

# **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 framework comprises the human rights dimension of access to medicines; 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, non-tariff measures, rules on trade in services, government procurement, and regional and bilateral free trade agreements (FTAs). In addition, it discusses the economics of innovation and access to medical technologies and outlines the interface between genetic resources, traditional knowledge and traditional medicine, IP and trade.

# Contents

A. Public health policy	44
B. Intellectual property, trade and other policy dimensions	63
C. Economics of innovation and access to medical technologies	108
D. Genetic resources, traditional knowledge and traditional medicine	112



# A. Public health policy

## Key points

- Ensuring access to essential medicines constitutes a core human rights obligation of states.
- Under United Nations Sustainable Development Goal (SDG) 3, target 3.8 specifically aims to achieve universal health coverage, including access to safe, effective, quality and affordable essential medicines and vaccines for all. Other SDGs deal with the need to put in place an environment that fosters innovation, including in low- and middle-income countries (SDG 9), and promote international cooperation to support their implementation (SDG 17).
- The WHO assesses the impact of trade agreements on public health and provides support to its member states on the implementation of TRIPS flexibilities in collaboration with other relevant international organizations.
- The WHO Global Strategy and Plan of Action on Public Health, Innovation, and Intellectual Property (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 by ensuring provision of the necessary information to enable the use of such products in a rational manner.
- The emergence of biotherapeutic products raises questions of how to build national capacities to regulate similar biotherapeutic products based on appropriate guidelines from the WHO and leading regulators.
- Antimicrobial resistance (AMR) is a global threat and has attracted increasing focus from health agencies, governments and international organizations. Among other things, a UN Interagency Coordination Group (IACG) on Antimicrobial Resistance has provided practical guidance for approaches needed to ensure sustained, effective action to address antimicrobial resistance at the global and national levels.
- Regulatory exclusivities (data exclusivity and market exclusivity) affect 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 the data.

As the epidemiological data presented in the previous chapter highlight, low- and middle-income countries (LMICs) are facing a double burden of infectious and non-communicable diseases (NCDs). 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),<sup>1</sup> 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, building on the Millennium Development Goals (MDGs), the Sustainable Development Goals (SDGs) reinforce and enhance the much-needed international platform for action on key concerns ranging from alleviating poverty to improving access to medicines, and are based on a commitment to global partnership and cooperation.<sup>2</sup>

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 SDGs, 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 creates binding obligations on parties. 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” (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, and the 1966 International Covenant on Economic, Social and Cultural Rights (ICESCR), as well as of regional human rights instruments and many national constitutions. It also constitutes the basis for the overall objective of the WHO – laid out in Article 1 of its Constitution – 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. Most countries adhere to one or more international or regional treaties and provide for certain forms of the right to health in their national constitutions (Hogerzeil and Mirza, 2011). In 2016, provisions that require governments to protect and/or fulfil the right to access quality medicines and to ensure their availability could be found in at least 22 national constitutions (Perehudoff et al., 2016).

The scope and content of the right to the highest attainable standard of health under Article 12 of the ICESCR, to which 166 countries are party, has been interpreted by the UN Committee on Economic, Social and Cultural Rights (CESCR) in General Comment No. 14.<sup>3</sup> 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.<sup>4</sup> In this context, the Special Rapporteur on the right to health identified four dimensions of access to medicines: medicines must be accessible in all parts of the country; they must be affordable to all, including those living in poverty; they must be accessible without discrimination on any of the prohibited grounds, such as sex, race, ethnicity and socio-economic status; and reliable information about medicines must be accessible

to patients and health professionals in order to facilitate informed decision-making.<sup>5</sup> 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.<sup>6</sup> The CESCR notes in paragraph 35 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 Comment No. 24, paragraph 24, the CESCR states that “parties should ensure that intellectual property rights do not lead to denial or restriction of everyone’s access to essential medicines necessary for the enjoyment of the right to health”.<sup>7</sup>

In the context of neglected diseases, where health interventions and research and development have long been inadequate and underfunded (although the picture has started to change), states are obliged to promote the development of new medical technologies through R&D and international cooperation (OHCHR and WHO, 2008).

