Korea and the United States, make available an extension of the patent term beyond the minimum of 20 years required by the TRIPS Agreement, generally to compensate for regulatory delays. This is because, unlike products in most other fields of technology, pharmaceutical products must undergo regulatory review in order to ensure safety and efficacy. The regulatory review process can considerably curtail the market exclusivity period that holders of pharmaceutical patents would otherwise enjoy.

For example, the United States provides for patent term extensions of up to five years, subject to a 14-year ceiling on the total market exclusivity period (the period after the market authorization until patent expiry) (see Box 4.17). Based on Regulation (EC) No 469/2009,¹⁰⁵ EU member states make available supplementary protection certificates (SPCs) for up to five years, subject to a 15-year limit on the total market exclusivity period after the marketing approval of the product. Since 2007, the European Union has also allowed for six-month extensions of SPCs in return for the completion of clinical studies of a product's effectiveness and safety in children.

In addition to serving as compensation for lengthy marketing approval procedures, patent term extensions are also made available by certain countries in order to compensate the right holder for any unreasonable curtailment of the patent term as a result of processing delays in the patent office. Patent term extension is also a standard feature in bilateral FTAs.

Many different views have been expressed about the impact of patent term extensions on public health. Some argue that such extensions hinder access to medicines because they delay the market entry of generic medicines. Others are of the view that extensions are favourable from a public health perspective because they support medical innovation and thus improve access to health in the long run.

(e) Enforcement of IP

An overview of IP enforcement standards is set out in Chapter II, Section B.1(f). This section looks at issues of enforcement that are specifically linked to access to medicines (see Box 4.17).

In the area of cross-border trade in medical products, public health and free trade interests intersect. The common objective is to ensure that free trade in legitimate medical products, including generic medicines, is not subject to unnecessary legal barriers to prevent movements of medicines between countries. This common objective is also reflected as a general principle in the enforcement section of the TRIPS Agreement (Article 41.1).

In 2009, Brazil and India, supported by a number of other developing countries, focused the international community's attention on the subject and expressed strong concerns at WHO and WTO meetings¹⁰⁶ about the detention of in-transit generic medicines by customs authorities at different EU ports on the basis of Council Regulation (EC) No 1383/2003.¹⁰⁷ The regulation allows customs authorities to detain goods suspected of infringing IPRs in the European Union. Since 2003, this has also included goods in transit which are suspected of infringing patents. In 2008, customs authorities in the Netherlands detained 17 consignments of generic medicines, reportedly on the grounds of alleged infringement of one or more patents which were valid and enforceable in the Netherlands. Of these 17 consignments, 16 originated in India and one in China. The majority of the consignments were in transit, destined for developing countries in Latin America and Africa. Included in one of these consignments was a hypertension drug, destined for Brazil. In 2009, German customs authorities detained a generic antibiotic shipped from India to Vanuatu through Frankfurt Airport for alleged trademark violation. In the reported cases, there was no suggestion that the medicines were infringing any IPRs in the countries of origin or countries of destination. The in-transit generics were therefore legitimate in the countries of origin and in the countries of destination. The consignments concerned were subsequently released.

In May 2010, Brazil and India initiated WTO dispute settlement proceedings by requesting consultations with the European Union on its customs measures. Among other things, Brazil and India claimed violation of the General Agreement on Tariffs and Trade (GATT) obligation to allow freedom of transit, as well as various provisions of the TRIPS Agreement on patent rights and enforcement.¹⁰⁸ In earlier TRIPS Council discussions, the European Union had concurred with the claimants that customs action should not affect legitimate trade in generic medicines. On the other hand, it defended its

regulation as being fully TRIPS-compliant, arguing that it was important for customs authorities to be allowed to control in-transit medicines, as this could help save patients' lives in developing countries. So far, further action in the WTO case has not been pursued and there has been no request for a WTO dispute settlement panel to be established.

In July 2011, the Indian government announced that India and the European Union had reached an informal settlement of the dispute ("Understanding") to guide border enforcement of IP in the European Union based on the principles agreed in the Understanding which are due to be reflected in the draft regulation to replace Regulation No. 1383/2003.¹⁰⁹

In the interim, the European Commission has issued "Guidelines concerning the enforcement by EU Customs authorities of IPRs with regards to goods, in particular medicines, in transit through the EU".¹¹⁰ These guidelines clarify the application of Council Regulation No 1383/2003 and take account of the findings in a European Court of Justice judgment of 1 December 2011.¹¹¹ In particular, the guidelines lay down the understanding that the mere fact that medicines are transiting through the EU territory and are subject to a patent rights in the European Union "does not in itself constitute enough grounds for customs authorities to suspect that those medicines are infringing patent rights". However, a substantial likelihood of diversion of such medicines onto the EU market "may constitute enough grounds for customs authorities to suspect that the medicines at stake infringe patent rights".

Taking into account the discussion about the detention of in-transit generic medicines, Switzerland also clarified that, under the Swiss Federal Act on Patents for Inventions, customs authorities may only prohibit the transit of patent-infringing goods if the right holder presents direct evidence concerning infringement of a patent in both Switzerland and in the country of destination.¹¹² These issues also came up in ACTA negotiations (see Box 4.18).

It is therefore important to ensure that enforcement provisions in trade agreements and trade rules do not create unnecessary barriers to legitimate trade in generic medicines. For this purpose, there is clearly a need to distinguish between counterfeit and generic medicines, in order to avoid definitional issues becoming a *de facto* barrier to access to generic medicines (definitional issues are also discussed in Chapter IV, Section B.7(e)(ii)). As the review of Kenya's 2008 Anti-Counterfeit Act has demonstrated (see Box 4.19), separating counterfeit from generic medicines has been an issue in the process of drafting national legislation (see Box 4.18). There has also been a trend in recent FTAs to include provisions on IPR enforcement (see Section 5 below).

Box 4.18. The Anti-Counterfeiting Trade Agreement

The Anti-Counterfeiting Trade Agreement (ACTA) constitutes another example of a proposed international instrument which has been the subject of substantive discussions on the potential impact of IP enforcement measures on access to medicines. Following two separate initiatives by Japan and the United States, a group of like-minded countries negotiated the ACTA, from 2007 to 2010. The ACTA aims to build on existing international rules in the area of IP, in particular on the TRIPS Agreement, and is intended to address a number of enforcement issues where participants identified perceived gaps in international legal framework.

According to the participants in the negotiations, the ACTA aims to:

- establish a state-of-the-art legal framework of enforcement measures to effectively respond to the growing phenomena of counterfeiting and piracy in international trade
- promote sound enforcement practices to foster the creation of additional mechanisms to combat the proliferation of illicit products
- ensure cooperation among the parties to address the challenges of cross-border trade in counterfeit and pirated goods.¹¹³

While WTO members are free to agree on higher standards, as long as those standards respect the provisions of the TRIPS Agreement (Article 1.1), the impact of higher enforcement standards under ACTA on trade in legitimate pharmaceutical products was extensively discussed at a number of TRIPS Council meetings. Concerns were voiced about ACTA's potential to negate decisions taken multilaterally, such as the Doha Declaration on the TRIPS Agreement and Public Health, as well as to deny the benefits of access to medicines under the Paragraph 6 System.¹¹⁴ Participants in the ACTA negotiations emphasized that these concerns had been addressed in the final version of the agreement which, among others, recognized the principles set out in the Doha Declaration. The ACTA does not provide for border measures to apply to products infringing patents and preserved the optional application of border measures to goods in transit. The ACTA text was circulated as a TRIPS Council document in October 2011.¹¹⁵

The Agreement has triggered an intense debate in many countries about, among others, its impact on access to medicines. As of December 2012, the number of countries which have ratified the agreement was not sufficient for it to enter into force.

Box 4.19. Drawing a line between counterfeit and generic products: Kenya's High Court ruling

In April 2012, the High Court of Kenya considered that the definition of "anti-counterfeit" in the country's 2008 Anti-Counterfeit Act was too ambiguous, as it failed to clearly distinguish between counterfeit and generic medicines, thus carrying the risk of adversely affecting access to generic medicines. The Court therefore ruled that the relevant passages of the Act could infringe the fundamental right to health guaranteed under Kenya's constitution and requested the State to reconsider the provisions concerned.¹¹⁶ Similar issues have been raised, among others, with respect to Uganda's draft Anti-Counterfeit Bill, Tanzania's 2008 Merchandise Marks Regulations, and the East African Community Anti-Counterfeiting Policy and Bill which was proposed in 2010.

4. Patent information and its relationship with public health policy

Access to patent information is an area of increasing importance for the procurement of medical products.¹¹⁷ When making procurement decisions relating to the purchasing of the best-priced quality products, procurement agencies may also need to consider the patent status of the products and the legal status of these patents in specific markets.

The joint technical symposium entitled "Access to Medicines, Patent Information and Freedom to Operate", held in February 2011, reviewed the linkages between

the patent information system and a range of policy questions associated with access and innovation in the field of public health.¹¹⁸

The symposium discussion on the need to make better use of patent information to support public health initiatives resulted in the following observations:

- Reliable domestic patent information is difficult to obtain in many countries.
- Health authorities and other stakeholders face difficulties in assessing the status of patents.
- Collaborative efforts are needed to build capacity and improve availability of data, particularly in developing countries.

- Patent information should be digitized, up to date and correct, and patent registers should be searchable online and easy to use.
- Where available, the international nonproprietary name (INN) should be submitted in patent applications, so as to aid patent searches.¹¹⁹
- Providing comprehensive patent information and enhancing access to national registers is the responsibility of national governments.
- Procurement agencies would benefit from tools to aid patent searches relating to health technologies, as well as a consultation service on how to find and interpret patent information.

Having access to complete patent information is also relevant, in order to build on the results of previous R&D – either by exploiting public domain technologies, inventing around protected technologies, or developing new technologies on the basis of public or protected technologies. Improving access to patent information related to health is also a concern of the GSPA-PHI, which addresses the need for access to user-friendly global databases containing public information on the administrative status of health-related patents. The WIPO Development Agenda, the work of the WIPO Committee on Development and Intellectual Property, the development and maintenance of WIPO Standards, the International Patent Classification,¹²⁰ as well as the establishment of Technology and Innovation Support Centers¹²¹ also aim to make patent information easier to obtain and to use.

5. Review of IP provisions in recent FTAs

Since the entry into force of the TRIPS Agreement, the number of FTAs containing provisions on IP protection and enforcement has increased. Some merely reaffirm the principles of the TRIPS Agreement, requiring adequate and effective protection of IP in accordance with the minimum standards set down in that agreement. There has been a recent trend for certain FTAs, in particular those involving developed countries, to require the parties to implement more extensive protection and enforcement of IPRs than provided for under the TRIPS Agreement. These higher and additional IP standards are often referred to as “TRIPS-plus” (see Chapter II, Section B.1(a)). While Article 1.1 of the TRIPS Agreement expressly allows WTO members to implement in their law more extensive protection than is required by the TRIPS Agreement, such protection must not contravene the provisions of that agreement, including its non-discrimination provisions. Such provisions generally require the parties to an FTA to extend the application of any higher standards to nationals of all other WTO members (as explained in Chapter II, Section B.5(b)).

This section provides an overview of the standards set down in certain FTAs that are of particular relevance to the pharmaceutical sector. For a broader overview, see Valdés and Tavengwa (2012). It also provides an overview of studies that have attempted to estimate the potential economic impact of these standards. It summarizes the approach adopted in a number of FTAs, and the role played by international organizations. Finally, it considers the potential implications for access to medical technologies. However, the focus on FTAs does not mean that no other types of agreements contain provisions which have a potential impact on the pharmaceutical sector. Such provisions may also be encompassed in bilateral investment treaties or specialized IPR agreements, for example, the ACTA, which represents a recent example of a plurilateral agreement dealing only with IPR enforcement (see Chapter IV, Section C.3(e)).

(a) Provisions affecting the pharmaceutical sector

The most common features found in virtually all FTAs are obligations to accede to a range of WIPO conventions and treaties, for example, the PCT, the Patent Law Treaty or the Trademark Law Treaty. FTAs also oblige signatories to respect TRIPS Agreement standards, in particular its principles of non-discrimination (national treatment and most-favoured-nation treatment). In addition, certain standards found in FTAs which relate to patent and test data protection, as well as IPR enforcement more generally, are particularly relevant to pharmaceutical products and other medical technologies. While there is no unique approach to IP standards in FTAs, certain commonalities in terms of clarifying and increasing TRIPS Agreement standards can nevertheless be observed. Provisions in FTAs that typically affecting the pharmaceutical sector cover (but are not necessarily limited to) one or more of the following subjects.

(i) Patentability

FTA provisions often cover various aspects of patentability. First, certain FTA standards do not provide for certain possible exclusions from patentability permitted under TRIPS, for example, by expressly preserving the patentability of plants and animals. Second, with regard to patentability criteria, a number of FTAs specify how some or all of the criteria (novelty, inventive step, industrial applicability), as well as the requirement of sufficient disclosure, are to be applied. Some FTAs expressly provide that patents must be available for a known product if a new use can be determined and the general patentability criteria are met in this respect.

(ii) Patent term extension

Certain FTAs require that an extension of the 20-year term of patent protection established by the TRIPS Agreement be available for pharmaceutical products to compensate the patent owner for any unreasonable curtailment of the

patent term as a result of the marketing approval process, or as a result of processing delays in the patent office.

(iii) Grounds for granting compulsory licences

While the TRIPS Agreement does not establish an exhaustive list of grounds for granting compulsory licences, certain FTAs limit such grounds to remedies under competition law, situations of extreme urgency and public non-commercial use.

(iv) Exhaustion

Under the TRIPS Agreement, as confirmed by the Doha Declaration, WTO members are free to choose the exhaustion regime that best meets to their domestic policy objectives (see Chapter IV, Section C.3(b)). However, the standards set by some FTAs specifically provide for the right of a patent owner to limit parallel imports through contracts.

(v) Test data protection

While Article 39.3 of the TRIPS Agreement requires countries to protect undisclosed test data against unfair commercial use, it does not specify the manner or duration of such protection (see Chapter II, Section B.1(c)). In contrast, some of the more recent FTAs specify that a period of exclusivity is required for the protection of such data; this is usually set at five years, but sometimes extends to eight years. During the exclusivity period, the regulatory authorities are not allowed to permit generic competitors to market the same or similar product on the basis of the approval granted to the originator company, unless the latter authorizes such reliance. In certain FTAs, data exclusivity also covers cases in which an FTA party permits the granting of a marketing approval of regulated products on the basis of an earlier marketing approval of the same or similar product in a third country. This has the effect of preventing generic companies from relying on the test data supplied by the originator company to another country's government, even if no test data have been supplied to the government of the country in which the generic company seeks to market its product. The TRIPS Agreement only requires test data protection when submission of data is mandatory.

(vi) Patent linkage

Although government authorities both may grant patents on pharmaceutical inventions and provide approval for patented pharmaceutical products for market entry, the two functions are not necessarily related. Most countries have separate agencies that grant patents (patent offices) and approve drug products and do not link these functions.

Nevertheless, it is possible to link regulatory approval, ordinarily based on safety and efficacy, to the patent status of the drug product. This so-called "patent linkage" can

take several forms. In its simplest form, linkage may involve a requirement that a patent owner simply be informed of the identity of any manufacturer seeking regulatory approval for a generic version of the originator's drug product. A stronger version of patent linkage could prohibit the granting of marketing approval for a drug product by a third party prior to the expiration (or invalidation) of a patent covering that product. An even stronger form of linkage could prohibit not only the granting of marketing approval, but also the consideration of a generic drug application during the patent period.

A number of FTAs include patent linkage provisions, such as the Colombia–Mexico FTA, the Japan–Thailand FTA, the Dominican Republic–Central America–United States FTA (CAFTA-DR), and several other FTAs to which the United States is a party.

Some stakeholders argue that patent linkage places regulatory agencies in the role of "patent enforcers", that some patent linkage provisions make no exception for generic medicines produced under compulsory licence, and that patent linkage provisions can unjustifiably extend exclusivity if the regulatory agency is unable to begin a review of the generic drug application during the patent period. On the other hand, proponents of patent linkage argue that it prevents unnecessary infringement, and increases transparency and predictability through the identification of patents relevant to each pharmaceutical product as part of the marketing approval process.

(vii) Enforcement

While enforcement standards set by FTAs are generally of broad application and are not sector-specific, a number of these standards have the potential to directly affect the pharmaceutical sector. Relevant enforcement provisions include, for example, the application of border measures to IPRs other than trademarks and copyright (for which they are already mandatory provisions under the TRIPS Agreement), as well as their application to goods in transit. In short, "border measures" allow right holders to work with customs authorities to prevent the importation of goods covered by IPRs.

(viii) Reaffirmation of TRIPS flexibilities and Doha Declaration principles

Some FTAs explicitly confirm the parties' agreement that the IPR standards set by the FTA neither affect the right of the parties to the FTA to take measures to protect public health nor their right to use the additional flexibility made available to WTO members through the Paragraph 6 System (see Chapter IV, Section C.3(iii)). For certain FTAs, this has been addressed by so-called "side letters" on public health. Other FTAs contain such provisions in the body of the agreement. Such confirmation is aimed at addressing concerns that FTA standards could limit the flexibilities available under the TRIPS Agreement and later instruments.

(b) Major players

As illustrated by Table 4.1, which lists provisions affecting the pharmaceutical sector, the FTAs which clarify or adopt higher standards of IPR protection and enforcement are clustered in and around three main geographical areas, namely the United States, the European Free Trade Association (EFTA) and the European Union:

- Since 2001, the United States has concluded 12 such FTAs with 17 countries. These agreements generally cover IPRs in a comprehensive manner, including most of the issues listed in Table 4.1.
- Since the early 1990s, the EFTA, which comprises Iceland, Lichtenstein, Norway and Switzerland, has concluded an extensive network of 24 agreements covering 33 countries and territories. As Table 4.1 shows, the majority of these agreements focus on higher standards with respect to patent term extension, test data exclusivity and enforcement measures at borders. Some other agreements are not listed in the table, because they do not contain an IPR chapter (Canada), are limited to reaffirming the TRIPS Agreement (Croatia and Mexico), or because they reiterate the commitments under international agreements, including the TRIPS Agreement, with a built-in review clause (Southern African Customs Union and Gulf Cooperation Council).
- Since the mid-1990s, the European Union has concluded a series of association, partnership

and trade agreements (see titles “European Community”, or “EC” in Table 4.1). The Stabilisation and Association Agreements (i.e. the agreements that countries enter into with a view to facilitating eventual accession to the European Union) with several central European countries aim to calibrate the level of protection to that in the Community *acquis* (i.e. the rights and obligations that EU member states share, including EU treaties and laws, declarations and resolutions, international agreements on EU affairs and the judgments given by the Court of Justice). This includes, among others, obligations to provide for patent term extension, test data exclusivity and higher enforcement standards. Most association agreements concluded with countries in the Mediterranean region, as well as the agreements with Chile, Mexico and South Africa, provide for protection in line with the “highest international standards”, without defining the precise meaning of such standards – in particular, whether the reference point is multilateral agreements (such as the TRIPS Agreement), or any standards set, for example those set down in other bilateral or regional agreements. The more recent agreements concluded with the Caribbean Forum of African, Caribbean and Pacific States (CARIFORUM) and the Republic of Korea illustrate the European Union’s new approach to the negotiation of a detailed IPR chapter, thus replacing the previously used references to “highest international standards”.