In April 2002, the UN 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.<sup>8</sup> The Special Rapporteurs<sup>9</sup> have prepared independent reports,<sup>10</sup> following consultations with many stakeholders, including the WHO. Some of these reports deal with access to essential medicines, the role of the pharmaceutical industry and IP issues (see Annex I).

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 Annex I). Resolutions of the HRC have called upon member states to promote access to medicines for all, including through using the full provisions in the TRIPS Agreement, which provide flexibilities for this purpose. The importance of IP protection as an incentive for the development of new medicines has been recognized, as have concerns about the effects of IP protection on prices.<sup>11</sup>

Putting the right to health in the context of the 2030 Agenda for Sustainable Development, Resolution 35/23 urged countries to fully implement the SDGs, including target 3.b, which calls for support of R&D and access to affordable essential medicines and vaccines in accordance with the Doha Declaration on the TRIPS Agreement and Public Health (Doha Declaration). Further, with regard to R&D, the HRC has called upon states

to "continue to collaborate, as appropriate, on models and approaches that support delinking the cost of new research and development from the prices of medicines, vaccines and diagnostics for diseases that predominantly affect developing countries, including emerging and neglected tropical diseases (NTDs), so as to ensure their sustained accessibility, affordability and availability and to ensure access to treatment for all those in need".<sup>12</sup>

Several UN General Assembly resolutions and political declarations have noted the need to ensure access to affordable medicines. The first such resolution was passed in 2001 and concerned HIV/AIDS.<sup>13</sup> Several others have followed, including the political declarations on AMR (2016), NCDs (2018), TB (2018), universal health coverage (2019), and further political declarations on HIV/AIDS (2011 and 2016) (see Annex I). 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.

A political declaration adopted by the UN General Assembly on 8 June 2016<sup>14</sup> included a commitment to remove obstacles that limit the capacity of LMICs to provide affordable and effective HIV/AIDS prevention and treatment, including by amending national laws and regulations, so as to optimize:

- (i) the use of the flexibilities contained in the TRIPS Agreement specifically geared to promoting access to, and trade in, medicines, and while recognizing the importance of the IPR regime in contributing to a more effective AIDS response, ensure that IPR provisions in trade agreements do not undermine the flexibilities, as confirmed in the Doha Declaration
- (ii) addressing barriers, regulations, policies and practices that prevent access to affordable HIV treatment by promoting generic competition
- (iii) encourage new partnerships to reduce treatment costs and encourage development of new medicines.

## 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 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 and universal health coverage. A lack of equity in the supply of essential medicines, high prices, informal payments and out-of-pocket payments for the medication required excludes the poor and vulnerable, and does not facilitate the realization of the right to health. Key segments of the population that in many cases face barriers to accessing essential medicines include people living in poverty or other situations of marginalization, children, older people, internally displaced people, persons with disabilities and detainees. 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: developing strategies and plans of action as elaborated in paragraph 43(f) of CESCR General Comment No. 14; establishing and/or strengthening participatory accountability mechanisms; and ensuring meaningful stakeholder participation in policy development, implementation and monitoring (Hogerzeil et al., 2006; Toebe et al., 2014). Selected reports on access to medicines are summarized in Box 2.1.

## 3. Universal access and the UN Sustainable Development Goals

The SDGs consist of a set of 17 goals and 169 targets.<sup>15</sup> The SDGs aim to continue the process initiated by the MDGs,<sup>16</sup> taking a broader and more comprehensive approach, recognizing the complexity of problems affecting humanity and their interdependence on one another. All the SDGs are designed to be cross-cutting, and the interlinkages and networks within the SDGs are as important as the individual goals themselves (WHO, 2015b). This collaborative approach is particularly suitable to the area of medical technologies, where the affordability, availability, quality and appropriateness of products are influenced by of a long chain of policy decisions, market forces and other factors.

SDG 3 aims to "Ensure healthy lives and promote well-being for all at all ages". Its 13 targets cover a wide range of health issues, from combating infectious diseases and NCDs to improving reproductive, maternal, newborn and child health.

Two of the 13 targets are specifically focused on the topics of this study: target 3.8 – "Achieve universal health coverage, including financial risk protection, access to quality essential health-care services and access to safe, effective, quality and affordable essential medicines and vaccines for all" – and target 3.b – "Support the research and development of vaccines and medicines for the communicable and non-communicable diseases that primarily affect developing countries, provide access to affordable essential medicines and vaccines, in accordance

### **Box 2.1: Selected reports on access to medicines and R&D**

#### **Report of the United Nations Secretary-General's High-Level Panel on Access to Medicines (2016)**

In November 2015, the United Nations Secretary-General convened a High-Level Panel on Innovation and Access to Health Technologies (known as the United Nations Secretary-General's High-Level Panel on Access to Medicines, UNHLP). It comprised individuals from diverse stakeholder groups acting in their individual capacities. A background note submitted by the WTO Secretariat to the UNHLP called for building policy coherence in public health, supported by greater transparency and accessibility of data and efforts to enable policy responses to be based on integrated health, trade and IP data.<sup>17</sup> The submission by the WHO summarized its previous work on the topic, highlighted issues concerning patentability standards and the magnitude of therapeutic benefit, and outlined alternative and new approaches to R&D, such as Global Antibiotic Research & Development Partnership (GARDP) (see Box 3.7). WIPO stated in its Information Note for the UNHLP that it remains committed to working within the UN system and with other multilateral organizations on policy issues related to innovation and global health and that it is pleased to share its expertise and specialized data on various forms of IP with the UNHLP and indeed with all interested stakeholders.

The Report of the UNHLP (UNHLP, 2016) recommended, among other things, to work together to facilitate access to medicines through legislation, and test and implement new models of financing and rewarding R&D, and to avoid the inclusion of provisions in FTAs that interfere with the right to health. It recommended that WTO members should respect the Doha Declaration and make full use of TRIPS flexibilities, including by applying "public health-sensitive patentability criteria" and implementing legislation that facilitates the issuance of compulsory licences that are "quick, fair, predictable and implementable" for legitimate public health needs. It recommended that the Secretary-General initiate a process for governments to negotiate global agreements on the coordination, financing and development of health technologies, including a binding R&D convention that delinks R&D costs from end prices. It recommended that governments should require manufacturers and distributors of health technologies to disclose the costs of R&D, manufacture, marketing and distribution, as well as public funding that supported the R&D.

The findings of the UNHLP Report have been discussed at the WTO TRIPS Council, the World Health Assembly and the UN Human Rights Council, among others.<sup>18</sup> Some WTO members brought the UNHLP Report to the attention of the TRIPS Council in order to facilitate an exchange of views on the Panel's recommendations, as well as national experiences regarding the use of TRIPS flexibilities. Some other members questioned the scope of the Panel's mandate and terms of reference, including the statement that there was policy incoherence between the justifiable rights of inventors, international human rights law, trade rules and public health in the context of health technologies.<sup>19</sup> In SCP meetings, WIPO member states either requested discussion of the UNHLP Report to guide future work of the SCP on patents and health or stated that the Report could not build a basis for discussions in the SCP since it did not reflect member states' views.<sup>20</sup> At the WHO Executive Board and World Health Assembly, a number of member states commended the Report and called for its recommendations to be implemented in the WHO's action plan, while other member states criticized the Report.<sup>21</sup>

The UN General Assembly, in December 2016, took note of the UNHLP Report and requested "the Secretary-General to promote discussion among member states and relevant stakeholders on appropriate policy options to promote access to medicines, innovation and health technologies, as well as other, broader aspects, bearing in mind, as appropriate, all relevant reports, such as the report of the High-level Panel on Access to Medicines" as well as this trilateral study.<sup>22</sup>

#### **The Lancet Commission on Essential Medicines Policies (2017)**

The Commission identified five "core challenges for essential medicines policies": adequate financing to pay for an appropriate set of essential medicines, ensuring the affordability of essential medicines, assuring the quality and safety of essential medicines, appropriate use of medicines, and "missing" essential medicines (as noted in SDG target 3.b):

1. To finance universal access to essential medicines, governments should reduce out-of-pocket spending on medicines, track expenditures on medicines and provide adequate financing, with assistance provided by the international community to low-income countries to achieve this, where necessary.
2. To ensure affordability, the Commission recommended the better monitoring of medicines' affordability, price and availability; comprehensive policies for affordability; benefit packages that guide procurement and reimbursement; and better international transparency.