Table 4.1. Key provisions affecting the pharmaceutical sector in selected FTAs

FTA	Provision on							
	Patentability	Patent term extension	Compulsory licensing	Exhaustion	Test data exclusivity	Patent linkage	Enforcement	Side letters/ reaffirmation of Doha Declaration
EC–Turkey (1995)	Level of protection similar to common body of EU legislation and jurisprudence (<i>acquis</i>)							
EC Stabilisation and Association Agreements with FYROM (2004), Croatia (2005), Albania (2009), Montenegro (2010)	Level of protection similar to EU <i>acquis</i>							
EC Association Agreements with Algeria (2005), Israel (2000), Jordan (2002), Morocco (2000), Tunisia (1998) and Interim Agreement with Lebanon (2003)	Protection in accordance with highest international standards							
EC Association Agreement with Egypt (2004)	Protection in accordance with prevailing international standards							
EC–Chile (2003), Mexico (2000), South Africa (2000)	Protection in accordance with highest international standards							
EC–CARIFORUM (pending as of August 2012)							✓	✓
EC–Korea (provisional application as of July 2011)		✓			Five years		✓	✓

Table 4.1 (Continued)

FTA	Provision on							
	Patentability	Patent term extension	Compulsory licensing	Exhaustion	Test data exclusivity	Patent linkage	Enforcement	Side letters/ reaffirmation of Doha Declaration
EFTA–Albania (2010)		✓			Eight years		✓	
EFTA–Chile (2004)		✓			Five years			
EFTA–Colombia (2011)		✓ (optional)			Reasonable period (normally five years)			✓
EFTA–Egypt (2007)					five years			
EFTA–Hong Kong, China (pending as of August 2012)					Eight years			
EFTA–Israel (1993)	Protection of patents on a level similar to that prevailing in EFTA							
EFTA–Jordan (2002)	Protection of patents on a level similar to that prevailing in the European Patent Convention (EPC)							
EFTA–Korea (2006)		✓			Adequate number of years or financial compensation			
EFTA–Lebanon (2007)					Six years or compensation			
EFTA–Montenegro (pending)		✓			Eight years		✓	
EFTA–Morocco (1999)	Protection of patents on a level similar to that prevailing in the EPC							
EFTA–Peru (2011)		✓ (optional)			Reasonable period (normally five years)			✓
EFTA–Serbia (2010–2011)		✓			Eight years		✓	
EFTA–Singapore (2003)		✓						
EFTA–Tunisia (2005)					Five years			
EFTA–Turkey (1992)	Protection of patents on a level similar to that prevailing in the EPC							
EFTA–Ukraine (pending)		✓			Five+one years		✓	
Japan–Switzerland		✓			Six years		✓	
NAFTA (1994)					Reasonable period (normally five years)			
United States–Australia (2005)	✓	✓	✓	✓	Five years	✓	✓	
United States–Bahrain (2006)	✓	✓			Five years	✓	✓	✓
CAFTA–DR (2006–2009)	✓	✓			Five years	✓	✓	✓
United States–Chile (2004)	✓	✓			Five years	✓	✓	
United States–Colombia (pending)	✓	✓ (optional)			Reasonable period (normally five years)	✓	✓	✓
United States–Jordan (2001)		✓	✓			✓		
United States–Korea (2012)	✓	✓			Five years	✓	✓	✓
United States–Morocco (2006)	✓	✓		✓	Five years	✓	✓	✓
United States–Oman (2009)	✓	✓			Five years	✓	✓	✓
United States–Panama (2011)		✓			Reasonable period (normally five years)	✓	✓	✓
United States–Peru (2009)		✓			Reasonable period (normally five years)	✓	✓	✓
United States–Singapore (2004)		✓	✓		Five years	✓	✓	

Source: WTO Secretariat.

Note: This only reflects provisions in FTAs that set higher standards, and does not reflect those that merely reaffirm the TRIPS Agreement).

That provisions affecting the pharmaceutical sector form an integral part of most of the FTAs concluded by the United States, the European Union and EFTA reflect the fact that the United States, the European Union and Switzerland are the world's largest producers and exporters of pharmaceutical products.¹²² Provisions on patents or test data protection are comparatively rare in, or absent from, FTAs concluded without the involvement of the United States, the European Union and EFTA, and especially in cases where such agreements are concluded among developing countries only, or where they involve LDCs. In some of these FTAs, detailed provisions on patents and/or test data protection are set out, but these usually restate TRIPS Agreement standards. A notable exception is the agreement between Colombia and Mexico, which provides for data exclusivity for a period "normally" of five years.

(c) Economic impact analysis

Some studies have looked at the economic impact of the FTA IPR provisions on the pharmaceutical sector. For example, a 2009 study commissioned by the ICTSD concluded that the CAFTA-DR would lead to an annual price increase for active ingredients in Costa Rica of between 18 per cent and 40 per cent by 2030, requiring increased public spending in the range of US\$ 2 million to US\$ 3.357 million. The strongest repercussions were expected from standards on patentability criteria and standards on test data exclusivity.¹²³ A similar 2009 study for the Dominican Republic predicted a modest price increase of 9 per cent to 15 per cent for active ingredients by 2027. It found that the strongest impact by far was to be expected from provisions on data exclusivity. Interestingly, the authors also reported that information asymmetries and government policy imperfections would have a higher impact on prices than regulatory changes in the IP regime.¹²⁴ A 2012 study, prepared by two civil society organizations in Colombia, found that the introduction of data exclusivity in exchange for trade preferences in 2002, and later confirmed in the FTA negotiations, has led to an additional expenditure of US\$ 412 million.¹²⁵ Finally, a 2007 Oxfam Briefing Paper estimated that prices for medicines in Jordan had increased by 20 per cent since the conclusion of the agreement with the United States. Here again, data exclusivity was singled out for delaying the market entry of almost 80 per cent of the generic versions of newly launched medicines between 2002 and 2006, with additional expenditures for medicines estimated at between US\$ 6.3 million and US\$ 22.04 million.¹²⁶

Assessing the economic impact of specific chapters in FTAs in an isolated fashion may, however, not do justice to the overall architecture of FTAs and their resulting effects in terms of wealth creation, improved living standards, and transparent and non-discriminatory procedures leading to delivering better value for money, among other things. Impact assessments that have been prepared by parties to a particular FTA, and that cover the effects of the FTA as a whole are more common.¹²⁷

Each of the higher standards adopted in FTAs – either on its own or in conjunction with other standards – has the potential to affect both the creation of, and subsequent access to, medical technologies. Typically, it can achieve this not only by incentivizing the invention of medical technologies in the first instance, but also by delaying the arrival of generics on the market for a period of time following the initial invention. Among the factors that can delay market entry of generics are narrower interpretations of or limitations to TRIPS flexibilities than otherwise available to WTO members. The trend towards the inclusion of detailed IPR provisions continues, including in the more recent FTAs negotiated by the European Union. At the same time, the readiness to include public health safeguards in these agreements – either in an IP chapter or in side letters – has also significantly increased over the past decade.

For its part, the WTO can contribute to monitoring and awareness-raising, among other things, through the examination of notified FTAs in the Committee on Regional Trade Agreements and through the regular review of national trade policies under the Trade Policy Review Mechanism. Based on Article 63.3 of the TRIPS Agreement, WTO members can also seek access to, or information on, bilateral agreements from other WTO members.

With regard to the WHO, a number of resolutions have also been adopted which explicitly call on WHO member states to take into account the flexibilities in the TRIPS Agreement and later instruments (e.g. the Doha Declaration and the Paragraph 6 System) in trade agreements (e.g. see Element 5.2(c) of the GSPA-PHI adopted by World Health Assembly Resolution WHA 61.21, which recommends that countries take into account the impact on public health when considering adopting or implementing more extensive IP protection than is required by TRIPS).¹²⁸

D. Other trade-related determinants for improving access

Key points

- International trade is crucial to ensuring access to medicines and other medical products.
- Developing countries, least-developed countries (LDCs) and transition economies comprise 85 per cent of the world's population but account only for 30 per cent of imports and 20 per cent of exports of internationally traded health-related products.
- Developed countries have largely eliminated tariffs on health-related products, in line with a WTO agreement on pharmaceutical trade. Tariffs applied by other countries have also fallen significantly, but the picture is still mixed.
- Competition policy is relevant to all stages in the process of supplying medical technology to patients – from the development and manufacture of medical technology to its eventual sale and delivery.
- Competition policy has an important role to play in preventing collusion among suppliers of medical technology participating in procurement processes.

1. International trade and tariff data of health products

No country is entirely self-reliant for the products and equipment it needs for its public health systems – most rely heavily on imports. Trade statistics therefore provide valuable insights into the evolution of patterns on access to health-related products. The factors affecting imports influence availability as well as prices of health-related products and technologies, and thus have immediate consequences for access. Tariffs are one of the key factors influencing imports, but price and availability are also determined by non-tariff measures (e.g. licences, regulations and import formalities) and import-related costs, such as transportation. In addition, national distribution costs, such as wholesale and retail mark-ups and dispensing fees, may increase prices dramatically.

Analysing trade statistics and tariffs on health-related products is difficult in the absence of a well-defined classification of health products in WTO agreements and the Harmonized Commodity Description and Coding System (HS) of tariff nomenclature (used to monitor international trade). Many products – such as chemical ingredients – have both medical and non-medical end uses. In the absence of a precise definition, this section reviews health-related products which are identified under 207 subheadings (334 tariff lines) of the HS for 139 countries. In all, this represents a total of 50,000 tariff lines for each of the years surveyed. The main categories are in HS29 (labelled as Organic Chemicals) and in HS30 (labelled as Pharmaceutical Products). One of the limitations of the data is that they do not reflect importation and immediate re-exportation. The products are clustered in six groups (see Table 4.2). While these

Table 4.2. Public health-related products

Group	Category	Sub-category	Description	HS Headings
Group A	Pharmaceutical industry	A1 Formulations	Nine tariff subheadings covering medicaments put up in measured doses and packaged for retail sale.	Headings 3002 and 3004 of the HS nomenclature.
		A2 Bulk medicines	Six tariff subheadings covering medicaments not put up in measured doses for retail sale, i.e. sold in bulk.	Headings 3003 and 3006 of the HS nomenclature.
		A3 Inputs specific to the pharmaceutical industry	57 tariff subheadings covering inputs specific to the pharmaceutical industry, e.g. antibiotics, hormones and vitamins.	Headings 2936, 2937, 2939 and 2941 of the HS nomenclature.
Group B	Chemical inputs	B Chemical inputs of general purpose	73 tariff subheadings covering chemical inputs used by the pharmaceutical industry as well as other industries and which correspond to the WTO Pharmaceutical Tariff Elimination Agreement.	Several headings of Chapter 29 as well as headings 2842, 3203, 3204 of the HS nomenclature.
Group C	Medical equipment, other inputs	C1 Hospital and laboratory inputs	28 tariff subheadings covering bandages and syringes, gloves, laboratory glassware, diagnostic reagents, etc.	Headings 3001, 3002, 3005, 3006, 3507, 3822, 4014, 4015, 7017, and 9018 of the HS nomenclature.
		C2 Medical technology equipment	33 tariff subheadings covering medical devices used in diagnosis or treatment covering furniture, X-rays, machinery, etc.	Headings 8419, 8713, 9006, 9018, 9019, 9021, 9022 and 9402 of the HS nomenclature.

Source: WTO Secretariat.

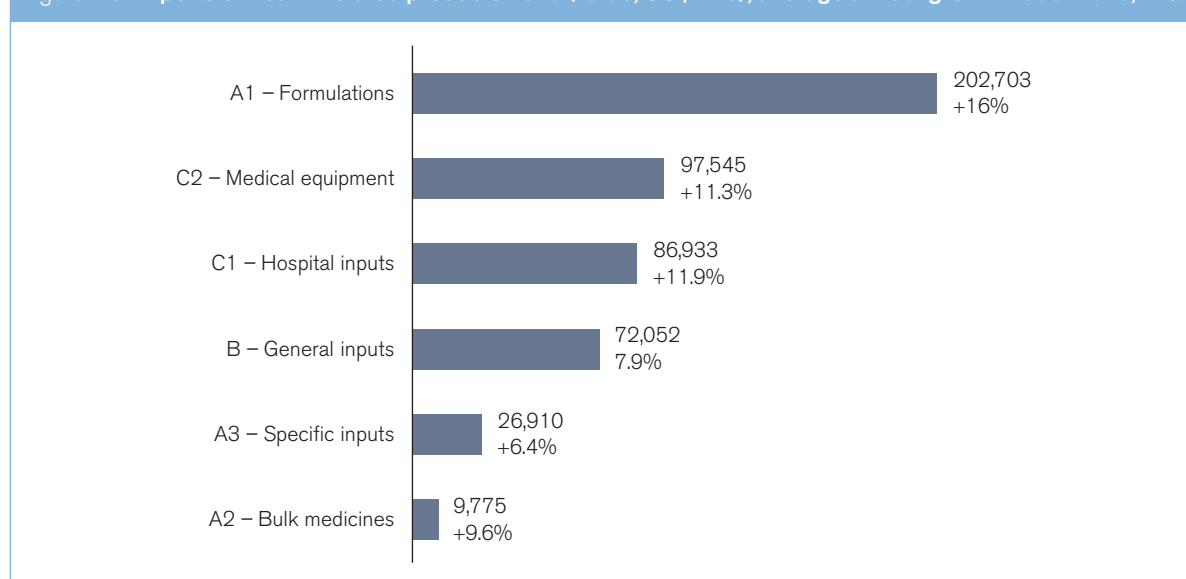
categories are not exhaustive, they provide useful insight into trade in health-related products.

(a) International trade in health-related products

International trade in the six groups of health-related products experienced very dynamic growth from 1995 to 2010, rising from US\$ 92 billion to about US\$ 500 billion. This represents an average annual rate of growth of almost 12 per cent – almost double the average growth rate of general merchandise trade.¹²⁹ In 2010, trade in health-related products accounted for approximately 4.2 per cent

of global merchandise trade. As can be seen in Figure 4.6, most of the trade in health-related products relates to formulations (Group A1), which is one of the fastest growing sectors of the health industry (average annual growth of 16 per cent since 1995), followed by trade in medical technology equipment (Group C2, average annual growth of 11.3 per cent since 1995). Medicines, in bulk and in formulations, accounted for over 60 per cent of all trade in health-related products in 2010. This trade is dominated by a small number of countries. The European Union and the United States together account for almost 50 per cent of all world imports. Overall, developed countries imported almost 70 per cent of traded health-related products (see Table 4.3). Developed countries' dominance of this trade has changed little over

Figure 4.6. Imports of health-related products 2010 (value, US\$ mio), average annual growth 1995–2010, in %



Source: COMTRADE, WTO Secretariat.

Table 4.3. International trade in health-related products: share of main importers, 2010, in %

	TOTAL	A1	A2	A3	B	C1	C2
European Union	26.3	20.8	24.4	37.8	26.4	34.9	26.9
United States	21.9	25.6	14.9	12.9	16.7	17.4	25.0
Japan	6.6	6.0	2.6	4.3	7.7	8.1	6.6
Switzerland	5.5	6.2	2.4	6.0	6.4	5.9	3.0
China	3.8	2.8	3.2	2.6	5.9	3.1	5.3
Canada	3.7	4.7	3.9	2.0	2.2	3.7	3.4
Russian Federation	3.1	4.6	2.0	0.9	0.9	2.3	3.1
Australia	2.7	3.6	1.1	1.3	1.4	1.6	3.0
Brazil	2.4	2.1	1.6	2.8	3.8	2.6	1.9
Mexico	1.9	1.6	3.1	1.7	2.5	1.8	1.9
Republic of Korea	1.8	1.3	1.9	1.7	3.7	1.5	1.9
Turkey	1.5	1.7	1.5	1.3	1.2	1.4	1.3
India	1.5	0.4	0.6	4.4	4.3	0.8	1.4

Source: COMTRADE, WTO Secretariat.

the past 15 years, possibly explained by these economies' relatively high share of private and public expenditures for health care, and their greater integration into vertical supply chains, thus boosting trade flows (see Box 4.20).

A small number of players also dominate export trade (see Table 4.4), with the United States and EU member states exporting approximately 60 per cent of traded health products, and developed countries accounting for almost 80 per cent of such products. Some variations are evident between categories. In comparison with individual EU member states, China, the fourth largest exporter of

health-related products, leads world exports in subgroup A3 (pharmaceutical inputs) and group B (chemical inputs). Some other developing countries rank higher in some categories: for example, Israel and India are significant exporters of medicines in bulk; and Mexico and Singapore are major exporters of inputs for hospitals and laboratories.

Overall, international trade has assumed increasing importance in ensuring supplies of goods required for public health, such as medicines, medical devices and other technologies. Of the 139 countries surveyed, only 24 were net exporters of health-related products in 2010.

Box 4.20. WTO "Made in the World Initiative": towards a measure of trade in value-added

The patterns of global production and trade have changed considerably, and are now based on globally integrated production chains. Manufactured products consumed all over the world are often produced within international supply chains where individual companies specialize in specific steps of the production process. Increasing numbers of products are composed of parts and components with various geographical origins, such products should be labelled "Made in the World" rather than "Made in any single country".

The trade taking place between various stakeholders in supply chains reflects their specialization in particular activities, and can thus be referred to as "Trade in tasks". The rise in global production has involved profound changes in international trade, mainly characterized by the marked increase of world trade in intermediate goods, the expansion of processing trade among developing countries and the important growth of intra-firm transactions.

Conventional trade statistics do not necessarily show the real picture of international trade in a globalized economy. For example, the "country of origin" recorded for imports of final goods is often the last country in the production chain, and this ignores the value of production from other contributors (origins). In order to provide innovative approaches to international trade statistics, the WTO launched its "Made in the World Initiative" (MIWI) in 2011. This initiative is aimed at fostering new methodologies to compile information on trade in value-added indicators. In January 2013, in the context of the MIWI, the WTO and the OECD unveiled the first set of data of trade in value-added.

Table 4.4. International trade in health-related products: share of main exporters, 2010, in %

EXPORTS	TOTAL	A1	A2	A3	B	C1	C2
European Union	38.2	20.5	43.8	24.5	25.9	30.2	31.9
United States	20.5	14.0	16.7	15.6	16.4	28.0	31.4
Switzerland	13.9	14.8	2.9	19.9	8.3	21.1	8.8
China	6.0	0.6	3.3	24.1	17.8	5.5	4.7
Japan	3.2	1.4	2.6	2.9	6.9	2.6	5.1
Singapore	3.0	2.4	0.6	3.3	6.6	2.1	2.6
India	2.6	2.8	6.5	4.2	6.3	0.4	0.5
Israel	1.8	2.9	9.7	0.2	0.9	0.2	1.3
Mexico	1.6	0.6	0.3	0.6	0.5	3.0	3.5
Canada	1.6	2.7	0.8	0.3	0.5	1.1	1.0
Australia	1.1	1.7	0.9	0.2	0.0	0.3	1.5
Republic of Korea	0.8	0.4	0.4	1.3	1.8	0.5	1.3
Hong Kong, China	0.8	0.5	6.2	0.6	0.5	0.6	1.5
Brazil	0.5	0.5	0.9	0.3	1.3	0.4	0.2

Source: COMTRADE, WTO Secretariat.

Note: Names of WTO members are those as used in the WTO.

Next to some EU member states¹³⁰ and Switzerland, the net exporters of health-related products include China, India, Israel and Singapore. The vast majority of developing countries are net importers of pharmaceutical products (see Tables 4.5 and 4.6).

Country	Value (US\$ mio)
European Union	50,272
Switzerland	18,355
Israel	4,984
India	4,839
Singapore	3,751
China	622
Jordan	241
Iceland	11

Source: WTO Secretariat.

Country	Value (US\$ mio)
United States	-25,208
Japan	-9,961
Russian Federation	-9,486
Canada	-5,302
Australia	-4,407
Brazil	-4,044
Turkey	-3,445
Saudi Arabia	-3,251
Mexico	-2,639
Venezuela, Bolivarian Rep. of	-2,256
Republic of Korea	-2,254
Ukraine	-2,088
South Africa	-1,812
Panama	-1,572
Algeria	-1,572
Thailand	-1,293
Iran	-1,279
Egypt	-900
Norway	-899
Colombia	-836

Source: WTO Secretariat.

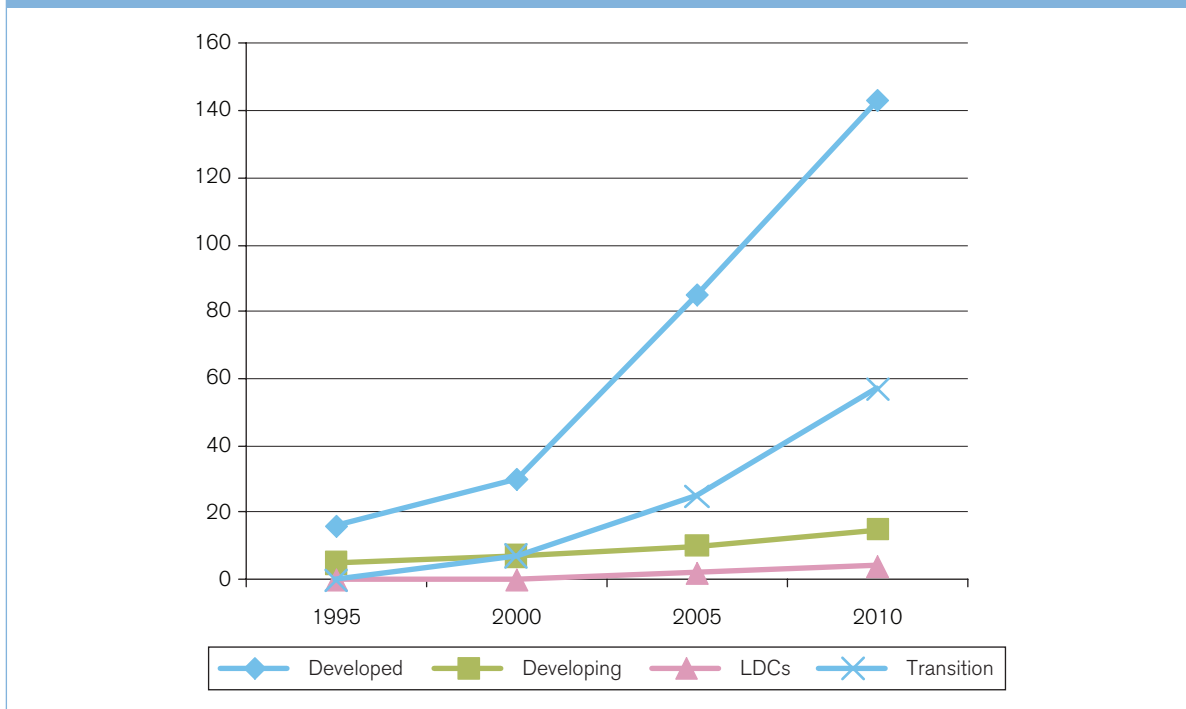
Structural shifts were evident in general trade in health products between 1995 and 2010. Many countries moved to a trade surplus, indicating growth and diversity in production capacity, with surpluses aimed at export markets. A number of countries (e.g. Costa Rica, Ireland and Singapore) prioritized the pharmaceutical and medical sector in national development strategies. Vigorous growth in health-related products and strong global demand mean that development strategies targeting the production and trade of health-related products offer developing countries promising avenues for economic growth and diversification. China became a major exporter, exporting US\$ 27.8 billion of health-related products in 2010, ten times its 1995 exports. From being a net exporter of health products (in all six categories), the United States became a very large net importer (only the Russian Federation and Japan import more). By contrast, the EU-27 (the 27 EU member states),¹³¹ which were net importers in 1995, exported more than they imported in 2010. For some countries, imports are highly significant domestically, even if they comprise a small share of global trade. Imports of health-related products represent 5 per cent or more of all imports for 40 countries in the world, with this share rising to 17 per cent in Panama, 14 per cent in the Bolivarian Republic of Venezuela and 12 per cent in Burundi (see Table 4.7).

Substantial, and widening, variations in per capita imports of health-related products were evident over the past 15 years between countries at different levels of development

Country	Share (%)
Panama	17
Switzerland	15
Venezuela, Bolivarian Rep. of	14
Burundi	12
Togo	11
Nicaragua	9
Mali	8
Barbados	8
Malawi	7
Australia	7
EU-27	7
Brazil	7
Colombia	6
French Polynesia	6
Russian Federation	6

Source: WTO Secretariat.

Figure 4.7. Per capita imports of formulations 1995-2010, in current US\$



Source: Helble (2012).

(see Figure 4.7), thus highlighting stark differences in access to medicines. Developed countries' per capita imports grew eightfold, from US\$ 16.02 to US\$ 127.42. Transition economies showed the strongest relative growth, rising from the lowest level of US\$ 0.20 to US\$ 48.21 in 2009. The rate for developing countries grew sixfold from US\$ 1.63 to US\$ 9.64. The per capita increase for LDCs was lowest and grew less, from US\$ 0.65 to US\$ 1.97. LDCs produce few medicines and rely very heavily on imports, and consequently, these import statistics are reasonable indicators of overall consumption of medicines: therefore, despite a modest improvement, the relative level remains very low, particularly given the high disease burden in LDCs. Overall, developing countries, LDCs and transition economies, comprising 85 per cent of the world's population, account only for 30 per cent of imports and 20 per cent of exports of internationally traded health-related products.

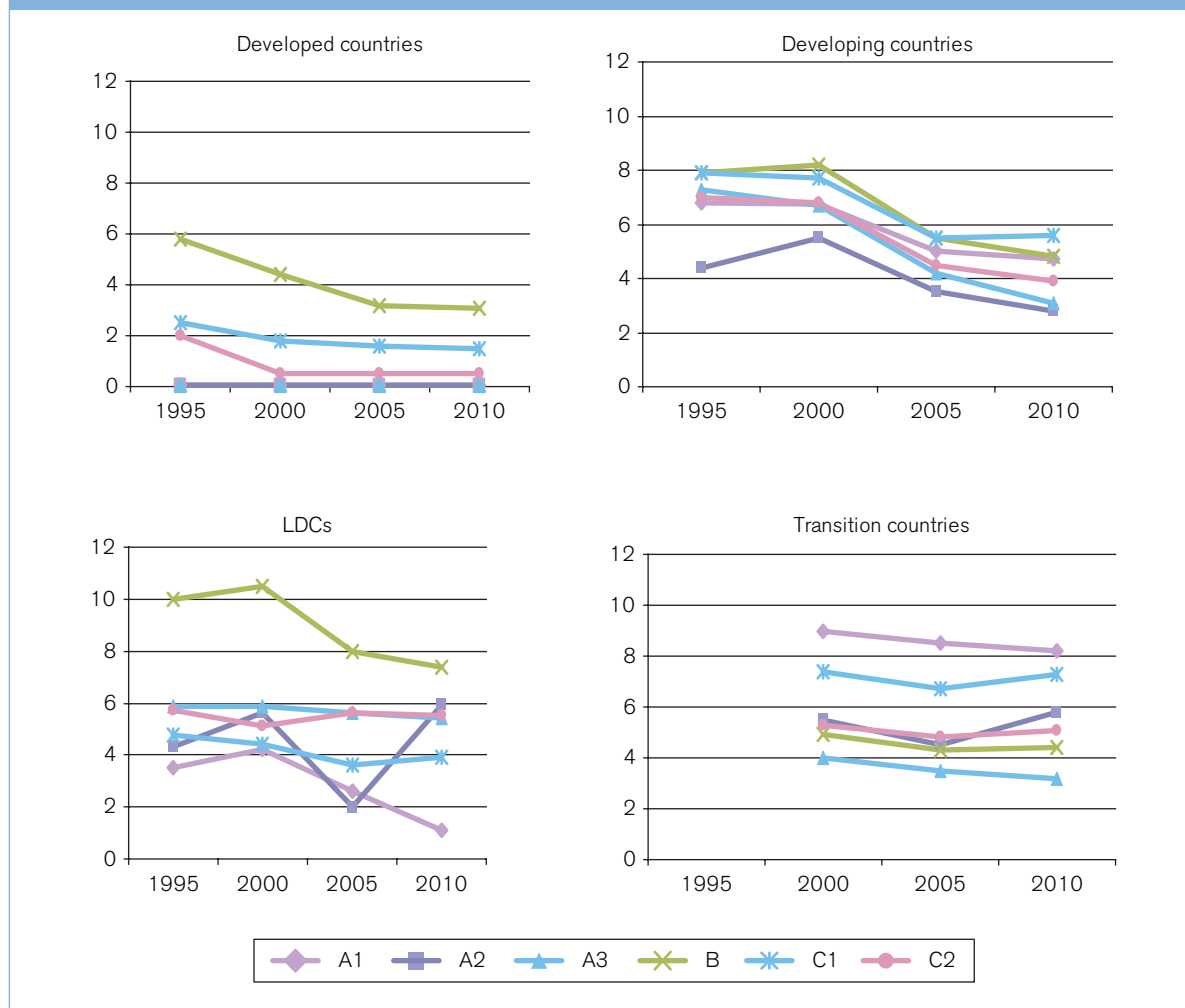
(b) Tariff policy for health-related products

Tariffs or import duties on pharmaceuticals affect prices, protection for local production capacity and generation of revenue (Olcay and Laing, 2005). The WHO has recommended that countries "reduce or abolish any import duties on essential drugs" (WHO, 2001d). Initiatives such as the Malaria Taxes and Tariffs Advocacy Project call for reductions of tariffs on products including treated mosquito nets, artemisinin-based combination therapies, diagnostic tests, insecticides and related equipment. Patterns of tariffs applied to the six health-related product groups therefore have a direct bearing on access.

Tariffs on all groups of health-related products have been reduced since 1996 (Figure 4.8). Tariffs on pharmaceutical products (Groups A1 and A2) have been markedly reduced in developing countries and LDCs, and remained close to zero in developed countries. Tariffs on general purpose chemical inputs remained the most protected product category in all three country groups. Economies in transition displayed contrasting patterns: formulations (A1) were, and remain, the most protected group of products, while tariffs on specific inputs (A3) and on inputs of general purpose (B) were lowest. Economies in transition reduced tariffs less than the other three country groups. Developing countries seem to have structured tariffs on formulations (A1), bulk medicines (A2) and pharmaceutical inputs (A3), with a view to promoting the local production of medicines through tariff protection (Levison and Laing, 2003), especially for generic products, but commentators have questioned the consistency of such policies (Olcay and Laing, 2005). By contrast, LDCs apply lower tariffs on formulations (A1) than on bulk medicines (A2) and specific inputs into the pharmaceutical industry (A3). Economies in transition apply lower tariffs to bulk medicines, pharmaceutical inputs and chemical inputs, thus suggesting the intent to provide cheap inputs for domestically manufactured medicines.

Governments can increase tariffs applied to health-related products at any time, as long as such increases are within the limits of tariff ceilings that WTO members prescribe for themselves (called bound duty rates or "tariff bindings"). Sometimes, the gap between actually applied tariffs and

Figure 4.8. Trade-weighted average rates applied to health-related products



Source: COMTRADE, WTO Secretariat.

the maximum WTO legal ceiling is very substantial (see Figure 4.9), creating doubts among traders about whether the effectively applied tariff rates might be increased again. Substantial cuts in bound rates to align them with actual rates, promote stability and predictability in tariff rates, and could promote trade in health products.

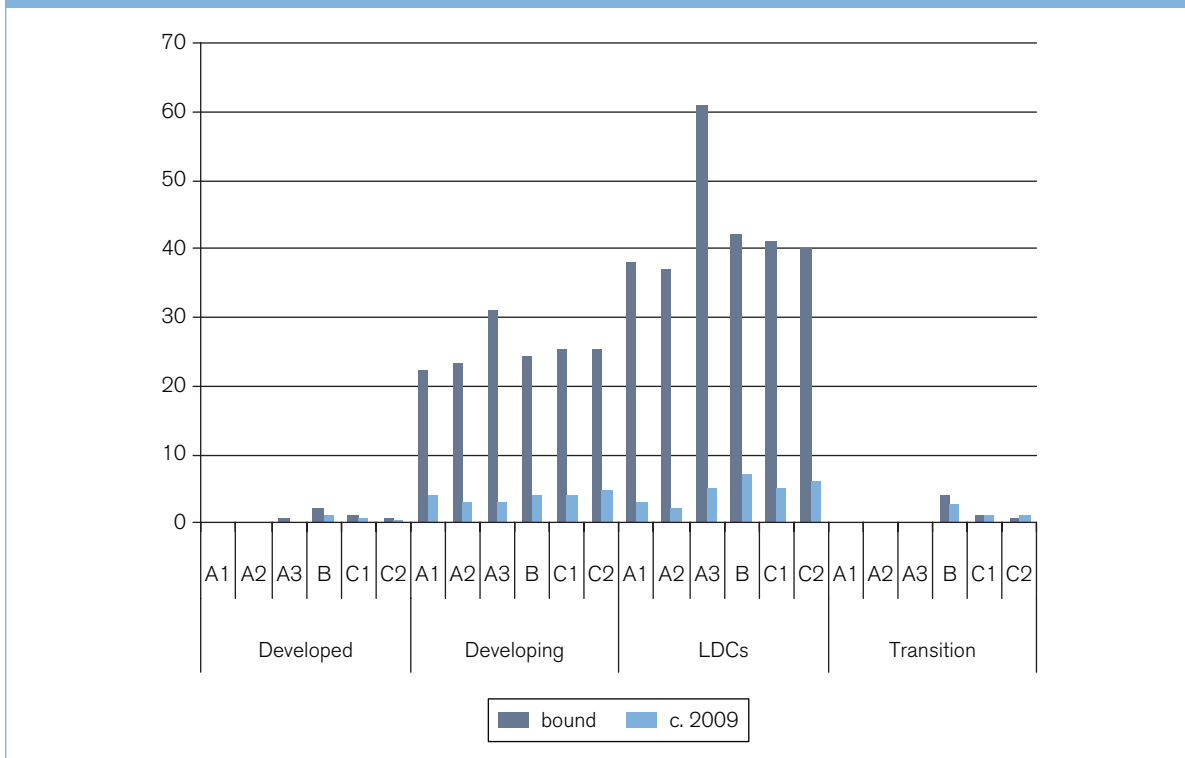
Governments sometimes apply special concessionary tariff regimes for certain strategic products, for example, waiving import duties on pharmaceuticals or health-related products so as to improve access. Several countries are reported (Krasovec and Connor, 1998) to apply such tariff exemptions for public health commodities, especially for not-for-profit purchasers.

FTAs frequently include provisions for preferential treatment between the agreement signatories. This may include reducing or removing import tariffs, which, in turn, results in more favourable market access than that afforded by multilateral (WTO) commitments. This section of the study only considers tariffs applied in the absence

of such preferential deals, i.e. on a most-favoured-nation (MFN) basis. The difference can be very significant for LDCs and developing countries: for example, syringes may be imported free of tariffs from a country with preferential market access, but they may be subject to a 16-per-cent tariff when imported from other WTO members. As a result, procurement of health-related products is skewed towards partners in FTAs. A comparison of preferential tariff rates with those applied in the absence of preferences reveals that, for Brazil, China, Mexico, India, South Africa and Turkey preferential tariffs for all three product groups (A, B and C) fell between 2005 and 2009 and were lower than the WTO MFN rate (by at least 0.4 per cent). The gap between preferential treatment and MFN treatment has thus widened, with the lowest tariffs applying to medicines (A) and the highest tariffs applying to medical devices (C).

Overall, but with significant exceptions, tariffs on health-related products have reduced substantially during recent years, and only represent one of the cost factors in the complex equation that determines access and affordability.

Figure 4.9. Tariffs on health-related products: simple applied average versus WTO simple bound average rates



Source: COMTRADE, WTO Secretariat.

However, tariffs often represent a cost increase at the beginning of a value chain (excise taxes, distribution services, mark-ups and retail services), so their impact on final prices may be considerably magnified by add-ons applied in the national distribution chain based on that higher import cost.

Apart from their impact on prices, tariffs also affect the conditions for local production initiatives – in terms of the cost of inputs such as chemical ingredients, the competitiveness and export focus of local producers, and

the protection afforded by tariffs on imported products. The trend towards lower tariffs for specific and general chemical inputs into the pharmaceutical industry (groupings A3 and B1) may help boost competitiveness of the local pharmaceutical industry. The tariff data above do not provide conclusive insights into the effectiveness of efforts to build up local production capacities, but it is clear that tariffs are losing overall significance in these policy efforts. Box 4.21 briefly describes sectoral tariff negotiations related to public health in the GATT and the WTO.

Box 4.21. Sectoral tariff negotiations in the GATT and WTO

During the Uruguay Round trade negotiations, some countries agreed to negotiate tariff reductions in specific economic sectors.¹³²

In 1994, Canada, the European Communities,¹³³ Japan, Norway, Switzerland and the United States concluded the WTO Pharmaceutical Agreement. These countries cut tariffs on pharmaceutical products and chemical intermediates used for their production (the “zero-for-zero initiative”), including all active ingredients with a WHO International Nonproprietary Name (INN). They agreed to periodically review and expand the list of items covered. The last such expansion took place in 2010.

Also during the Uruguay Round, some WTO members agreed to harmonize tariffs on chemical products, bringing them to zero, 5.5 per cent and 6.5 per cent, in what is referred to as the “Chemical Harmonization” initiative.

In 2006, in the context of the Doha Round negotiations on Non-Agricultural Market Access, some WTO members have put forward a proposal on “Open access to enhanced healthcare”. It aims to reduce or eliminate tariffs and non-tariff barriers on a wide range of health-related products. The list of products to be covered includes chemical and pharmaceutical products, and a range of other items such as surgical gloves, bednets, sterilizers, wheelchairs, surgical instruments, orthopaedic appliances, as well as medical, surgical, dental and veterinary furniture. The proposal is still under consideration by WTO members.

2. Competition policy issues

The importance of competition (antitrust) policy in promoting innovation and ensuring access to medical technology derives from its cross-cutting relevance to all stages and elements involved in the process of supplying medical technology to the patient – from the development and manufacture of such technology to its eventual sale and delivery (see Chapter II, Section B.2). While a full analysis of all competition policy issues involved in that process is beyond the scope of this study, this section outlines a number of areas where competition policy has direct relevance.¹³⁴ The main focus in this section is on the link with the access dimension.

(a) Competition in the pharmaceutical sector

Once a pharmaceutical has been developed, one of the main determinants of access is affordability, for instance, the end-price paid by the consumer. The prices charged by manufacturers are an important factor in determining this end-price, and competition between different manufacturers has been found to have a beneficial effect on the affordability of and access to pharmaceuticals.

In that context, two forms of competition take place. The first form is between-patented-product competition, which is competition between manufacturers of different originator medicines within a given therapeutic class. The second form is competition between the originator companies and producers of generic products (as well as among the generic companies themselves), usually after expiry of the patent. The following sections discuss particular issues relating to competition law and policy.

(b) Application of competition law to manufacturers of originator products

Depending on the availability of alternative products, IPRs can influence the degree of competition in the pharmaceutical sector. The question of how competition law is applied to IP right holders has therefore plays an important role in the discussion on access to medicines.

In some countries, competition authorities have implemented a twofold strategy. On the one hand, they have conducted sector inquiries and have published reports, for example on the interrelationship between patents and competition, so as to gain a better understanding of competition concerns in the pharmaceutical sector and to identify relevant market structures. On the other hand, they have then used the knowledge gained to provide policy guidance and enforce competition law more effectively.

Several potentially anti-competitive strategies in relation to IPRs involving medical technology have been observed and documented. These strategies mostly are designed to extend patent protection for originator drugs and to prevent market entry by generic competitors after patent expiry (see Box 4.22). The following examples describe some anti-competitive practices that may be considered detrimental for access to medical technology.

(i) *Strategic patenting*

The European Commission Pharmaceutical Sector Inquiry Final Report (see Box 4.23) found that originator companies file for numerous patent applications (on process, reformulation, etc.) in addition to the base patent, with the aim of creating several layers of defence against generic competition. It showed that individual blockbuster medicines were protected by almost 100 INN-specific EPO patent families, which in one case led to up to 1,300 patents

Box 4.22. US Federal Trade Commission reports on patents and related enforcement actions

In 2003, the US Federal Trade Commission (FTC), an independent agency of the US government, published a report on the effects of patents on competition.¹³⁵ The report proposed a number of recommendations designed to ensure that patents, while continuing to provide appropriate incentives for innovative activity, do not unnecessarily impede competition. A 2007 joint report by the FTC and the US Department of Justice highlighted the need to balance efficiencies with competitive concerns, in particular with regard to certain licensing practices.¹³⁶ In 2011, the FTC published a report which focused on patent notices and remedies and their effects on competition.¹³⁷

The FTC has also pursued numerous antitrust enforcement actions against both originator and generic medicines manufacturers at times when the agency had reason to believe that such companies had abused patent rights in violation of the antitrust laws. These actions have included cases of patent settlement agreements between originator companies and generic applicants, sham litigations, and agreements between generic drug manufacturers. The FTC has also addressed patent settlement agreements between originator companies and generic applicants in cases where the market entry of one or more generic applicants was delayed through manipulation of the 180-day exclusivity period provided by the 1984 Hatch-Waxman Act.