(Continued)

*(Continued)*

3. To assure medicines' quality and safety, quality assurance mechanisms should be internationally harmonized, duplication among national regulatory agencies should be minimized and these agencies should be transparent and accountable, the WHO Prequalification Team should be involved, and payers and procurement agencies should have transparent quality assurance mechanisms.
4. To strengthen use of quality medicines, independent pharmaceutical analytics units should be established to generate information to promote quality use in collaboration with other stakeholders, and stakeholder groups should implement interventions to tackle local medicines use problems, guided by information from the analytics units.
5. To develop "missing" essential medicines, a global R&D policy framework that includes new financing mechanisms should be created by governments, a general "Essential Medicines Patent Pool" should be created, and the pharmaceutical industry should better align its R&D with global health needs and develop strategies for ensuring access to medicines (Wirtz et al., 2017).

with the Doha Declaration on the TRIPS Agreement and Public Health, which affirms the right of developing countries to use to the full the provisions in the Agreement on Trade-Related Aspects of Intellectual Property Rights regarding flexibilities to protect public health, and, in particular, provide access to medicines for all".

Other SDGs also have a close link to achieving public health objectives. In particular, this concerns the SDGs dealing with the need to put in place an environment that enables innovation, including in LMICs, as well as those promoting international cooperation to support the implementation of the SDGs. SDG 9 is to "Build resilient infrastructure, promote inclusive and sustainable industrialization and foster innovation". Innovation takes place on all levels along the value chain of medicines and health products (Cornell University, INSEAD and WIPO, 2019). Actions under SDG 9 can play an important role for technology transfer and the development and commercialization of medical technologies, by enhancing manufacturing capacities, reducing logistic costs, increasing timeliness by the use of information and communication technologies and decreasing red tape in order to facilitate expeditious trade (WTO, 2018). SDG 17 stresses the need to "Strengthen the means of implementation and revitalize the global partnership for sustainable development" to support and achieve the ambitious targets of the 2030 Agenda, bringing together national governments, the international community, civil society, the private sector and other actors. Targets 17.6, 17.7 and 17.8 stress the importance of international cooperation for enhancing knowledge-sharing and the development, transfer, dissemination and diffusion of technology. In addition, as regards the contribution of trade, target 17.10 calls for the promotion of a "universal rules-based, open, non-discriminatory and equitable multilateral trading system", recognizing the key role trade plays for the overall implementation and achievement of the SDGs. This has implications for providing access to affordable medicines for all (see Chapter II, section B and Chapter IV, section A).

#### 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".<sup>23</sup> Since then, the interface of public health, IP and trade has been the subject of many debates and resolutions that reflect a growing consensus over the years (see WHO Document EB 144/17 for a list of key WHO resolutions). The 52nd World Health Assembly (WHA), in 1999, provided the WHO Secretariat with a mandate to work with WHO member states on monitoring 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.<sup>24</sup> The implementation of the resolution included the establishment of a WHO network for monitoring the implications of the TRIPS Agreement on public health. Over the years, the mandate of the WHO was further expanded to include, where requested by individual member states, technical and policy support on formulating coherent trade and health policies and the implementation of TRIPS flexibilities,<sup>25</sup> while noting that this should be done in collaboration with other relevant international organizations. The WHA recognized the importance of IPRs in fostering R&D, 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)”.<sup>26</sup> Many subsequent resolutions contain similar language. With regard to HIV/AIDS, in the same year member states highlighted “the difficulties faced by developing countries in effective use of compulsory licensing in accordance with the Doha Declaration on the TRIPS Agreement and Public Health (Doha Declaration)”.<sup>27</sup>

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 policies,<sup>28</sup> as well as to provide, on request and in collaboration with other competent international organizations, technical and policy support to countries on TRIPS flexibilities<sup>29</sup> (see Annex II for a list of the relevant WHA resolutions).

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 the 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.