The FTC has furthermore reviewed and, in many cases, blocked or placed appropriate conditions on mergers in health-related sectors that would have created anti-competitive effects.

Box 4.23. European Commission inquiry into the pharmaceutical sector and related enforcement action

In 2008, the European Commission began an inquiry into the pharmaceutical sector to examine the reasons why fewer new medical technologies were being brought to market and why market entry of generic medicines seemed to be delayed in some cases.

Based on an in-depth investigation of a sample of 219 medical pharmaceutical substances in the period between 2000 to 2007 in 17 EU member states, the final report found that the first generic version of medicines developed during this period had entered the market on average more than seven months after the originator medicines had lost exclusivity.

The inquiry revealed that originator companies use a variety of instruments to delay the market entry of generics for as long as possible. Such instruments include:

- **Strategic patenting** to extend the breadth and duration of patents: companies file numerous patents for the same medicine, thus creating “patent clusters”, as well as voluntary divisional patent applications.
- **Litigation:** although originator companies use their patents to initiate the majority of court cases, the European Commission found that generic companies won the majority of cases in which a final judgment was given.
- **Settlement agreements:** originator and generic companies sometimes enter into agreements that resolve patent disputes or opposition procedures in which the generic company agrees not to enter the market until a certain date.
- **Interventions before national regulatory authorities and/or pricing and reimbursement bodies:** originator companies interfere with the process of marketing authorization and/or determination of pricing/reimbursement status.
- **life cycle strategies for follow-on products** that aim to switch patients from products facing patent expiry to newer, more expensive products.¹³⁸

and/or pending patent applications across the EU member states. The report referred to such a multitude of patents as a “patent cluster”. It described the effect of this strategy: that generic companies, even if they manage to invalidate the base patent before its regular expiry, still cannot enter the market.

The report describes the filing of divisional patent applications as another strategy used by originator companies. This strategy involves keeping subject matter that is contained in a parent application pending even if the parent application as such is withdrawn or revoked. Divisional patent applications allow the applicant to divide out from a patent application (parent application) one or several patent applications (divisional application). Divisional applications must not go beyond the scope of the parent application. The division must be made while the parent application is still pending, leading to separate applications, each with a life of its own. These applications have the same priority and application date as the parent application, and, if granted, have the same duration as the parent application. In cases where the parent application is refused or withdrawn, the divisional application remains pending.

The European Commission stated that both practices are aimed at strategically delaying or blocking the market entry of generic medicines by creating legal uncertainty for generic competitors. However, the findings by the European Commission have not resulted in competition law cases related to the creation of “patent clusters” or the use of divisional patent applications.

(ii) Patent litigation and patent settlements

Litigation proceedings initiated by manufacturers of originator medical technology in multiple jurisdictions

can constitute a deterrent to market entry of generics irrespective of the final outcome. Furthermore, in some cases, courts may grant preliminary injunctions in favour of patent holders while litigation is pending and before the ultimate determination of the validity of patents is made.

Similarly, settlement agreements that are reached during opposition proceedings or patent litigation between generic manufacturers and originator companies sometimes include negotiated restrictions on the generic companies’ ability to enter the market, sometimes in return for a cash payment made by the originator company to the generic company (for the EU experience, see Box 4.24).

(iii) Refusal to deal and restrictive licensing practices

In some jurisdictions, and in particular circumstances, the refusal of an IP right holder to license the protected technology may be considered an anti-competitive abuse of dominance (see Box 4.25). Compulsory licensing can arguably provide an effective remedy in circumstances where a refusal to license may be abusive in character. It is important, however, to note that refusals to license per se are not necessarily actionable abuses. On the contrary, the right of such refusal may be viewed as implicit in the grant of the IP rights.

In many jurisdictions, other licensing practices, whose effects on competition are normally evaluated on a case-by-case basis, are regulated by competition law. Such practices may include:

- “Grant-backs” that legally grant back to the holder of a particular patent the right to use improvements made by a licensee to the licensed technology. Where

Box 4.24. Competition issues arising from patent settlements: the EU experience

Patent settlements are commercial agreements between private-sector companies to settle actual or potential patent-related disputes, for example, questions of patent infringement or validity in the context of opposition procedures or litigation. While patent disputes, like any other types of law suits between private entities, may legitimately be settled in order to avoid costly litigation, such settlements can have effects that restrict competition and can therefore be undesirable from the standpoint of competition policy.

Follow-up studies after the European Commission Pharmaceutical Sector Inquiry report (see Box 4.23) have found that the number of patent settlements that are problematic under EU antitrust rules fell significantly in the years following the publication of the report. The European Commission's third report on its monitoring of patent settlements in the pharmaceutical sector, which was published in July 2012, confirmed that while the overall number of concluded settlements has significantly increased, the proportion of settlements that may be problematic for competition has stabilised at a low level of 11 per cent vis-à-vis 21 per cent in the findings of the sector inquiry. This shows that the Commission's action has not hindered companies from concluding settlements, contrary to fears expressed by certain stakeholders in that respect. At the same time, the monitoring exercises may have generally increased stakeholders' awareness of competition law issues, given the lower number of problematic settlements.¹³⁹

Box 4.25. Abuse of dominance on antiretroviral markets in South Africa

In 2003, the Competition Commission of South Africa concluded settlements with two major pharmaceutical companies relating to allegations that the two companies had abused their dominant position in their respective antiretroviral (ARV) markets by charging excessively high prices and by refusing to issue licences to generic manufacturers.

The Commission agreed not to ask for the imposition of a fine and, in return, the companies undertook to:

- expand the licensing of the drugs to a number of generic manufacturers
- permit the licensees to export the relevant ARV drugs to other sub-Saharan countries charging royalties of no more than 5 per cent of the net sales of the relevant drugs.

In 2007, a third major pharmaceutical company agreed to grant licences to produce and sell ARVs following a complaint about a refusal to license, which was brought before the South African Competition Commission.

These cases concern settlements rather than fully litigated competition law decisions. Nevertheless, the settlements reached are understood to have contributed to the substantial reduction in prices of ARVs in South Africa.¹⁴⁰

such licences are exclusive, they are likely to reduce the licensee's incentive to innovate since it hinders the exploitation of his/her improvements, including by way of licensing any such improvements to third parties.

- "Exclusive dealing requirements" requiring a licensee to use or deal only in products or technologies owned by a particular right holder.
- "Tie-ins" or "tying arrangements" requiring that a given product or technology (the "tied product") be purchased or used whenever another product or technology (the "tying product") is purchased or used.
- "Territorial market limitations" limiting the territories within which products manufactured under licence may be marketed.
- "Field-of-use" restrictions limiting the specific uses to which patented or other protected technologies may be put by a licensee.
- "Price maintenance clauses" stipulating the price at which products manufactured under licence may be sold. Relevant clauses in licensing contracts can either be declared invalid in patent laws or other IP laws, or invalidated as violations of (general) competition law.

(c) Competition law and policy in relation to the generic sector

The effect of generic competition, including between generic manufacturers, on medicine prices after patent expiry has been highlighted in various studies carried out by the OECD and also carried out in developed countries, including Canada, EU member states and the United States. In general, these studies have found that savings from generic competition can be substantial. For example, a Prepared Statement by the US Federal Trade Commission (FTC) before a US Congressional Committee refers to possible savings in the range of 20 per cent to 80 per cent, depending on the number of generic market entrants.¹⁴¹ The European Commission found that in rare cases, for some medicines in some member states, the decrease in the average price index was as high as 80 per cent to 90 per cent.¹⁴² Other studies exploring these issues have been conducted by the Canadian Competition Bureau and the OECD.¹⁴³

Where market entry of generics has occurred, the application of competition law to generic manufacturers

is necessary in order to prevent anti-competitive practices by such companies and also oversee mergers that may restrict competition (see also Box 4.26 on applying competition law to generic manufacturers).

Aside from the enforcement of competition law, it is also important to ensure that competitive market structures are supported through regulation. Once patents on medical technology have expired, competition is best achieved by regulatory regimes that allow market entry of generics by removing unnecessary legal and administrative barriers while maintaining the required quality, safety and efficacy standards.

(d) Application of competition policy to the health care and retail sectors

Competition needs to be ensured not only with regard to manufacturers, but also with regard to the health care and retail sectors. Both restrictions of competition along the value chain (vertical restriction) and market restraints in the health care or retail sectors (horizontal restrictions) can have highly detrimental effects on access to medical technology. First, vertical mergers between different companies that operate along the value chain can pose a threat to competition. For example, the FTC has reviewed the acquisition by a research-based pharmaceutical company of pharmacy benefit management (PBM) companies. As well as carrying out a range of other activities, PBMs help to determine which prescription drug claims to reimburse. The acquisition may have resulted in the PBMs unfairly favouring the products of this pharmaceutical company, and thus the FTC required the PBMs to implement measures to remain neutral in the process that leads to decisions on which medicines are reimbursed.

Second, cartelization can restrict competition horizontally. Associations of pharmacies or pharmacists have been found in several OECD countries to have coordinated prices or restrict entry to the profession. In some cases, the associations restricted the ability of individual

pharmacists to deal with third-party payers individually, thus establishing control over possible defectors and stabilizing cartel agreements.

At the same time, both public-sector initiatives and contracted or franchised NGO participation in retail have been found to increase competition and improve access to low-priced medical technology. For example, Uganda has contracted non-profit organizations to provide health services, and has allowed them to establish retail pharmacy outlets selling medical technology at affordable prices.

(e) The role of competition policy with regard to public procurement markets

The role of public-sector procurement and distribution is not to be underestimated. Competition policy is relevant in two key respects.

First, good procurement policies can maximise competition in the procurement process. Moreover, it can be cost-effective to procure bulk quantities of medicines.¹⁴⁴ However, this may mean that a balance needs to be struck between achieving the lowest price in a given tender (through bulk purchases) and maintaining a competitive market structure over the medium to longer term.

Second, competition policy has an important role to play in preventing collusion among suppliers of medical technology. Although transparency is generally considered conducive to integrity in the procurement process, it can also facilitate anti-competitive behaviour by, for example, facilitating the ability of competitors to match each other's prices. Competition policy and law therefore need to complement general procurement regulations and practices in order to guard against such behaviour, and competition authorities should be encouraged to monitor anti-competitive behaviour not only with regard to competition in private markets but, equally, with regard to competition in public markets for medical technology (Anderson et al., 2011).

Box 4.26. Applying competition law to generic manufacturers

The FTC has found cases where generic companies have entered into anti-competitive agreements so as to control markets for generic medical technology and ancillary markets. For example, in 2000, the FTC found that four companies had concluded exclusive licensing agreements for the supply of raw materials for producing lorazepam and clorazepate, which resulted in a dramatic increase in the price of these products. In a move designed to not only deter such behaviour, but also to compensate the public for the welfare losses incurred, the FTC ordered one company to pay US\$ 100 million to consumers and state agencies who had suffered losses as a result of excessive prices.

The FTC has also reviewed takeovers of one generic manufacturer by another to assess whether the merged company would reduce competition in medical technology markets. For example, in the case of a merger of two generic companies in 2006, the FTC required the companies to divest certain assets needed to manufacture and/or market 15 generic products.¹⁴⁵

Endnotes

- 1 See www.who.int/mediacentre/factsheets/fs331/en/index.html.
- 2 Availability represents the degree of fit between existing services and clients' needs (e.g. the correct medicines and therapies available for the current disease burden; personnel able to diagnose and treat diseases). Accessibility represents how well the geographical location of health service delivery matches the location of patients and whether patients can physically access these services (e.g. the distances and transport to health services). Affordability represents how prices for health services match clients' ability to pay (e.g. patients can pay fees out of pocket but without selling important assets; patients can pay through health insurance; services are free). Adequacy represents how the health services organization and logistics meets clients' expectations and needs (e.g. the hours of service match the schedules of clients and they are acceptable also to health personnel). Acceptability represents how well the match is between the provider and clients (e.g. how well the provider communicates with the client during medical consultations; how satisfied the clients are with the quality of care).
- 3 WHO Medicines Strategies 2004-07 and 2008-13 are available at: http://whqlibdoc.who.int/hq/2004/WHO_EDM_2004.5.pdf and www.who.int/medicines/publications/medstrategy08_13/en/index.html.
- 4 See www.who.int/medicines/areas/policy/access_noncommunicable/NCDbriefingdocument.pdf.
- 5 See http://erc.msh.org/dmpguide/pdf/DrugPriceGuide_2010_en.pdf.
- 6 See <http://apps.who.int/medicinedocs/documents/s18767en/s18767en.pdf>.
- 7 See www.who.int/globalatlas/autologin/hrh_login.asp.
- 8 See www.who.int/alliance-hpsr/projects/medicines/en/index.html.
- 9 See http://whqlibdoc.who.int/publications/2011/9789241502986_eng.pdf.
- 10 For example, see the WHO Global price reporting mechanism, at www.who.int/hiv/amds/gprm/en/. See also <http://utw.msfacecess.org/>.
- 11 See <http://utw.msfacecess.org/>.
- 12 For more details on this situation, see <http://utw.msfacecess.org/>.
- 13 See Chapter II, Section B.1(g).
- 14 See www.worldbank.org/depweb/english/modules/social/pgr/.
- 15 See Chapter I, Section C.2(b).
- 16 "New Drugs and Indications in 2011. France is Better Focused on Patients' Interests after the Mediator® Scandal, But Stagnation Elsewhere", translated from *Rev Prescrire*, 2012, 32(340): 134-40.
- 17 See www.who.int/medicines/areas/policy/access_noncommunicable/NCDbriefingdocument.pdf.
- 18 UN document A/RES/66/2.
- 19 See http://whqlibdoc.who.int/hq/2007/a95078_eng.pdf.
- 20 See http://whqlibdoc.who.int/hq/2004/WHO_EDM_PAR_2004.7.pdf.
- 21 See www.who.int/childmedicines/prioritymedicines/en/index.html.
- 22 See Annex 5 in *Forty-Sixth Report of the WHO Expert Committee on Specifications for Pharmaceutical Preparations*, available at www.who.int/medicines/areas/quality_safety/quality_assurance/expert_committee/TRS-970-pdf1.pdf.
- 23 See www.biomedcentral.com/content/pdf/1471-2431-10-74.pdf.
- 24 Ibid.
- 25 See www.gavialliance.org.
- 26 See http://apps.who.int/gb/pip/pdf_files/OEWG3/A_PIP_OEWG_3_2-en.pdf.
- 27 For a general overview of pricing policies, see OECD (2008).
- 28 ATC system information is available from www.whocc.no/atc_ddd_index.
- 29 See <http://whocc.goeg.at/Glossary/About>.
- 30 For a definition, see www.eunethta.eu.
- 31 See www.ft.com/intl/cms/s/0/f0b1e114-e770-11e0-9da3-00144feab49a.html#axzz1c404Fdtv.
- 32 Sources: <http://apps.who.int/medicinedocs/documents/s19111es/s19111es.pdf>; <http://apps.who.int/medicinedocs/documents/s19110es/s19110es.pdf>; and <http://apps.who.int/medicinedocs/en/m/abstract/Js19110es/>.
- 33 A revised version of 2003 is available at <http://siteresources.worldbank.org/PROCUREMENT/Resources/health-ev4.pdf>.
- 34 Available at www.who.int/hiv/amds/en/decisionmakersguide_cover.pdf.
- 35 For further information, see: www.who.int/phi/access_medicines_feb2011/en/index.html; www.wipo.int/meetings/en/2011/who_wipo_wto_ip_med_ge_11/; and www.wto.org/english/tratop_e/trips_e/techsymp_feb11_e/techsymp_feb11_e.htm.
- 36 For a review of initiatives supporting investment in local production and technology transfer in pharmaceuticals, see WHO (2011e).

- 37 See www.who.int/medicines/areas/quality_safety/quality_assurance/production/en/index.html.
- 38 See Chapter II, Section B.1(g)(v).
- 39 See http://whqlibdoc.who.int/hq/2006/WHO_IVB_06.13_eng.pdf.
- 40 See <http://apps.who.int/prequal/>.
- 41 See <http://apps.who.int/prequal/query/productregistry.aspx?list=in>.
- 42 See www.who.int/medical_devices/policies/en/.
- 43 See Directive 90/385/EEC, Directive 93/42/EEC and Directive 98/79/EC, available at http://ec.europa.eu/health/medical-devices/regulatory-framework/index_en.htm
- 44 See www.who.int/medicines/services/counterfeit/en/.
- 45 See www.who.int/medicines/services/counterfeit/WHO_ACM_Report.pdf.
- 46 See www.who.int/medicines/services/expertcommittees/pharmprep/43rdpharmprep/en/index.html.
- 47 See www.who.int/mediacentre/factsheets/fs275/en/.
- 48 Ibid.
- 49 Ibid.
- 50 WHA, *Resolution: WHA41.16: Rational use of drugs*.
- 51 See www.who.int/impact/en/.
- 52 WHA, *Decision: WHA 63(10): Substandard/spurious/falsely-labelled/falsified/counterfeit medical products*. Documents of the Working Group and the new member state mechanism are available at <http://apps.who.int/gb/ssffc/>.
- 53 WHA, *Resolution: WHA65.19: Substandard/spurious/falsely-labelled/falsified/counterfeit medical products*.
- 54 [1999] RPC 253 (Pat. Ct.) [51], *aff'd in part* [2001] RPC 1 (CA) (United Kingdom).
- 55 See WIPO document SCP/12/3 Rev.2, Annex II, for information on national laws regarding exclusion from patentable subject matter.
- 56 This information may be accessed at on www.wipo.int/patent-law/en/guidelines.html.
- 57 See www.wipo.int/pct/en/texts/gdlines.html.
- 58 WIPO document WIPO/SCP/12/3 Rev.2.
- 59 See www.wipo.int/pct/en/quality/authorities.html.
- 60 See www.wipo.int/meetings/en/topic.jsp?group_id=61.
- 61 For more information on prior art, see Chapter II, Endnote 67.
- 62 Source: WIPO Statistics Database.
- 63 See http://ec.europa.eu/competition/sectors/pharmaceuticals/inquiry/communication_en.pdf.
- 64 In the Matter of Patent Application No. 712/del/2002, Order of 18 March, 2009.
- 65 This exception is sometimes called the “Bolar” exception after the 1984 U.S. court decision *Roche Products v. Bolar Pharmaceuticals* that had considered this type of use to be patent infringement, leading to US legislation that defined this type of use as a permissible exception to the patent right (*Roche Products v Bolar Pharmaceuticals*, 733 F.2d. 858 (Fed. Cir. 1984).
- 66 WTO document WT/DS114.
- 67 WIPO document CDIP/5/4, Annex II.
- 68 This issue was raised in consultations requested by the United States with Brazil under the WTO dispute settlement mechanism. The mutually agreed solution can be found in WTO document WT/DS199/4
- 69 See Article L613-16 of the French *Code de la propriété intellectuelle* and Article 67 of Morocco's *Loi relative à la propriété industrielle*.
- 70 WIPO document CDIP/5/4, p. 16.
- 71 Available at http://ipindia.nic.in/ipoNew/compulsory_License_12032012.pdf. At the time of writing (December 2012), the appeal of the patentee was pending.
- 72 WTO document IP/C/57, para. 19. See Chapter II.
- 73 WTO document IP/C/M/65, para. 151.
- 74 See www.citizen.org/documents/PresidentialDecree20121.pdf.
- 75 WTO document WT/TPR/S/255, para. 173.
- 76 For more details, see WTO documents IP/C/M/63, paras. 359-70, WT/TPR/S/254/Rev.1, para. 140 and IP/C/57, para. 113.
- 77 See www.iepi.gob.ec/module-contenido-viewpub-tid-4-pid-184.html.
- 78 See 't Hoen (2009).
- 79 See: WTO document IP/C/61, paras. 50-55; and Khor (2007, p. 18).
- 80 See www.twobirds.com/English/News/Articles/Pages/italy_court_quashes_decision_1012.Aspx.
- 81 See www.wto.org/english/tratop_e/trips_e/amendment_e.htm.
- 82 See www.cptech.org/blogs/drugdevelopment/2006/11/noah-novogrodsky-on-compulsory.html.
- 83 WTO document IP/C/64, para. 104.
- 84 WTO document IP/N/9/RWA/1.

- 85 WTO document IP/N/10/CAN/1.
- 86 WTO document IP/C/M/64, para. 116.
- 87 See www.apotex.com/apotriavir/default.asp.
- 88 Source: WTO document IP/C/M/64.
- 89 See Annex to the Chairman Statement in WTO document WT/GC/M/82.
- 90 See www.medicinespatentpool.org/LICENSING/Current-Licences.
- 91 See www.pharmalot.com/2011/12/johnson-johnson-rebuffs-medicines-patent-pool/.
- 92 See: www.medicinespatentpool.org/LICENSING; www.i-mak.org/publications/; and www.msfacecess.org/content/msf-review-july-2011-gilead-licences-medicines-patent-pool.
- 93 See www.i-mak.org/storage/Oxfam%20-%20Voluntary%20Licensing%20Research%20IMAK%20Website.pdf.
- 94 www.cptech.org/ip/health/d4T.html.
- 95 See www.medicinespatentpool.org/patentdata/patentstatusofarvs/.
- 96 See: <http://utw.msfacecess.org/>; and www.msfacecess.org/sites/default/files/MSF_assets/Access/Docs/ACCESS_book_GlobalPolitics_tHoen_ENG_2009.pdf.
- 97 Source: www.accesstomedicineindex.org/.
- 98 See WIPO document CDIP/5/4 REV., Annex II.
- 99 See www.iprcommission.org/graphic/documents/final_report.htm.
- 100 See WIPO document CDIP/5/4 REV., Annex II.
- 101 See www.wipo.int/sme/en/ip_business/export/international_exhaustion.htm.
- 102 See WIPO document CDIP/5/4 REV., Annex II.
- 103 See www.weko.admin.ch/aktuell/00162/index.html?download=NHZLpZeg7tInp6IONTU042I2Z6In1ad1IZn4Z2qZpnO2YUq2Z6gpJCDdH94fWym162epYbg2c_JjKbNoKSn6A-&lang=en.
- 104 WTO document WT/DS170.
- 105 Official Journal of the EU L152/1 of 16 June 2009.
- 106 The issue was first raised at the 124th Executive Board meeting of the WHO in January 2009. Brazil and India raised it again under "Other Business" at the WTO's General Council meeting on 3 February 2009, as well as at the TRIPS Council meetings on 3 March 2009 (WTO document IP/C/M/59, paras. 122-91) and on 8 June 2009.
- 107 Official Journal of the EU 2003 L196/7.
- 108 WT documents WT/DS408/1 and WT/DS409/1.
- 109 See <http://pib.nic.in/newsite/erelease.aspx?relid=73554>.
- 110 See http://ec.europa.eu/taxation_customs/resources/documents/customs/customs_controls/counterfeit_piracy/legislation/guidelines_on_transit_en.pdf.
- 111 Joined cases C-446/09 (Philips v LuchengMeijing) and C-495/09 (Nokia v Her Majesty's Commissioners of Revenue and Customs).
- 112 See www.ige.ch/en/legal-info/legal-areas/patents.html.
- 113 See the statements of the participants in the ACTA negotiations at the TRIPS Council meeting in October 2011, WTO document IP/C/M/67, paras. 457-508.
- 114 WTO documents IP/C/M/69, paras. 230-310; IP/C/M/67, paras. 456-543; and IP/C/M/63, paras. 248-336. See also Chapter III and Annex II)
- 115 WTO document IP/C/W/563.
- 116 See www.aidslawproject.org/wp-content/uploads/2012/04/Judgment-Petition-No-409-of-2009-Anti-counterfeit-case.pdf.
- 117 The content and the sources of patent information are explained in Chapter II, Section B.1(b)(viii).
- 118 See: www.who.int/phi/access_medicines_feb2011/en/index.html; www.wipo.int/meetings/en/2011/who_wipo_wto_ip_med_ge_11/; and www.wto.org/english/news_e/news11_e_trip_18feb11_e.htm.
- 119 In early development stages, the INN of a product would have not yet been assigned. A potentially useful way of recording compounds would be using text-based structure representations (e.g. the International Union of Pure and Applied Chemistry (IUPAC) International Chemical Identifier (InChI), www.iupac.org/home/publications/e-resources/inchi.html). InChI presently does not support, for example, Markush structures, but ongoing projects exist to extend the scheme and allow it to describe numerous types of chemical structures.
- 120 The IPC, established by the Strasbourg Agreement Concerning the International Patent Classification, provides for a hierarchical system of language independent symbols for the classification of patents and utility models according to the different areas of technology to which they pertain. The standardized application of IPC symbols to patent documents by experts enables language independent patent searches and makes the IPC an indispensable search tool. For further information, see www.wipo.int/classifications/ipc/en.
- 121 See www.wipo.int/tisc/en/.
- 122 See IFPMA (2011, p. 46).
- 123 See <http://ictsd.org/i/publications/68413/>.
- 124 See <http://ictsd.org/i/publications/68155/>.
- 125 A Spanish version of the report is available at www.ifarma.org.
- 126 See <http://dontradeourlivesaway.files.wordpress.com/2011/01/all-costs-no-benefits.pdf>.

- 127 See, for example, the Office of the United States Trade Representative website for the agreements concluded with its trading partners, available at www.ustr.gov/trade-agreements/free-trade-agreements.
- 128 In 2010, the East Mediterranean Regional Office of the WHO produced a policy guide on "Public health related TRIPS-plus provisions in bilateral trade agreements" for negotiators and implementers in the region (El Said, 2010). See www.who.int/phi/publications/category_ip_trade/en/index.html
- 129 The annual growth rate of world merchandise trade in value terms was about 6.1 per cent according to the WTO Statistics Database.
- 130 Austria, Belgium, Bulgaria, Denmark, Finland, France, Germany, Hungary, Ireland, Latvia, Lithuania, Malta, Slovenia, Sweden and the United Kingdom.
- 131 Intra-trade of today's 27 EU member states has been consolidated into EU-27 group since 1995, in order to work over a stable group over the period analysed.
- 132 See WTO document TN/MA/S/13 for further information regarding sector-specific negotiations in goods in the GATT and WTO.
- 133 Refers to the European Communities and its 12 member states in 1994. Since then, the European Communities has evolved into the European Union and its 27 member states. All countries which adhered to the European Union since 1994 have subscribed to the same tariff commitments of the previous European Communities with respect to the elimination and harmonization of tariffs in health-related products.
- 134 For additional details, see Müller and Pelletier (forthcoming).
- 135 See www.ftc.gov/os/2003/10/innovationrpt.pdf.
- 136 See www.ftc.gov/reports/innovation/P040101PromotingInnovationandCompetitionrpt0704.pdf.
- 137 See www.ftc.gov/os/2011/03/110307patentreport.pdf.
- 138 Sources: <http://ec.europa.eu/competition/sectors/pharmaceuticals/inquiry/>; <http://europa.eu/rapid/pressReleasesAction.do?reference=MEMO/12/593&format=HTML&aged=0&language=EN&guiLanguage=en>.
- 139 Source: <http://ec.europa.eu/competition/sectors/pharmaceuticals/inquiry/>.
- 140 Sources: <http://cyber.law.harvard.edu/people/tfisher/South%20Africa.pdf>; www.wcl.american.edu/pijip_static/competitionpolicyproject.cfm.
- 141 See www.ftc.gov/os/testimony/P859910%20Protecting_Consume_%20Access_testimony.pdf. See also www.fda.gov/AboutFDA/CentersOffices/OfficeofMedicalProductsandTobacco/CDER/ucm129385.htm.
- 142 See http://ec.europa.eu/competition/sectors/pharmaceuticals/inquiry/preliminary_report.pdf.
- 143 See: [www.competitionbureau.gc.ca/eic/site/cb-bc.nsf/vwapj/GenDrugStudy-Report-081125-fin-e.pdf/\\$FILE/GenDrugStudy-Report-081125-fin-e.pdf](http://www.competitionbureau.gc.ca/eic/site/cb-bc.nsf/vwapj/GenDrugStudy-Report-081125-fin-e.pdf/$FILE/GenDrugStudy-Report-081125-fin-e.pdf); and www.oecd.org/regreform/liberalisationandcompetition/interventioninregulatedsectors/46138891.pdf.
- 144 For further background information, see www.oecd.org/document/25/0,3746,en_2649_37463_48311769_1_1_1_37463,00.html.
- 145 Source: www.haiweb.org/medicineprices/05062011/Competitionpercent20finalpercent20Maypercent202011.pdf.

Annex I. Overview of international key stakeholders

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Chapter I describes the trend, notably over the past decade, towards the expression of a more diverse range of views and perspectives in policy discussions about public health, intellectual property (IP) and trade, and also in debates about the issue of access and innovation relating to medical technologies such as pharmaceuticals. This study acknowledges the inputs of many stakeholders and their essential contribution to a necessarily multidisciplinary and pluralistic set of policy discussions. Annex I is not exhaustive. It contains information on a selection of some of the most active participants in the policy discussions about public health, IP and trade, other than the WHO, WIPO and the WTO. The first section covers international organizations and the second section introduces other

stakeholders such as public health advocates and industry representatives. These are listed in alphabetical order. This annex does not contain information on many important practical initiatives, as these are covered in the main body of the study.

The descriptions of the mandates, roles and priorities of the organizations listed in Annex I are based on, and summarized from, material provided and published by these organizations. The descriptions cannot be attributed to the WHO, WIPO or the WTO. Readers are encouraged to contact the organizations for authoritative and up-to-date information on any of the programmes and other activities described in this study.

A. International organizations

1. Global Fund to Fight AIDS, Tuberculosis and Malaria

Created in 2002, the Global Fund to Fight AIDS, Tuberculosis and Malaria (Global Fund) is a public-private partnership and international financing institution dedicated to attracting and disbursing additional resources to prevent and treat HIV/AIDS, tuberculosis (TB) and malaria. The Global Fund's model is based on the concepts of country ownership and performance-based funding, with recipients of its funding implementing their own programmes based on their priorities, on the condition that verifiable results are achieved.

The Global Fund urges recipients of its funding to adhere to good procurement practices, including competitive purchasing from qualified manufacturers and suppliers. It encourages them to apply national laws and applicable international obligations in the field of IP, including the flexibilities contained in the TRIPS Agreement and interpreted in the Doha Declaration on the TRIPS Agreement and Public Health (Doha Declaration), in a manner that achieves the lowest possible price for products of assured quality.

The Global Fund encourages recipients who face challenges on the procurement and supply of health products, including challenges in relation to the management of issues related to intellectual property rights (IPRs), to obtain the requisite technical assistance and support as part of the Global Fund grant.

The Global Fund maintains a public web-based Price and Quality Reporting (PQR) system which tracks procurement transactions for key health products purchased by its recipients.¹ It aims to promote transparency on pricing, monitor compliance with the Global Fund's Quality Assurance Policy and enable recipients to make informed procurement decisions.

Website: www.theglobalfund.org

Contact: The Global Fund to Fight AIDS, Tuberculosis and Malaria
Chemin de Blandonnet 8
1214 Vernier
Geneva, Switzerland
Tel: +41 58 791 1700
Fax: +41 58 791 1701

2. United Nations Human Rights Council and Office of the United Nations High Commissioner for Human Rights

The United Nations Human Rights Council (HRC), a subsidiary body of the United Nations General Assembly, is responsible for promoting universal respect for the protection of all human rights and fundamental freedoms for all. The HRC was established by the United Nations General Assembly to replace the former Commission on Human Rights.² The Office of the United Nations High Commissioner for Human Rights (OHCHR) provides substantive and technical support to the HRC in all areas of its work, including its regular and special sessions and the meetings of its subsidiary bodies.

Special Rapporteurs are appointed by the HRC to address either specific country situations or thematic issues in all parts of the world. The OHCHR provides them with personnel, policy, research and logistical support for the discharge of their mandates. Special Rapporteurs operate within their respective mandates through different means and activities.³ These include monitoring the situation of the right to health throughout the world, as well as presenting annual and thematic reports to the HRC and interim reports to the United Nations General Assembly. During his tenure (2002-2008), the first Special Rapporteur, Mr Paul Hunt,

regularly analysed the issue of access to medicines as a component of the right to the highest attainable standard of health. In 2008, he published *Human Rights Guidelines for Pharmaceutical Companies in relation to Access to Medicines*.⁴ His successor closely examined the relationship between the right to health, specifically with regard to access to medicines, and IPRs in his 2009 report to the HRC.⁵ Making use of the flexibilities in the Agreement on Trade-Related Aspects of Intellectual Property Rights (TRIPS Agreement) and avoiding higher IP standards in free trade agreements (FTAs) than provided by the TRIPS Agreement are among the actions recommended by the Special Rapporteur. Following his 2011 report on expert consultation on access to medicines,⁶ the HRC mandated the Special Rapporteur to explore existing challenges with regard to access to medicines in the context of the right to health, ways to overcome these challenges, and good practices.⁷

The Intergovernmental open-ended Working Group on the Right to Development and the High-Level Task Force on the implementation of the right to development also examined and reported on their findings with respect to trade issues from a human rights perspective, including Target E of Millennium Development Goal (MDG) 8, which concerns providing access to affordable medicines in developing countries.⁸

The Committee on Economic, Social and Cultural Rights (CESCR), established under the International Covenant on Economic, Social and Cultural Rights (ICESCR), has also considered the right to health and IPRs. Like the considerations underlying the broader debate on the appropriate balance in the IP system as it relates to public health, the need to strike an adequate balance between the various rights guaranteed in the Covenant is also recognized.⁹

Website: www.ohchr.org

Contact: Office of the UN High Commissioner for Human Rights (OHCHR)
Palais Wilson
Rue des Pâquis 52
CH-1201 Geneva, Switzerland
Tel: +41 22 917 9220

3. South Centre

The South Centre is an intergovernmental organization comprising 52 developing countries. Based in Geneva, it was established to provide policy advice to developing countries and to contribute to south-wide collaboration in promoting common interests and coordinated participation by developing countries in international forums dealing with South–South and North–South matters.

The three main activities undertaken by the South Centre are: research and policy analysis; policy advice; and

capacity-building and training. The Centre has developed a strong reputation for working consistently on issues related to IP, innovation and access to pharmaceutical products. In its day-to-day operations, it uses an interdisciplinary approach, and relies on a team of experienced experts in various fields, including law, economics, development studies, political science and international relations.

The provision of policy advice is the main activity undertaken by the South Centre in order to meet its objective of assisting developing country governments in decision-making with respect to standard-setting and rule-making in so far as these relate to IP and access to pharmaceutical products. The Centre provides analysis of the main international treaties and ongoing international negotiations, as well as advice on regional and national processes, such as the negotiation of FTAs and their implications for public health – in particular the issue of access to pharmaceutical products. It also provides training for pharmaceutical patent examiners.

In line with its work in the field of IP and access to pharmaceutical products, the South Centre has published a number of books, research papers and policy briefs.

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4. Joint United Nations Programme on HIV/AIDS

The Joint United Nations Programme on HIV/AIDS (UNAIDS) is an innovative partnership which provides global inspiration and leadership towards the achievement of universal access to (HIV) prevention, treatment, care and support. Two political declarations on HIV/AIDS, adopted by the United Nations General Assembly in 2001 and 2006, established the framework for a global response to the epidemic. In 2011, the General Assembly adopted a third Declaration which commits member states to a set of ambitious targets, including ensuring that 15 million people living with HIV have access to treatment by 2015, and halving new HIV infections. In the absence of a vaccine, and given the need for ever simpler and more tolerable antiretroviral (ARV) medicines, UNAIDS calls for continued and increased investments in research and development (R&D).

UNAIDS fully supports the use of flexibilities contained in the TRIPS Agreement and clarified by the Doha

Declaration by developing countries. Such flexibilities are critical to enable countries to expand access to HIV treatment and are central to the 2010 UNAIDS Treatment 2.0 initiative, which aims to accelerate access to cheaper, more effective and tolerable drug combinations and diagnostics. In March 2011, UNAIDS, the WHO and the United Nations Development Programme (UNDP), produced a policy brief which reviewed available trade-related aspects of intellectual property rights (TRIPS) flexibilities and urged countries to make use of such flexibilities where appropriate, in order to obtain access to affordable generic ARV medicines, including through local production, where feasible.¹⁰ In its capacity as an observer, UNAIDS has been monitoring TRIPS Council discussions in so far as these relate to IP and public health since 2002.

UNAIDS is also fully committed to the recently launched Medicines Patent Pool, an innovative mechanism for managing IPRs, in the hope that this mechanism will help to advance its Treatment 2.0 initiative.

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5. United Nations Conference on Trade and Development

The United Nations Conference on Trade and Development (UNCTAD) has undertaken a number of activities related to trade and health, in particular in the area of IPRs. Since 2001, the UNCTAD IP programme has been running a major project which aims to address concerns voiced by developing countries with respect to the implementation of the TRIPS Agreement and new developments in the area of IPRs. One of the key results of this programme was the publication in 2005 of the *Resource Book on TRIPS and Development* in conjunction with the International Centre for Trade and Sustainable Development (ICTSD). The Resource Book, conceived as a practical guide to the TRIPS Agreement, provides detailed analysis of each of its provisions, aimed at a sound understanding of WTO members' rights and obligations. It is designed to help negotiators and policy-makers engage in informed participation in negotiations and decision-making processes. It is also designed to assist national authorities in the implementation and adoption of policies on IPRs.¹¹ UNCTAD and the ICTSD have also worked on the so-called "Development Dimension of Intellectual Property Reports", with the objective of assisting developing countries, for example, Cambodia and Uganda, in integrating IP issues into their overall development goals.¹²

In 2005, UNCTAD was mandated to engage in work specifically related to the local manufacturing and supply of pharmaceutical products.¹³ The overall objective of UNCTAD is to assist developing countries to establish domestic IP regimes that will facilitate increased access to affordable medicines and, where feasible, to support the creation of local or regional pharmaceutical production and supply capacities, including in cooperation with investors. Among a range of programme activities, UNCTAD has produced a series of comprehensive publications, including *Using Intellectual Property Rights to Stimulate Pharmaceutical Production in Developing Countries: A Reference Guide*¹⁴ and *Investment in Pharmaceutical Production in the Least Developed Countries: A Guide for Policy Makers and Investment Promotion Agencies*.¹⁵ It has also provided training courses on TRIPS flexibilities for local pharmaceutical production. The work of UNCTAD in the field of medical products is complemented by a series of case studies focusing on examples of technology transfer for pharmaceutical production and access to medicines in selected developing and least-developed countries.¹⁶ This activity is part of a larger project, which is based on the WHO Global Strategy and Plan of Action on Public Health, Innovation and Intellectual Property (GSPA-PHI), which includes UNCTAD as one of the stakeholders. The project, conducted in partnership with the WHO and the ICTSD, examines possibilities to improve access to medicines in developing countries by identifying the main challenges and obstacles to local pharmaceutical production and related technology transfer in selected developing countries.

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6. United Nations Development Programme

The United Nations Development Programme (UNDP) is the UN global development network and is represented in 177 countries around the world. In cooperation with a broad range of stakeholders, the UNDP helps countries to create knowledge and share experience and resources in order to find solutions to global and national development challenges to achieve positive social change and to realize the MDGs.