Based on this mandate, the WHO has published a wide range of materials,<sup>30</sup> including on: access to hepatitis C treatment (WHO, 2016a, 2018c), the role of IP in local production, as well as patent data on specific medicines (WHO, 2016b, 2016c), the intersection between trade and health policies (WHO, 2015d), access to HIV treatment (WHO, 2014a, 2014d), making use of TRIPS flexibilities for improving public health (e.g. UNAIDS et al., 2011), developing a public health perspective on the examination of pharmaceutical patents (e.g. Correa, 2007), remuneration guidelines for the non-voluntary use of patents on medical technologies (e.g. WHO, 2005) and implementation of the WTO General Council Decision on paragraph 6 of the Doha Declaration (e.g. Correa, 2004).

The establishment of the Commission on Intellectual Property Rights, Innovation and Public Health (CIPIH) (see section 4(b) below) and the subsequent adoption of the WHO Global Strategy and Plan of Action on Public Health, Innovation and Intellectual Property (GSPA-PHI) (see section 4(c)) were key milestones in implementing this mandate.

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

In 2003, the WHO established the CIPIH “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”.<sup>31</sup>

In its final report of April 2006, the CIPIH 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 (CIPIH, 2006). 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; and the regulation of quality, safety and efficacy of medicines, as well as the impact of FTAs on access to medicines.

The report led to the GSPA-PHI, which was adopted in 2008 and 2009.<sup>32</sup>

### (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. 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 in which the potential paying market is small or uncertain.<sup>33</sup> The lack of financing for R&D into diseases disproportionately affecting developing countries was subsequently addressed by two WHO expert working groups.<sup>34</sup>

Overall, WHO 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

**Box 2.2: The Global Strategy and Plan of Action on Public Health, Innovation and Intellectual Property**

Main aims:

- 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

GSPA-PHI elements:

- 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

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 Box 2.2).<sup>35</sup>

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 that were given to the WHO through the resolutions adopted since the TRIPS Agreement came into effect. On the other hand, this overall 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".<sup>36</sup> 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",<sup>37</sup> also provides the basis for the trilateral cooperation established by the Secretariats of the WHO, WIPO and the WTO.<sup>38</sup>

Following a request approved by the WHA in 2015,<sup>39</sup> an expert panel reviewed the GSPA-PHI. Its recommendations for the overall programme review of the GSPA-PHI were adopted by the WHA in 2018.<sup>40</sup>

(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<sup>41</sup> (see Chapter III, section E)
- The Political Declaration on the Prevention and Control of Non-communicable Diseases, adopted after the First Global Ministerial Conference on Healthy Lifestyles and Non-communicable 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<sup>42</sup> (see Chapter IV, section B.4)
- A range of activities to tackle AMR, including the establishment of a non-profit R&D organization – the Global Antibiotic Research & Development Partnership (GARDP) – initiated by the WHO and Drugs for Neglected Diseases initiative (DND)<sup>43</sup> (see Chapter II, section A.5; Chapter III, section C.2; Chapter IV, section B.2)
- The establishment of the Global Observatory on Health R&D, a centralized and comprehensive source of information and analyses on global health R&D<sup>44</sup> (see Chapter III, section C.5(a))
- An initiative on the fair pricing of medicines, and associated biennial Fair Pricing Forums, in which WHO member states, non-governmental and patient organizations, and the pharmaceutical industry discuss options for a fairer pricing system that is sustainable

- for both health systems and the pharmaceutical industries<sup>45</sup> (see Chapter IV, section A.4)
- A series of analyses directed at developing a framework that could bring together and guide policy-makers and others from all relevant fields to support the local production of medicines, vaccines and diagnostics in a manner that should improve access, maximizing the potential to improve public health<sup>46</sup> (see Chapter IV, section A.10).

## 5. Cross-cutting efforts to tackle antimicrobial resistance

AMR occurs when bacteria, parasites, viruses and fungi become resistant to antimicrobial medicines that are used for treating the infections they cause. Every time an antimicrobial medicine is used, it diminishes the effectiveness for all users, because its usage increases the possibility of the development of resistance.<sup>47</sup> AMR has been recognized by the United Nations as a global threat and has attracted increasing focus from health agencies, governments and international organizations. The drivers of AMR lie in humans, animals, plants, food and the environment (IACG, 2019).<sup>48</sup> Since the impact of AMR is global, it goes beyond human health and will have economic and other consequences, and a sustained, comprehensive response needs to involve different actors and sectors, such as human and veterinary medicine, agriculture, finance, environment and consumers.<sup>49</sup> This approach is called “One Health”, and it endeavours to engage all stakeholders to address the global AMR challenge. The Food and Agriculture Organization of the United Nations (FAO), the World Organisation for Animal Health (OIE), the UN Environment Programme (UNEP) and the WHO signed a memorandum of understanding in 2018 and developed a common work plan to address AMR in a holistic manner.<sup>50</sup>