In order to reduce costs and increase access to HIV treatment and treatment of coinfections, as well as access to relevant technologies, the UNDP advocates the implementation and use of the public health-related

flexibilities contained in the TRIPS Agreement. In furtherance of this objective, the UNDP provides technical and policy support to countries which are engaged in reviewing legislation with a view to incorporating TRIPS flexibilities into such legislation. It also provides support to countries involved in WTO accession negotiations or FTA negotiations, in particular where such negotiations may have IP-related implications. The UNDP also analyses and disseminates knowledge on the experience of countries in utilizing the TRIPS flexibilities to reduce cost and increase access to essential medicines. For example, in 2010, the UNDP published the *Good Practice Guide: Improving Access to Treatment with Flexibilities in TRIPS*. In early 2011, the UNDP, UNAIDS and the WHO released a joint policy brief on using the TRIPS flexibilities to increase access to HIV treatment.¹⁷

The UNDP has been supportive of the Doha Declaration and has advocated for the simplification of national laws in order to remove obstacles that prevent the effective use of the 30 August decision, and also in order to give effect to the Paragraph 6 System.

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7. United Nations Children's Fund

Created in 1946 and formerly known as the United Nations International Children's Emergency Fund, UNICEF is the key advocate for children within the UN system. UNICEF is the world's leading procurement agency of vaccines for children. It works in partnership with national governments, donor agencies and other organizations to obtain quality pharmaceutical products at reasonable prices. UNICEF is also committed to improving access to treatment for children affected by HIV/AIDS.

In order to ensure the safety and efficacy of medicines, UNICEF has a quality assurance system for purchasing medicines. This is based on the principles of the WHO Model Quality Assurance System for Procurement Agencies.¹⁸ As part of the system, pre-qualification of suppliers based on the WHO Good Manufacturing Practice Guidelines is required, documentation provided by suppliers is assessed, products are evaluated, and visits to manufacturing sites are organized. When purchasing medical products, UNICEF is mindful of the need to take into account patents and other IPRs, as they apply to the products concerned, in accordance with the international and national legal framework. Where appropriate, UNICEF fully supports the use of TRIPS flexibilities as clarified

by the Doha Declaration. The UNICEF Supply Division therefore reviews the patent and regulatory status of individual products in order to find the best supply solutions for each country. To ensure that IP issues do not impede UNICEF procurement efforts, and in line with paragraph 7 of the Doha Declaration, least-developed country (LDC) WTO members must provide a certification of non-recognition and non-enforceability of patents and test data in the pharmaceutical sector. Developing countries, on the other hand, must state which TRIPS-compliant measures have been taken, or are intended, to authorize generic medicines in their respective domestic markets.

UNICEF is committed to working with manufacturers to increase the affordability of quality medicines. It contributes to the publication of prices for HIV/AIDS medicines through the WHO Global Price Reporting Mechanism.¹⁹ Prior to 2011, UNICEF had a practice of publishing only the average prices paid for vaccines. In 2011, in an attempt to increase transparency and thus stimulate competition, UNICEF decided to systematically publish details of prices paid to individual producers.²⁰ This measure is expected to lead to lower prices for vaccines needed in developing countries, and will enable purchasers to procure vaccines at reasonable prices from quality sources.

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8. UNITAID

Created in 2006, UNITAID is an international drug purchase facility. The objective of this facility is to scale up access to prevention and treatment products for HIV/AIDS, TB and malaria in developing countries. In order to achieve this, prices are negotiated, often in cooperation with relevant partners (such as the Clinton Foundation and Stop TB), for already existing forms of medication and by bulk purchasing and pooled procurement. UNITAID also encourages follow-on innovation, so as to ensure that medicines are available in formulations and combinations that are best suited to target populations and treatment conditions in developing countries.

UNITAID raises money through a combination of taxes on airline tickets and long-term government funding. It does not administer the distribution of drugs. Rather, it provides the necessary resources to facilitate the purchase of needed drugs by other organizations. As a consequence, its activities are mainly focused on the identification of current needs by potential recipients, on the negotiation

of long-term contracts with pharmaceutical companies, and the maintenance of relations with major stakeholders in the field. In cases where it is appropriate to achieve competition and price reductions, UNITAID supports the use by countries of compulsory licensing under the framework of the Doha Declaration. UNITAID was the main driving force behind the proposal that patent holders be asked to share their IPRs in a pool which would then make licences available to other producers, thus facilitating the production of affordable generic medicines and the development of adapted formulations. This process ultimately led to the establishment of the Medicines Patent Pool.

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9. The World Bank

While recognizing the importance of innovation for improving health care, the World Bank is also cognizant of the financial strain that high-priced innovative technologies place on health systems and citizens in all countries.

Incentivizing innovation through IP protection has been shown to be effective in sustaining funding for innovators of products with significant commercial potential. In order to encourage innovation that benefits the poor, and also in order to make new technologies affordable for them, alternative innovation models as well as options for segmentation of product markets need to be explored.

The World Bank's key role in the health sector is to assist countries in building stronger health systems, including sustainable mechanisms for financing. As part of that role, the World Bank staff and consultants have published a number of articles and guides designed to assist countries in navigating the complexities of IP rules, for example in procuring medicines for HIV/AIDS. Going forward, it will be important to broaden the discussion beyond the issues surrounding IP protection and to explore alternative incentive models for innovators and public-private partnerships. In addition, it will be important to ensure the implementation of contractual arrangements that improve access to new technologies for commercially marginalized groups without undermining the sustainability of health financing.

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B. Other international key stakeholders

1. Bill & Melinda Gates Foundation

The Global Health Program of the Bill & Melinda Gates Foundation harnesses advances in science and technology to save lives in poor countries. It focuses on the health problems that have a major impact in developing countries but get too little attention and funding. Where proven tools exist, the Global Health Program supports sustainable ways to improve their delivery. Where such tools do not exist, it invests in R&D of new interventions, such as vaccines, drugs, and diagnostics. Most of the work of the Global Health Program is done through grants to partners in priority areas of focus, with extensive input from external experts and from the Program's Global Health advisory panel.

The Global Health Program's work in the field of infectious diseases focuses on developing ways to fight and prevent enteric and diarrhoeal diseases, HIV/AIDS, malaria, pneumonia, TB, and neglected and other infectious diseases. It also works on integrated health solutions for family planning, nutrition, maternal, neonatal and child health, tobacco control and vaccine-preventable diseases.

The Bill & Melinda Gates Foundation's three cross-cutting programmes include:

- **Discovery:** closing gaps in knowledge and science and creating critical platform technologies in areas where current tools are lacking.
- **Delivery:** implementing and scaling up proven approaches by identifying and proactively addressing the obstacles that typically lie in the path of adoption and uptake.
- **Policy and Advocacy:** promoting more and better resources, effective policies, and greater visibility of global health, so as to effectively address the foundation's priority health targets.

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2. Clinton Health Access Initiative

In 2002, the Clinton Health Access Initiative (CHAI) began as the Clinton HIV/AIDS Initiative to address the HIV/AIDS crisis in the developing world and strengthen health

systems there. On 1 January 2010, the CHAI became a separate non-profit organization.

The CHAI currently operates four programme areas: HIV/AIDS; Health Systems; Maternal and Child Health; and Access to Medicines. Through these programmes, the CHAI is saving lives in low- and middle-income countries (LMICs) by helping people gain access to essential medicines and health services. The CHAI works closely with governments and other partners to improve the management and organization of in-country health systems and global commodity markets while addressing key health systems barriers. The CHAI does not implement stand-alone programmes; neither does it create parallel health systems. Rather, at the invitation of individual governments, it works to strengthen and sustain their capacity to provide long-term health care to their citizens.

The CHAI negotiates price reductions for drugs and diagnostics and it also works to increase the quality of these commodities. It reports that more than 70 countries can now avail of lower drug prices as a result of the CHAI's work with pharmaceutical companies. Moreover, some 3.9 million people – representing almost 70 per cent of people being treated for HIV/AIDS globally – have benefited from lower prices for HIV/AIDS medicines. The CHAI has helped countries save more than US\$ 1 billion by reducing the price of some drugs by 60 per cent to 90 per cent between 2008 and 2011.

Website: www.clintonhealthaccess.org

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3. The COHRED Group

The COHRED Group is an international non-governmental organization (NGO) established following the merger in March 2011 of the Council on Health Research for Development (COHRED) with the Global Forum for Health Research.

The COHRED Group believes that research and innovation are key drivers for development and the improvement of people's health. Sustainable development in LMICs is only possible where governments recognize the importance of fostering an environment where research and innovation are valued and can prosper.

COHRED was established in 1993, and has focused on strengthening the governance, management and systems of LMICs to use research, science and technology and innovation to improve health, equity and development. The Global Forum for Health Research has provided a key focal point for debate on the role of research in the improvement of health in LMICs, organizing 13 global meetings between 1997 and 2010 alone.

The COHRED Group is actively engaged in discussions around the interaction between public health, IP and trade. Key examples include:

- Strengthening pharmaceutical innovation in Africa: in partnership with the New Partnership for African Development (NEPAD) and the African Union, the COHRED Group is developing a framework through which LMIC governments can understand the benefits of pharmaceutical innovation, and design effective national innovation strategies.²¹
- Supporting the implementation of the GSPA-PHI: in collaboration with the WHO, the COHRED Group is developing a monitoring and evaluation platform to track global progress towards achieving the GSPA-PHI indicators.²²
- The Global Forum for Health Research: Forum 2012 marks the first in a new series of Global Forum for Health Research meetings. It focused on moving “beyond aid” – achieving health, equity and development through research and innovation. This will include looking at important framework conditions, such as IP.²³

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4. Drugs for Neglected Diseases initiative

The Drugs for Neglected Diseases initiative (DNDi) is a collaborative, patients’ needs-driven, non-profit R&D organization.²⁴ It was established in 2003 by Médecins Sans Frontières, the Indian Council for Medical Research, the Oswaldo Cruz Foundation in Brazil, the Kenya Medical Research Institute, the Ministry of Health of Malaysia, and the Pasteur Institute in France, with the Special Programme for Research and Training in Tropical Diseases (WHO-TDR) as a permanent observer. It aims at bridging gaps in

existing R&D in essential drugs for neglected diseases through collaboration with public and private sector entities.²⁵ For this purpose, it identifies significant unmet medical needs, R&D opportunities such as candidate compounds and improved formulations to address these needs, possible organizations to partner with in the R&D process, as well as adequate funding sources. DNDi is dedicated to developing new, field-adapted treatments for neglected tropical diseases, such as African sleeping sickness, Chagas disease and visceral leishmaniasis.²⁶ Malaria was also an early focus of DNDi, and new R&D programmes for pediatric HIV²⁷ and specific helminth infections²⁸ were added in 2011. Thus far, DNDi has delivered five new treatments that are safe, effective, field-adapted and affordable.²⁹

DNDi regards drug research as a public good that should, primarily lead to the advancement of health. As such, DNDi’s mission is also to make research outputs available through open access scientific databases in order to further facilitate and stimulate neglected diseases R&D. In 2011, DNDi published more than 20 pre-clinical datasets related to fexinidazole (a clinical candidate for the treatment of human African trypanosomiasis) on the Public Library of Science-Neglected Tropical Diseases (PLoSNTD) website. DNDi also provided raw data to WIPO Re:Search.

DNDi’s approach to IP is characterized by two major guiding principles: (i) to ensure that drugs developed by DNDi are affordable and that access is equitable for patients who need them; (ii) to develop these drugs as public goods whenever possible.³⁰ Negotiations regarding ownership of patents and licensing terms are therefore made on a case-by-case basis in order to guarantee the best possible conditions for patients. Depending on the status of any IP that predates DNDi partnership agreements, the IP generated in collaboration with DNDi may be individually or jointly owned by DNDi and/or its partners. If DNDi does not own the IP, it secures non-exclusive, sub-licensable, royalty-free licences on the pre-existing IP and the newly-generated IP, in order to retain control of the outcome of the joint research in the field of neglected diseases. Such non-exclusive licences provide DNDi with the freedom to coordinate R&D and manufacturing activities globally with third parties on a sustainable basis, should any partner discontinue its collaboration with DNDi.

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5. Health Action International

Health Action International (HAI) is a Dutch civil society NGO, with a coordinating office (HAI Global) in Amsterdam and partner regional offices in Africa (Nairobi), Asia-Pacific (Penang), Latin America (Lima) and Europe (Amsterdam). Recognized globally for its medicines policy expertise, it is a non-profit, independent, worldwide network of over 270 members, including consumer groups, public interest NGOs, health care providers, academics, media and individuals in more than 70 countries. Due to the HAI's work on access to essential medicines, including price, affordability, availability, quality, safety, efficacy and the rational use of medicines, it is in a position to make a valuable contribution to the trade, health and innovation debate.

The HAI Medicines, Access Trade & Health (MATH) programme was established in 2008 and is coordinated by HAI Europe. The programme has both facilitated and strengthened a global expert civil society dialogue on trade and health issues between the five HAI regions. An analysis of EU and US trade policy and the global importance of IP protection and enforcement suggest that civil society organizations such as the HAI should play a bigger role in international trade negotiations.

The HAI also works towards the exploration and implementation of new models of innovation, engaging in discussions at the WHO and at regional and national levels. Together with other organisations, the HAI has been supporting the exploration of an essential health and biomedical R&D treaty, in order to ensure needs-driven and accessible innovation.

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6. International Centre for Trade and Sustainable Development

Founded in Geneva in September 1996, the International Centre for Trade and Sustainable Development (ICTSD) aims to influence the international trade system such that it advances the goal of sustainable development. The ICTSD promotes the use and management of knowledge and technology conducive to sustainable development, in the context of balanced and development-oriented IP regimes. Its programme activities focus

on: facilitating pro-development and pro-competitive outcomes in international IP and trade negotiations; helping to implement IP norms that balance private rights and public interests; maximizing incentives for innovation, creativity and technology transfer to developing countries; and promoting greater integration between IP, technology transfer, foreign direct investment and competition policies. The IPRsonline.org internet portal offers a useful source of information regarding further resources, documents and news on IPRs and sustainable development.³¹

More specifically, in the context of the relationship between IPRs and public health, the ICTSD cooperates closely with key stakeholders, in particular UNCTAD and the WHO. Relevant activities have focused on identifying options for the use of public health-related TRIPS flexibilities by developing countries. Such activities have included: publication of the *Resource Book on TRIPS and Development*,³² a comprehensive guide to the TRIPS Agreement from a development and public policy perspective which was co-published with UNCTAD; guidelines for the examination of pharmaceutical patents to support the development of a public health perspective through improved transparency and efficiency of patentability examination of pharmaceutical inventions, which was co-published with UNCTAD and the WHO³³; and a policy guide on public health-related TRIPS-plus provisions in bilateral trade agreements for negotiators and implementers in the WHO Eastern Mediterranean region, co-published with the WHO Regional Office for the Eastern Mediterranean.³⁴ Technology transfer, including as a means to support local production of pharmaceuticals in developing countries, has also been dealt with comprehensively by the ICTSD, in particular in the context of a joint project with the WHO and UNCTAD.³⁵ In addition, the ICTSD has undertaken extensive policy-oriented research on a variety of issues relevant to the relationship between IPRs and public health, such as an analysis of IP technical assistance and capacity-building, as well as an analysis of bilateral and regional trade agreements. In this regard, it has commissioned and published two major country studies on the impact of TRIPS-plus standards in FTAs on the prices of medicines in Central America.

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7. International Federation of Pharmaceutical Manufacturers & Associations

The International Federation of Pharmaceutical Manufacturers & Associations (IFPMA) was founded in 1968 as a global, non-profit NGO representing the research-based pharmaceutical industry, including the biotechnology and vaccine sectors. The primary role of the IFPMA is to represent its members' views in dialogue with intergovernmental organizations, with diplomatic missions of national governments and with specialized NGOs. The IFPMA participates in meetings organized by international organizations, such as the WHO and WIPO. It also participates in technical cooperation activities organized by the WTO.

The mission of the IFPMA is to advocate policies that encourage discovery of, and access to, life-saving and life-enhancing medicines to improve the health of people everywhere. To fulfill its mission, the IFPMA follows a number of guiding principles, including encouraging a global policy environment that is conducive to medicines innovation, both therapeutic and preventive, for the benefit of people around the world. For this purpose, effective IP systems in both developed and emerging developing countries, supported by sound regulatory processes and health care financing, are regarded as a key enabling factor to encourage innovation and manage the resulting IPRs. IFPMA member companies and associations also cooperate closely with country authorities to combat counterfeit medicines. The promotion of high standards of manufacturing practices and quality assurance for pharmaceutical products is another key IFPMA objective.

A number of IFPMA-sponsored projects provide detailed information on the research-based pharmaceutical industry's activities, with a special focus on global public health. The IFPMA Developing World Health Partnerships Directory lists the research-based pharmaceutical industry's long-term partnership programmes aimed at helping to achieve the MDGs and improve other aspects of global health. The directory is searchable by country, by disease, by programme type and by partner organization.³⁶ Dedicated events and public health-related material on the IFPMA website provide, among others, information relating to clinical trials, vaccines, biotech medicines and ethical marketing.

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8. International Generic Pharmaceutical Alliance

The International Generic Pharmaceutical Alliance (IGPA) is an informal network of five national/regional associations of generic medicines manufacturers from Canada (CGPA), Europe (EGA), USA (GPhA), Japan (JGA) and South Africa (NAPM), with three observer associations. The IGPA represents the generic industry in relations with the International Conference on Harmonization of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH), the WTO, WIPO, the WHO and other international organizations. The IGPA Science Committee has worked with various international institutions to encourage the adoption of high quality standards for generic medicines, including the application of good manufacturing practices (GMP) standards and bioequivalence studies. The IGPA Intellectual Property Committee is responsible for reviewing relevant IP issues and formulating positions. One of the objectives of the IGPA is to promote affordable access to high-quality medicines, including biosimilars. In line with this objective, it provides guidance on regulatory matters relating to the registration and marketing of generic medicines. It also supports policies that cultivate both innovation and competition in pharmaceutical markets.

The IGPA advocates a balanced approach to IP, taking into account different national health care priorities and IP systems, as well as the flexibilities provided in the TRIPS Agreement. Unwarranted periods of IP protection prevent the dissemination of established knowledge in the public domain and hinder the progress of technology.

It has expressed strong concerns about the evergreening of patents and has advised countries to resist the inclusion of TRIPS-plus provisions in FTAs. Further, the IGPA contends that the Paragraph 6 System is cumbersome, and is lacking any practical applicability. It supports the flexibilities provided in the exception clause in Article 30 of the TRIPS Agreement, which it views as being applicable to situations identified in paragraph 6 of the Doha Declaration. In addition, because of its strong interest in the production of quality medicines, the IGPA has lent its support to the implementation of strict and effective controls of production and trade in medicines, in order to avoid the proliferation of counterfeit versions of both originator and generic products.

Website: <http://198.170.119.137/igpa.htm>

Contact: For IGPA Members and Contact information see the website above.

9. Knowledge Ecology International

Knowledge Ecology International (KEI) is a not-for-profit NGO that searches for better outcomes, including new solutions, to the management of knowledge resources.

The KEI focuses on the human rights dimension of IP and innovation policy, and the protection of consumer interests.

Since the 1990s, the KEI (formerly known as the Consumer Project on Technology) has been involved in discussions about norms and practices relating to IP and innovation. Issues addressed in these discussions have included the following: the role of public sector R&D; the use of compulsory licences; the control of anti-competitive practices; the collective management of IPRs (including the UNITAID-sponsored Medicines Patent Pool); the exhaustion of rights and other limitations and exceptions to patent rights (including those relevant to the enforcement of rights in Part III of the TRIPS Agreement); pricing of medical technologies; the global trade framework for both IP and medicine pricing.

The KEI has been very active in efforts to explore alternative incentive systems for R&D that delink R&D incentives from medicine prices, such as through the use of prize funds, the implementation of the “open source dividend”, the consideration of a medical R&D treaty (a public health paradigm to support global funding of R&D), and a new WTO agreement on the supply of public goods.