The UN Political Declaration of the High-Level Meeting of the General Assembly on Antimicrobial Resistance of 16 December 2016<sup>51</sup> suggested a number of actions needed to prevent a “post-antibiotic era,” among which was the establishment of the *ad hoc* UN Interagency Coordination Group (IACG) on Antimicrobial Resistance to provide practical guidance for approaches needed to ensure sustained, effective global action to address antimicrobial resistance.<sup>52</sup> The IACG brought together a range of multilateral organizations, including the WHO, FAO, UNEP, WIPO, the OIE and the WTO, as well as a number of individual experts.<sup>53</sup> The IACG report to the UN Secretary-General for submission to the UN General Assembly in September 2019 made a number of recommendations, which aimed at providing practical guidance for approaches needed to ensure sustained effective global action to address antimicrobial resistance (IACG, 2019). The 14 recommendations were structured into the five following areas: A. Accelerate progress in countries; B. Innovate to secure the future; C. Collaborate

for more effective action; D. Invest for a sustainable response; E. Strengthen accountability and global governance. *Inter alia*, the report aimed at supporting mobilization of action by all stakeholders; highlighted the urgency of the action needed; took a consistent “One Health” approach to AMR, cutting across human, terrestrial and aquatic animal and plant health, as well as food and feed production and the environment; focused on strengthening existing systems; and considered options for further international collaboration.

In his report to the UN General Assembly, the Secretary-General called upon the Tripartite Organizations to establish a joint secretariat and, through the support of the joint secretariat, in close collaboration with UNEP, other UN system entities, member states and other stakeholders, to further define the modalities of implementation of the IACG report in a transparent manner and undertake the required institutional and governance arrangements.<sup>54</sup>

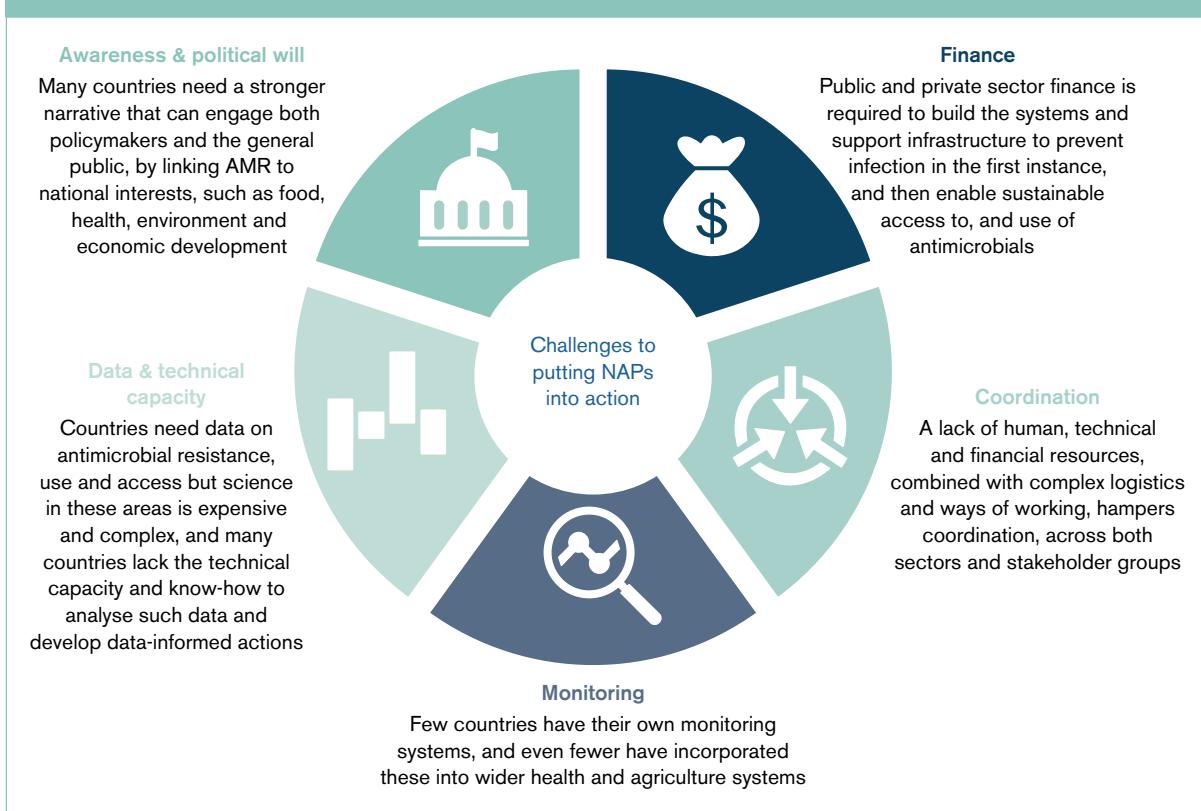
In a resolution adopted by the General Assembly on 10 October 2019, member states agreed to enhance cooperation to address AMR, as it poses a challenge to achieving universal health coverage, noting the work of the UN IACG and its recommendations as contained in the report of the Secretary-General.<sup>55</sup> AMR was the subject of the sixth WHO–WIPO–WTO Joint Technical Symposium in 2016,<sup>56</sup> and is covered in trilateral technical assistance activities.<sup>57</sup>