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10. Medicines Patent Pool Foundation

Established in 2010 with the support of UNITAID, the Medicines Patent Pool (“the Pool”) aims to improve the health of people living in LMICs by increasing access to quality, safe, efficacious, appropriate and affordable ARV medicines, with a special focus on HIV/AIDS. For this purpose, the Pool negotiates with patent holders – companies, researchers, universities and governments – to share their IP. The Pool makes licences available on a non-exclusive and non-discriminatory basis to other producers. The easier availability of needed licences will result in facilitating the production of affordable generic medicines and the development of adapted formulations of HIV/AIDS medicines, such as heat-stable or pediatric formulations, which are needed in target countries.

The Pool is a voluntary mechanism. It operates within the current IP framework and provides a collaborative platform for all parties involved. In this way, patent holders receive royalties for sharing their patents; generic drug manufacturers obtain access to broader markets; and, most importantly, people living with HIV/AIDS will have expanded access to affordable, appropriate medicines.

The Pool has amassed a large database of patent information related to critical medicines for the treatment of HIV/AIDS and. It has decided to make this information publicly available, so that others can benefit from it and add to it. The database contains information on the patent status of selected ARVs in a large number of LMICs. It is searchable by country/region and by medicine.

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11. Médecins Sans Frontières

Médecins Sans Frontières (MSF) is an international, independent, medical humanitarian organization that delivers emergency aid to people affected by armed conflict, epidemics, natural disasters and exclusion from health care. It was founded in 1971 and currently works in more than 60 countries, providing high-quality care to those in need.

MSF’s actions are guided by medical ethics and the principles of neutrality and impartiality. Since it was founded, it has been an active advocate for improved medical treatments and protocols. It has drawn attention to neglected health crises as well as to challenges of the aid system.

In 1999, MSF established the Campaign for Access to Essential Medicines as a response to the growing frustration of MSF volunteers who were experiencing difficulties in providing treatment for patients because the medicines and diagnostic tools they needed were unavailable, unaffordable or unsuitable. The objective of the campaign is to improve access to existing medical technologies (medicines, diagnostics and vaccines) and to stimulate the development of new medical tools that have, or could have, a major impact on morbidity and mortality. As part of this campaign, MSF has encouraged countries to make use of flexibilities in international trade rules to facilitate access to patented medicines. Along with a number of other organizations, MSF played an important advocacy role in the lead-up to the Doha Declaration.

The current key priority areas of the campaign include improving: the availability and affordability of HIV and TB treatment options; promoting the change to improved treatment guidelines for severe malaria; improving the quality of food aid to meet the nutritional needs of growing children; and campaigning for improved, more affordable, more suitable versions of existing vaccines and the development of new vaccines to address the needs of developing countries. In addition, MSF advocates for fundamental changes to the framework for stimulating medical innovations, so that it is driven by health needs rather than by profits. For this purpose, it supports delinking R&D costs from the price of the resulting medical innovation. MSF regularly publishes a guide to the prices of ARVs entitled *Untangling the Web of Antiretroviral Price Reductions*. It includes information on the evolution in price for each ARV over time, charting the difference between the originator price and the prices available from generic producers for developing countries.³⁷

MSF has been very active in the discussions on the seizure of medicines in transit in the European Union to developing countries for alleged patent infringement. In addition, it has repeatedly urged pharmaceutical companies to participate in the Medicines Patent Pool.

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12. Oxfam

Oxfam is an international confederation of 17 organizations working together in 90 countries and with partners and allies around the world to find lasting solutions to poverty and injustice. It believes that all people should have access to health services, including HIV services, free at the point of use. This includes meeting needs for water and sanitation and hygiene promotion (WASH) in crises, supporting rights holders to campaign for the provision of essential services, and holding governments to account to meet the needs of people in poverty.

Oxfam has worked with other civil society organizations to ensure that IP rules do not create barriers to access to affordable medicines. It has called for new approaches to innovation to stimulate innovation for medicines, vaccines and diagnostics for diseases that disproportionately affect poor people in developing countries. In addition, it has called for increased innovation

and access to medicines through engagement in key multilateral, rules-setting bodies – especially the WTO and the WHO. It has engaged with other organizations on this issue – in particular organizations that purchase significant quantities of medicines and vaccines on behalf of LMICs. Oxfam thus works with a number of global institutions involved in health, in particular the World Bank, the GAVI Alliance, the Global Fund, UNITAID and the WHO. Through research and advocacy at global and national levels, it seeks to influence the policies and practices of these institutions, so that they ensure improved access to health care and medicines for poor people.

Oxfam works with civil society organizations around the world to ensure that governments fully respect key safeguards and flexibilities in the TRIPS Agreement and the Doha Declaration. This involves lobbying developed countries – the European Union and the United States in particular – to not introduce TRIPS-plus rules through bilateral and regional trade agreements, including, but not limited to, the Anti-Counterfeiting Trade Agreement, and to not punish developing countries that make legal use of TRIPS safeguards and flexibilities to promote and protect public health. Oxfam also lobbies developing countries to not introduce TRIPS-plus rules that will undermine efforts to improve access to medicines. It encourages LMICs to incorporate safeguards and flexibilities into national legislation and to utilize these safeguards to ensure affordable medicine prices.

Oxfam lobbies multinational pharmaceutical companies, and their shareholders, to encourage these companies to adopt changes to their business models. Such changes would see access to medicines placed at the heart of their business models. Additionally, major companies would be benchmarked on their approaches to IP, pricing and R&D.

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13. Third World Network

The Third World Network (TWN) is an independent non-profit international NGO involved in issues relating to development, developing countries and North–South affairs. It aims to deepen the understanding of the development dilemmas and challenges facing developing countries and to contribute to policy changes in pursuit of just, equitable and ecologically sustainable development.

It also works to bring about a greater articulation of the needs and rights of peoples in the South.

A key focus of the work of the TWN work is on IP and public health, particularly with regard to access to medicines. The objective is to ensure that IP rules and standards do not undermine public health and, in particular, do not undermine access to affordable medicines in developing countries. For this purpose, the TWN carries out research, engages in advocacy and provides technical assistance and support for capacity-building, aimed at enhancing the use of TRIPS flexibilities in developing countries in order to protect public health.

The TWN broadly represents developing countries' interests and perspectives at international forums and conferences, in discussions with UN agencies, and also in discussions with WIPO, the WHO and the WTO. The TWN actively monitors international negotiations on IP

and public health that take place in the WTO, WIPO and the WHO.

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Endnotes

- 1 See www.theglobalfund.org/en/procurement/pqr/.
- 2 General Assembly resolution A/RES/60/251 of 3 April 2006.
- 3 Particularly relevant for this study is the mandate of the Special Rapporteur on the right of everyone to the enjoyment of the highest attainable standard of physical and mental health (right to health), which was established by the Commission on Human Rights in April 2002 by Resolution 2002/31.
- 4 UN document A/63/263, Annex.
- 5 UN document A/HRC/11/12.
- 6 UN document A/HRC/17/43.
- 7 UN document A/HRC/RES/17/14.
- 8 For the final reports of the high-level task force on the implementation of the right to development, see UN documents A/HRC/15/WG.2/TF/2 and Add. 1 and 2.
- 9 See "the right of everyone to the enjoyment of the highest attainable standard of physical and mental health" (Article 12) and General Comment 14 as well as "the right to the protection of the moral and material interests resulting from any scientific, literary or artistic production of which he is the author" (Article 15.1(c)) and General Comment 17.
- 10 See www.unaids.org/en/media/unaids/contentassets/documents/unaidspublication/2011/JC2049_PolicyBrief_TRIPS_en.pdf.
- 11 See www.iprsonline.org/unctadictsd/ResourceBookIndex.htm.
- 12 For Uganda, see www.unctad.org/en/docs/diaepcb200913_en.pdf.
- 13 See UN document TD/B/COM.2/L.22 and www.unctad.org/Templates/Page.asp?intItemID=4567&lang=1.
- 14 See www.unctad.org/en/docs/diaepcb2009d19_en.pdf.
- 15 See www.unctad.org/templates/Download.asp?docid=14956&lang=1&intItemID=2068.
- 16 See http://www.unctad.org/en/PublicationsLibrary/diaepcb2011d7_en.pdf.
- 17 See www.unaids.org/en/media/unaids/contentassets/documents/unaidspublication/2011/JC2049_PolicyBrief_TRIPS_en.pdf.

- 18 See www.who.int/medicines/publications/ModelQualityAssurance.pdf.
- 19 See www.who.int/hiv/amds/gprm/en/.
- 20 Available at www.unicef.org/supply/index_57476.html.
- 21 See www.cohred.org/pharmainnovation.
- 22 See www.healthresearchweb.org/phi_beta/.
- 23 See www.forum2012.org.
- 24 See <http://dndi.org/index.php/overview-dndi.html?ids=1>.
- 25 For agreements signed with pharmaceutical companies, see www.dndi.org/press-releases/866-sanofi-dndi-agreement.html. For agreements signed with biotech companies, see www.dndi.org/portfolio/oxaborole.html.
- 26 See <http://dndi.org/index.php/diseases.html?ids=2>.
- 27 See <http://jama.ama-assn.org/content/306/6/597.extract>.
- 28 See www.dndi.org/press-releases/918-flubendazole.html.
- 29 See www.dndi.org/index.php/portfolio.html?ids=2.
- 30 DNDi's Intellectual Property Policy is available at www.dndi.org/dndis-policies/intellectual-property-policy.html.
- 31 Available at www.iprsonline.org.
- 32 Available at www.iprsonline.org/unctadictsd/ResourceBookIndex.htm.
- 33 Available at <http://ictsd.org/i/publications/11393/>.
- 34 Available at <http://ictsd.org/downloads/2011/12/public-health-related-trips-plus-provisions-in-bilateral-trade-agreements.pdf>.
- 35 See www.who.int/phi/implementation/TotLCProject.pdf.
- 36 See www.ifpma.org/healthpartnerships.
- 37 See www.msfacecess.org/content/untangling-web-antiretroviral-price-reductions-14th-edition.

Annex II. Special compulsory licences for export of medicines

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A. Operation of the System: context and scope

While Chapter IV, Section C.3(a)(iii), outlines the policy context of the Paragraph 6 System and why it allows special compulsory licences for export of medicines in limited circumstances, this annex provides supplementary information setting out its operation and use. The System is the only flexibility in the TRIPS Agreement that specifically entails action by (at least) two countries (i.e. an importer and an exporter). It operates on the basis of notifications to the TRIPS Council by these countries, which, in turn, result in the various actions described in this annex.

1. What is the Paragraph 6 System?

As outlined in Chapter IV, Section C.3(a)(iii), the Doha Declaration on the TRIPS Agreement and Public Health (paragraph 6) recognized that WTO members with insufficient or no manufacturing capacity in their pharmaceutical sector could face difficulties in making effective use of compulsory licensing under the TRIPS Agreement, as the agreement then stood. To overcome those difficulties, WTO members adopted the Paragraph 6 System. It addresses a particular scenario for access to medicines:

- A country needs to import a medicine from a foreign supplier because it lacks sufficient manufacturing capacity in its pharmaceutical sector.
- The medicine can be produced under a compulsory licence in another country.

- Export of the non-predominant part of the production in that country does not satisfy the needs of the importing country.
- Therefore, the importing country has to use the Paragraph 6 System in order to import medicines produced under a compulsory licence from another country.

The System provides WTO members with an additional flexibility, which is a special type of compulsory licence permitting production of medicines exclusively for export. The System links demand in importing countries with supply from exporting countries. In addition, it waives the obligation on importing countries to pay adequate remuneration to the right holder following the grant of a compulsory licence (Article 31(h) of the TRIPS Agreement), if such remuneration is provided for in the exporting country.

2. What products are covered by the System?

The System is available for any pharmaceutical sector products (including active ingredients and diagnostic kits) that are patented or manufactured under a patented process and are needed to address public health problems afflicting developing countries and least-developed countries (LDCs), especially those resulting from HIV/AIDS, tuberculosis (TB), malaria and other epidemics. This list of public health problems is based on paragraph 1 of the Doha Declaration and is not intended to be exhaustive.

B. Use of the System

This section describes which WTO members can use the System as importers and exporters; and the terms and conditions under which the System may be used.

1. Which countries can use the System as importers and exporters?

While all WTO members are eligible to use the System as importers, developed countries have elected not to use the System for their imports,¹ and some higher-income developing countries and territories have agreed that they would use the System as an importer only in situations of national emergency or other circumstances of extreme urgency.² Nevertheless, the System itself is not restricted to emergency situations. Most WTO members have not indicated that they would limit its use to such situations. Some WTO members have implemented the System so as to enable exports to developing countries and LDCs that are not WTO members. While any WTO member may participate in the System as an exporter, they are not under any obligation to do so.

2. How is the System used?

The essence of the System is the grant of a compulsory licence by the exporting country to meet the need(s) identified by the importing country. The entitlement to do so is triggered by notifications sent for information to the WTO TRIPS Council, including:

1. An importing country's general notification of intent to use the System (not required for LDCs).
2. An importing country's specific notification of needed pharmaceutical product(s).
3. An exporting country's notification of a compulsory licence issued for exports to meet the needs of the importing country or countries.

Notifications need only be very brief, and may be in the form of a letter sent by fax or email, and signed by any authorized government official. Such notifications are required for transparency purposes. It is expressly provided that they are not subject to approval by any WTO body. No standard form is established. The WTO Secretariat provides model notifications on its website (see Figure A.1).³ Further guidance is also provided by the World Bank (Abbott and Van Puymbroeck, 2005) and the WHO (Correa, 2004).

- (a) How does an importing country use the System?

(i) *Notifying general intention to use the System*

Countries other than LDCs need to submit a general notification of intent to use the System. This can be done at any time prior to actual use, and it does not commit these countries to use the System. Rather, they simply reserve the right to do so in the event of potential future need. The general notification comprises the simple statement by a WTO member that it intends to use the System.

(ii) *Notifying the need to import specific pharmaceutical products*

When a country wishes to create the option of importing particular products under the System, it submits a specific notification of its import needs.

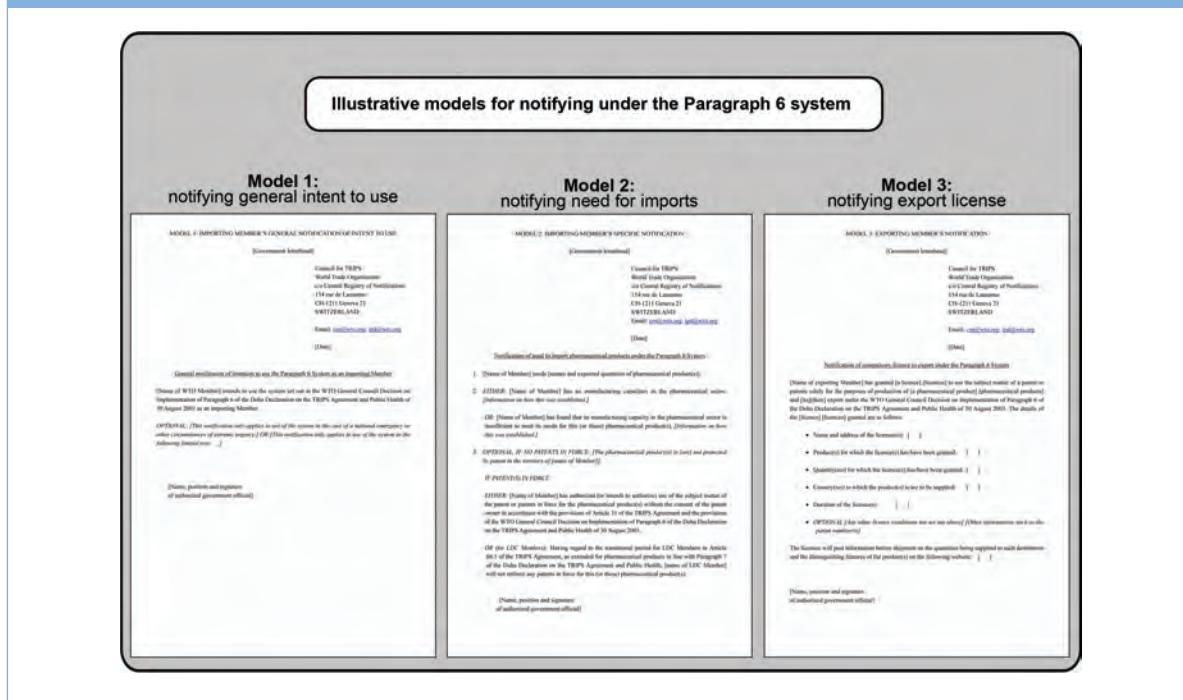
The specific notification includes:

- Names and expected quantities of the products the country needs to import.
- if a patent is in force in the country for any of the pharmaceutical products listed, an indication that a compulsory licence has been or will be granted. LDCs may simply indicate an intent to use the extended transition period under the TRIPS Agreement.
- An indication that the country has established that it lacks the capacity to manufacture the product. LDCs are already deemed to have insufficient manufacturing capacity, and thus they are exempt from adhering to this requirement.

This notification can be submitted at an early stage of the procurement process, before any final decision about preferred sources of supply. It does not create any obligation to use the System should a better alternative emerge. A country is therefore free to notify expected medicine requirements as a routine step in the procurement planning process, thus facilitating assessment of the full range of access options, signalling demand for potential suppliers, and clearing the way for actual use of the System should it present the most commercially viable option.

Countries pooling their procurement needs can make joint notifications. Given that the System recognizes the need for economies of scale in a regional context, joint notifications by countries with similar needs may provide a pathway for the establishment of commercially viable level(s) of demand for production and shipment.

Figure A.1. Screenshot from WTO web site providing practical guidance on the system



Source: www.wto.org/medicinesnotifications.

If a compulsory licence is needed on a patent in force in the importing country, that country must still respect general TRIPS Agreement requirements for compulsory licensing. There is no obligation to seek a voluntary licence from the patent holder in cases of public non-commercial use, or if there is a national emergency or other circumstances of extreme urgency. (The Doha Declaration clarifies that countries have the right to determine when such situations exist.) Furthermore, there is no obligation to seek a voluntary licence if the compulsory licence was issued to remedy an anti-competitive practice. However, in all other cases, the importer should make prior efforts to obtain authorization from the patent holder on reasonable commercial terms and conditions. To avoid double payment to the patent holder, the licensee in the importing country is exempted from the requirement to pay remuneration under a compulsory licence if payment has already been made in the exporting country.

(b) How does an exporting country use the System?

Any country can export under the System if it has a pharmaceutical industry with the capacity to manufacture the needed product – and if its domestic law allows the grant of a compulsory licence to export. If there is no patent in force for the products in the exporting country, then there is no need to resort to the Paragraph 6 System. Equally, if the product is already being produced under a compulsory licence for the domestic market, the

non-predominant portion of the production quantity can be exported without using the System.

Once a compulsory licence for export under the System has been issued, the exporting country submits a notification.

The exporting country's notification of the licence(s) for export contains the following details:

- name of the licensee(s)
- product(s) for which the licence(s) has/have been granted
- quantity(ies) for which the licence(s) has/have been granted
- country(ies) to which the product(s) is/are to be supplied
- duration of the licence(s)
- optionally, any other licence conditions and other information, such as the patent number(s)
- address of website providing information on quantities shipped and distinguishing features of the product(s).

When granting the special licence for export, the exporting country needs to apply the standard TRIPS Agreement requirements for compulsory licences, except that:

- the limit is removed on the quantity that can be exported under compulsory licence, and the entire production quantity is exported to the beneficiary countries

- the requirement for adequate remuneration is calculated on a different basis, namely the economic value of the authorization in the importing country.

3. Do regulatory authorities have to approve products manufactured under a special compulsory licence?

While the System does not deal with marketing authorization for pharmaceutical products, use of the System may entail facilitating regulatory clearances. It remains a separate responsibility of health authorities to determine whether products are safe and effective, and it is up to the exporting and importing countries to decide whether their respective pharmaceutical regulatory authorities will review the products manufactured under the System or whether they will rely on regulatory reviews carried out by counterpart authorities either in the countries using the System or even in another jurisdiction.

4. Which safeguards against diversion need to be put in place?

In order to ensure that products exported under the System are used to address the public health problems afflicting the importing country or countries, specific safeguards against diversion apply:

- Production carried out in the exporting WTO member as a result of a compulsory licence is limited to the quantity necessary to meet the needs of the importing WTO member(s), and the entire quantity produced must be exported to the importing WTO member(s).
- The products must have specific labelling or marks. They should have distinctive packaging and/or be specially coloured or shaped – as long as these latter requirements are feasible and do not have a significant impact on price. Before shipment, the manufacturer must post on a website details of the quantity of products it has manufactured under the compulsory licence, as well as details of the way in which it has specially labelled or packaged them. The WTO website is available for the manufacturer to utilize for the purpose of publishing this information, but such use is not mandatory.
- Importing WTO members must take reasonable measures within their means to prevent re-exportation. Such measures should be proportionate to these members' administrative capacity and the risk of trade diversion. Importing WTO members are entitled to receive technical and financial assistance from

developed-country WTO members so as to meet this obligation.

- Other WTO members need to have in place effective legal procedures and remedies in order to prevent importation into their markets of diverted pharmaceutical products produced under special compulsory licences for export, using the means that are already available to them under the TRIPS Agreement.

5. How can the System be used at regional level?

Under a regional mechanism established by the System, the condition otherwise applicable to compulsory licences (i.e. that they be used to predominantly supply the domestic market), is also waived. The purpose is to allow WTO members who are party to a regional trade agreement (RTA) to better harness economies of scale in their regional economic community and also enhance their purchasing power by combining demand to facilitate bulk imports or local production of pharmaceutical products for distribution within the relevant region. The regional mechanism enables the exporting and re-exporting of products that have been manufactured under a compulsory licence to take place more easily among WTO members who are party to an RTA, provided that:

- the RTA complies with the General Agreement on Tariffs and Trade (GATT) and the so-called Enabling Clause (the name given to a 1979 GATT Decision permitting preferential arrangements among developing countries and LDCs in goods trade)
- at least half the WTO members who are party to the RTA are LDCs
- these WTO member share the public health problem(s) in question.

The WTO does not state which RTAs satisfy these requirements, and thus no list of RTAs qualifying for this regional mechanism is available.

The regional mechanism can cover pharmaceutical products manufactured within the regional trade area under compulsory licence. It can also cover products manufactured elsewhere under compulsory licence and imported by one RTA party under the Paragraph 6 System. Either way, the products can be traded among the parties to the RTA without any further notification or adherence to any additional requirements other than those that apply at the time of the importation into the regional trade area under the Paragraph 6 System.

The regional mechanism does not override patents or national marketing approval requirements. Where a patent is in force for any country in the region seeking

to use this mechanism, either a voluntary or compulsory licence would be required in the country that is seeking to use the mechanism. Equally, the product should still be approved for distribution in each of the countries concerned.

6. What does the WTO General Council Chairman's statement add?

The General Council decisions to establish the System were both adopted in light of a statement by the General Council Chairman which reflected several key shared understandings of WTO members,⁴ notably:

- The System should be used in good faith to protect public health and should not be used to pursue industrial or commercial policy objectives.
- The requirements on product differentiation apply to active ingredients produced and supplied under the

System. They also apply to finished products containing such ingredients. In general, special packaging and/or special colouring or shaping should not have a significant impact on the price of pharmaceuticals. (In relation to the prevention of diversion of products, members and producers are encouraged to draw from and use best practices guidelines and to share information on their experiences and practices in preventing diversion).

- Importing countries should include information on how they established that they had insufficient or no manufacturing capacities in their local pharmaceutical sector.

The Chairman also noted that developed countries had agreed to opt out of the System as importers (also reflected in footnote 3 of the 2003 Decision/ Protocol Amending the TRIPS Agreement)⁵ and that 11 higher-income developing countries and territories had agreed to restrict the use of the System as importers to situations of national emergency or other circumstances of extreme urgency.

C. Domestic implementation

Countries can implement the Paragraph 6 System as importing countries, exporting countries, or as both.⁶ There is no obligation on WTO members to use the System in either capacity, and it remains one option among many that can be used to enable access to medicines.

1. Importing members

Importing WTO members will generally need to make legislative changes in order to exercise the option of dispensing with remuneration on imports under a compulsory licence, where remuneration has already been paid in the exporting country. While the required submission of a notification to the WTO does not necessitate special legislation, such notification requirement may be addressed in laws or implementing regulations. Importing WTO members are obliged to take reasonable measures to prevent the re-export of imported products but, again, this is possible without the need to use special legislation. For example, in the Philippines, the law simply requires that the compulsory licence “shall also contain a provision directing the grantee of the license to exercise reasonable measures to prevent the re-exportation of the products imported under this provision”.⁷

2. Exporting members

Exporting WTO members typically need to make limited legislative changes in order to use the Paragraph 6 System,

except where it is directly applicable under national law (this is reportedly the case in Japan, for example). Countries that have already incorporated the 1994 TRIPS Agreement standards into law will have restricted compulsory licences (i.e. predominantly to supply the domestic market). Therefore, at a minimum, this limitation will need to be amended so as to allow for the export of the entire quantity produced under a compulsory licence issued under the System. Implementation of compulsory licences for export under the System would also need to take account of the need to limit the volume of production to that referred to in the importing country(ies) notification(s), the obligation to export the full quantity of production, and special marking or labelling of the products.

3. Regional mechanism

Implementation of the regional mechanism would entail ensuring that the relevant legislation in exporting countries in the region does not limit the proportion of exports under a compulsory licence, as would be the case under the limitation predominantly to supply the domestic market, which applies to standard compulsory licences under the TRIPS Agreement. For countries that intend only to import, changes may be required in their domestic law so that the licensee can be exempted from paying remuneration to the right holder in a situation where a compulsory licence to import has been granted and where remuneration has already been paid in the exporting country.

Endnotes

- 1 See footnote 3 to the 2003 Decision/Protocol Amending the TRIPS Agreement, WTO documents WT/L/540 and WT/L/641.
- 2 See the list contained in the Chairman's Statement, WTO documents WT/GC/M/82, para. 29 and WT/GC/M/100, para. 29.
- 3 See www.wto.org/medicinesnotifications
- 4 WTO documents WT/GC/M/82, para. 29 and WT/GC/M/100, paras. 28–29.
- 5 WTO documents WT/L/540 and WT/L/641.
- 6 A collection of laws implementing the Paragraph 6 System is available at www.wto.org/english/tratop_e/trips_e/par6laws_e.htm.
- 7 Rule 13 of the Implementing Rules and Regulations of Republic Act 9502 Otherwise Known as the "Universally Accessible Cheaper and Quality Medicines Act of 2008", notified in WTO document IP/N/1/PHL/1/10.

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Abbreviations

ACTA	Anti-Counterfeiting Trade Agreement
AFRO	WHO Regional Office for Africa
AMC	Advance Market Commitment
AMF	Access to Medicine Foundation
AMRH	African Medicines Regulatory Harmonization
ANDI	African Network for Drugs and Diagnostics Innovation in Africa
API	active pharmaceutical ingredient
ARIPO	African Regional Intellectual Property Organization
ARV	antiretroviral
ASAQ	artesunate and amodiaquine
ASEAN	Association of Southeast Asian Nations
ATC	Anatomical Therapeutic Chemical
BTA	bilateral trade agreement
BVGH	BIO Ventures for Global Health
CAFTA-DR	Dominican Republic–Central America–United States Free Trade Agreement
CAM	complementary and alternative medicine
CAMR	Canada's Access to Medicines Regime
CAN	Andean Community
CARIFORUM	Caribbean Forum of African, Caribbean and Pacific States
CBD	Convention on Biological Diversity
CDIP	Committee on Development and Intellectual Property
CEWG	Consultative Expert Working Group on Research and Development: Financing and Coordination
CESCR	Committee on Economic, Social and Cultural Rights
CHAI	Clinton Health Access Initiative
CIOMS	Council for International Organizations of Medical Sciences
CIPIH	Commission on Intellectual Property Rights, Innovation and Public Health
CMH	Commission on Macroeconomics and Health
COHRED	Council on Health Research for Development
COPD	chronic obstructive pulmonary disease
CSIR	Council of Scientific and Industrial Research
CTD	Common Technical Document
DALY	disability-adjusted life year
DMEPA	Division of Medication Error Prevention and Analysis
DNDi	Drugs for Neglected Diseases initiative
Doha Declaration	Declaration on the TRIPS Agreement and Public Health
EAC	East African Community
EBS	equitable benefit-sharing
EDCTP	European and Developing Country Clinical Trials Partnership
EFTA	European Free Trade Association
EMA	European Medicines Agency
EMRO	WHO Regional Office for the Eastern Mediterranean
EML	Model List of Essential Medicines
EPC	European Patent Convention
EPO	European Patent Office
EWG	Expert Working Group on Research and Development: Financing and Coordination
FDA	US Food and Drug Administration
FDI	foreign direct investment
FTA	free trade agreement
FTC	US Federal Trade Commission
FTO	freedom to operate
GACP	good agricultural and collection practices
GATS	General Agreement on Trade in Services
GATT	General Agreement on Tariffs and Trade
GBD	global burden of disease
GCC	Gulf Cooperation Council
GDP	gross domestic product
GHTF	Global Harmonization Task Force
GISRS	Global Influenza Surveillance and Response System
Global Fund	Global Fund to Fight AIDS, Tuberculosis and Malaria
GMP	good manufacturing practice
GPA	Agreement on Government Procurement

GPO	Government Pharmaceutical Organization
GPP/GCC	Group Purchasing Program of Gulf Cooperation Council
GR	genetic resources
GSPA-PHI	WHO Global Strategy and Plan of Action on Public Health, Innovation and Intellectual Property
HAI	Health Action International
Hib	Haemophilus influenzae type b
HPV	human papillomavirus
HRC	United Nations Human Rights Council
HS	Harmonized Commodity Description and Coding System
IAVI	International AIDS Vaccine Initiative
ICDRA	International Conference of Drug Regulatory Authorities
ICESCR	International Covenant on Economic, Social and Cultural Rights
ICH	International Conference on Harmonization of Technical Requirements for Registration of Pharmaceuticals for Human Use
ICT	information and communications technology
ICTRP	International Clinical Trials Registry Platform
ICTSD	International Centre for Trade and Sustainable Development
IFPMA	International Federation of Pharmaceutical Manufacturers & Associations
IGC	Intergovernmental Committee on Intellectual Property and Genetic Resources, Traditional Knowledge and Folklore
IGO	intergovernmental organization
IGPA	International Generic Pharmaceutical Alliance
IGWG	Intergovernmental Working Group on Public Health, Innovation and Intellectual Property
IMDRF	International Medical Device Regulators Forum
IMPACT	International Medical Products Anti-Counterfeiting Taskforce
InChI	International Chemical Identifier
INN	international nonproprietary name
IP	intellectual property
IPC	International Patent Classification
IPRs	intellectual property rights
IRCH	International Regulatory Cooperation for Herbal Medicines
IRP	international reference price
IUPAC	International Union of Pure and Applied Chemistry
KEI	Knowledge Ecology International
LDC	least-developed country
LMIC	low- and middle-income country
Madrid System	Madrid System for the International Registration of Marks
MATH	Medicines, Access, Trade & Health
MDG	Millennium Development Goal
MPP	Medicines Patents Pool
MPR	median price ratio
MERCOSUR	Southern Common Market
MFN	most favoured nation
MIWI	"Made in the World" initiative
MMV	Medicines for Malaria Venture
MSF	Médecins Sans Frontières
Nagoya Protocol	Nagoya Protocol on Access to Genetic Resources and the Fair and Equitable Sharing of Benefits Arising from their Utilization to the Convention on Biological Diversity
NCD	non-communicable disease
NCE	new chemical entity
NCI	National Cancer Institute
NEPAD	New Partnership for African Development
NGO	non-governmental organization
NIC	National Influenza Centre
NICHSR	National Information Center on Health Services Research and Health Care Technology
NIH	National Institutes of Health
NME	new molecular entity
NRG	(Invented) Name Review Group
NTD	neglected tropical disease
NTM	non-tariff measure
OECD	Organisation for Economic Co-operation and Development
OECS	Organisation of Eastern Caribbean States
OHCHR	Office of the United Nations High Commissioner for Human Rights
OSDD	Open Source Drug Discovery

OWEG	Open-Ended Working Group of Member States on Pandemic Influenza Preparedness: Sharing of Influenza Viruses and Access to Vaccines and other Benefits
PAHO	Pan American Health Organization
PANDRH	Pan American Network for Drug Regulatory Harmonization
Paris Convention	Paris Convention for the Protection of Industrial Property
PARLATINO	Latin American Parliament
PATH	Programme for Appropriate Technology in Health
PBM	pharmacy benefit management
PCT	Patent Cooperation Treaty
PCV	pneumococcal conjugate vaccine
PDP	product development partnership
PEPFAR	President's Emergency Plan for AIDS Relief
PhRMA	Pharmaceutical Research and Manufacturers of America
PIC	prior informed consent
PIP Framework	Pandemic Influenza Preparedness Framework for the Sharing of Influenza Viruses and Access to Vaccines and other Benefits
PLoSNTD	Public Library of Science-Neglected Tropical Diseases
PPP	public-private partnership
PQR	Price and Quality Reporting
PRV	priority review voucher
PTA	preferential trade agreement
R&D	research and development
RTA	regional trade agreement
SARS	severe acute respiratory syndrome
SCP	Standing Committee on the Law of Patents
SCT	Standing Committee on the Law of Trademarks, Industrial Designs and Geographical Indications
SDR	Special Drawing Right
SFFC	spurious/falsely-labelled/falsified/counterfeit
SMTA	Standard Material Transfer Agreement
SPC	supplementary protection certificate
SPS	sanitary and phytosanitary
SPS Agreement	Agreement on the Application of Sanitary and Phytosanitary Measures
TB	tuberculosis
TBT	technical barriers to trade
TBT Agreement	Agreement on Technical Barriers to Trade
TBT Committee	Committee on Technical Barriers to Trade
TCM	Traditional Chinese Medicine
TDR	WHO Special Programme for Research and Training in Tropical Diseases
TK	traditional knowledge
TKDL	Traditional Knowledge Digital Library
TRIPS	trade-related aspects of intellectual property rights
TRIPS Agreement	Agreement on Trade-Related Aspects of Intellectual Property Rights
TWN	Third World Network
UNAIDS	Joint United Nations Programme on HIV/AIDS
UNCTAD	United Nations Conference on Trade and Development
UNDP	United Nations Development Programme
UNECA	United Nations Economic Commission for Africa
UNFPA	United Nations Population Fund
UNICEF	United Nations Children's Fund
USPTO	United States Patent and Trademark Office
VAT	value added tax
WASH	Water, Sanitation and Hygiene for All
WHA	World Health Assembly
WHO	World Health Organization
WIPO	World Intellectual Property Organization
WMA	World Medical Association
WTO	World Trade Organization
YLD	years lost due to disability
YLL	years of life lost

The word "country" is sometimes used to describe what are officially "customs territories", and not necessarily countries in the usual sense of the word.

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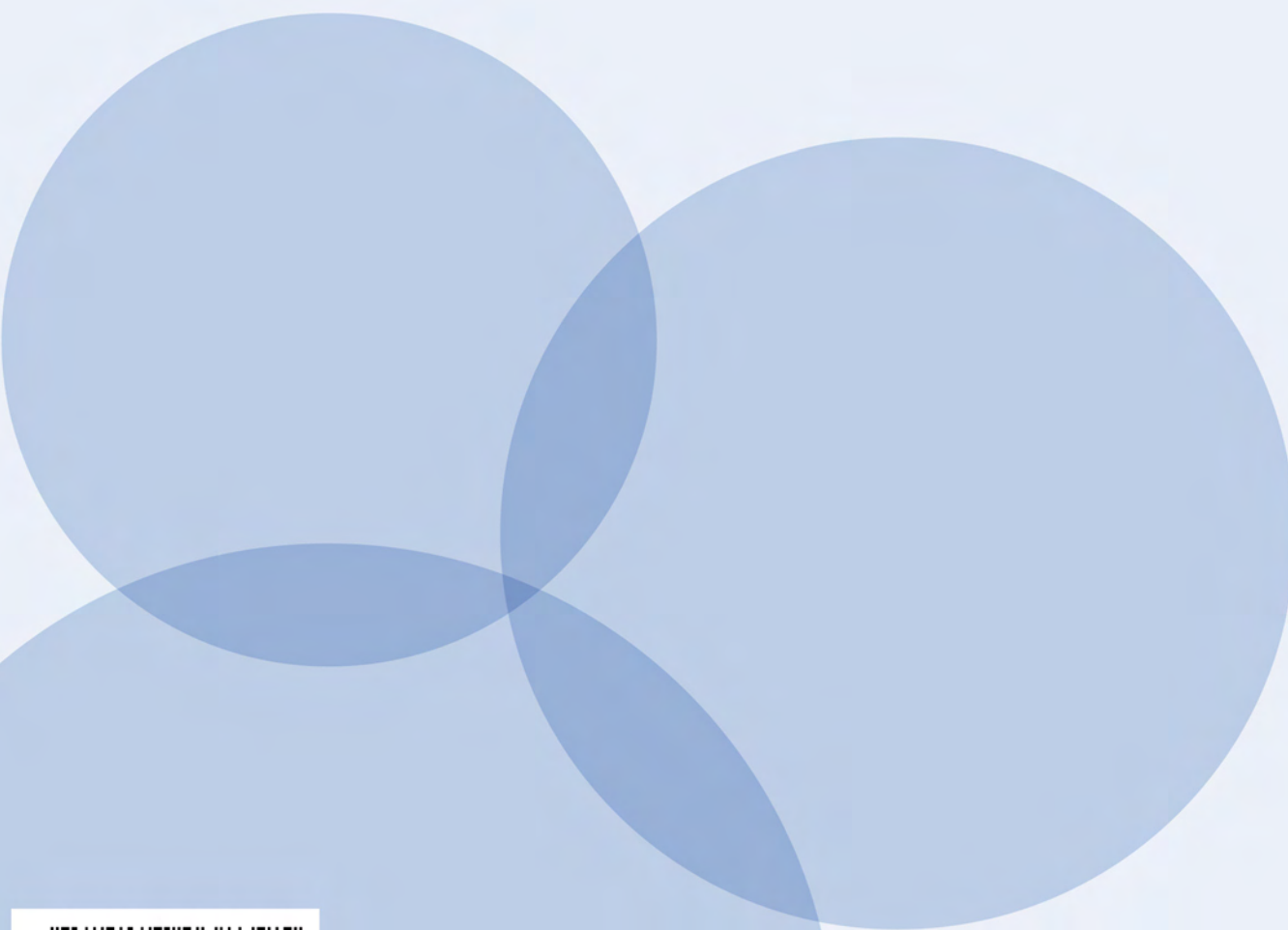
Promoting Access to Medical Technologies and Innovation

Intersections between public health, intellectual property and trade

Medical technologies – medicines, vaccines and medical devices – are essential for public health. Access to essential medicines and the lack of research to address neglected diseases have been a major concern for many years. More recently, the focus of health policy debate has broadened to consider how to promote innovation and how to ensure equitable access to all vital medical technologies.

Today's health policy-makers need a clear understanding both of the innovation processes that lead to new technologies and of the ways in which these technologies are disseminated in health systems. This study seeks to reinforce the understanding of the interplay between the distinct policy domains of health, trade and intellectual property, and of how they affect medical innovation and access to medical technologies. It captures a broad range of experience and data in dealing with the interplay between intellectual property, trade rules and the dynamics of access to, and innovation in, medical technologies. A collaborative effort by the World Health Organization, the World Intellectual Property Organization and the World Trade Organization draws together the three Secretariats' respective areas of expertise.

The study is intended to inform ongoing technical cooperation activities undertaken by the three organizations and to support policy discussions. Based on many years of field experience in technical cooperation, the study has been prepared to serve the needs of policy-makers who seek a comprehensive presentation of the full range of issues, as well as lawmakers, government officials, delegates to international organizations, non-governmental organizations and researchers.



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