The work of the WHO on AMR is based on the Global Action Plan on Antimicrobial Resistance, adopted by the WHA in 2015,<sup>58</sup> and spans a range of awareness-raising, policy implementation and technical activities.<sup>59</sup> The WTO works on AMR concerns by, among other things, administering relevant aspects of the WTO Agreement on Sanitary and Phytosanitary Measures (SPS Agreement) and Agreement on Technical Barriers to Trade (TBT Agreement) (see section B.3(b)). Trade law can potentially support the implementation of international standards for appropriate use of antibiotics, including in animal husbandry and/or good manufacturing practice. While WIPO does not have an official mandate to work on AMR-related issues, WIPO collaborates with the WHO and the WTO on public health, trade and IP issues, including in relation to AMR, and has published research on the interface between antibiotic innovation and IP (Sampat, 2015; WIPO, 2015c; Jenner et al., 2017).

To address the challenge of AMR, many countries have developed national action plans.<sup>60</sup> However, a number of factors make the implementation of a national action plan difficult for many countries, among them awareness and political will, finance, coordination, monitoring, and data and technical capacity (see Figure 2.1).

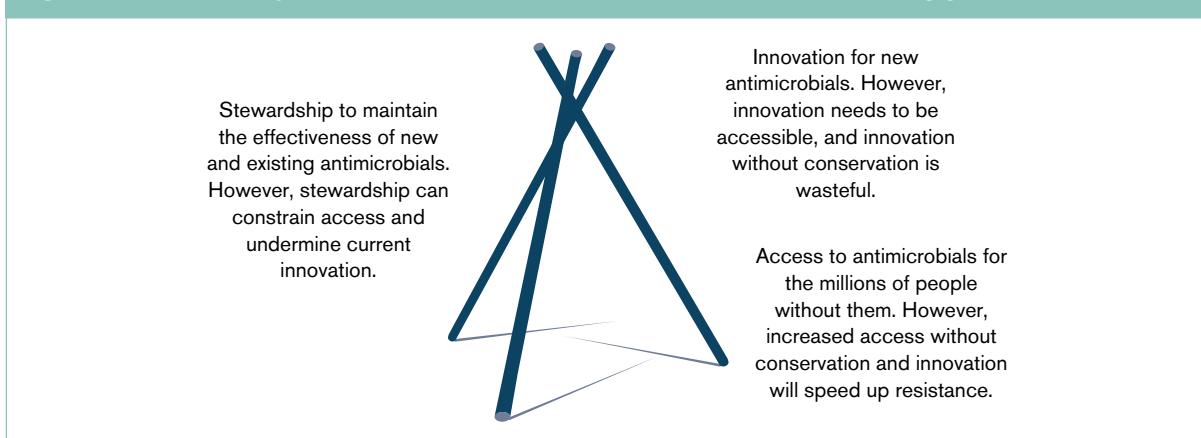
Possible measures against AMR include: improvement of hygiene; infection control to prevent the spread of resistant

**Figure 2.1: Key challenges in implementing national action plans**



Source: Interagency Coordination Group on Antimicrobial Resistance (IACG) (2018), "Antimicrobial Resistance: National Action Plans", IACG Discussion Paper.

**Figure 2.2: Stewardship, innovation and access: a delicate balance of conflicting goals**



Source: "Antimicrobial Resistance – A Global Epidemic", Background paper for the Technical Symposium on Antimicrobial Resistance: How to Foster Innovation, Access and Appropriate Use of Antibiotics? Prepared by the Secretariats of WHO, WIPO and WTO (2016).

bacteria; development of new antimicrobials against which bacteria are not resistant; and improved conservation efforts to maintain the effectiveness of new antimicrobials and of existing drugs. Stewardship, innovation and access are three key objectives in addressing AMR (see Figure 2.2). R&D in antimicrobials is further discussed in Chapter III, section C.2. Access to antimicrobial medicines is further discussed in Chapter IV, section B.2.

## 6. Regulation of health technologies

Regulation of health 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 quality, safety, effectiveness and performance of such devices (WHO, 2003b). Regulation also plays an important role in influencing access to

new products. However, unjustified regulatory measures and/or a lack of transparency in the regulatory process and slow procedures can become obstacles to access. Higher safety standards and other additional regulatory requirements may require manufacturers to provide more data to prove the safety of products or further invest in production facilities in order to 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.

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 frameworks and authorities with a clear mission, sound legal basis and realistic objectives. The authorities should have an appropriate organizational structure, an adequate number of qualified staff, sustainable financing, and access to up-to-date evidence-based technical literature, equipment and information, coupled with the capacity to exert effective market control. 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.<sup>61</sup>

Most countries have a regulatory authority and formal requirements for providing marketing authorization for medicines.

Other medical technologies, such as medical devices, are often subject to lower regulatory requirements. But the regulation of medical devices, which is done in accordance with their risk level, can be more complex and requires expert professionals to review dossiers. The WHO has published guidance in this regard – *WHO Global Model Regulatory Framework for Medical Devices Including in vitro Diagnostic Medical Devices* (2017) – and has prepared country profiles on the regulation of medical devices in order to analyse regulatory gaps and better understand needs (WHO, 2017).<sup>62</sup>

Another challenge facing regulatory agencies is the growing complexity of supply chains for pharmaceutical manufacture. For example, a company that has received good manufacturing practice (GMP) certification to supply active pharmaceutical ingredients (APIs) from a stringent regulatory authority may also purchase APIs from other manufacturers who have not been certified.

The role of the WHO in strengthening health technology regulation includes the issuance of recommended norms and standards through its expert committees, the assessment of regulatory systems and support to regulatory capacity-building at national or regional levels, and support for post-marketing activities, in addition to

the prequalification of essential medicines, vaccines and certain medical devices, in particular, in vitro diagnostics, so as to facilitate the procurement of adequate quality products internationally (see Chapter IV, section A.8).

It is a complex task to balance the benefits of the early access to new products with uncertainties regarding their quality, efficacy and safety, 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.

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

### (a) Why regulate medical products?

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
- manufacturing and trade of substandard and falsified (SF) products 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, where legal, is fair, balanced and aimed at rational use
- access is not hindered by unjustified regulatory barriers
- adequate pharmacovigilance is in place (e.g. monitoring at the population level serious adverse events).

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, governmental responses to various medical catastrophes effectively served to accelerate the development of medicines regulation. For example, the 1938 US Federal Food, Drug, and Cosmetic Act, with its 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, originally prescribed as a sedative, was given to expectant mothers experiencing morning sickness. Between 1958 and 1960, thalidomide was introduced in 46 countries worldwide, resulting in an estimated 10,000 babies being born with severe birth defects (Rägo and Santoso, 2008). In the field of medical devices, about 300,000 women in 65 countries were reportedly affected by the production of certain silicone breast implants sold from 2001 to 2010, which had a substantially higher risk of rupture and leakage than other implants.<sup>63</sup>

These disasters created a concerted push for more oversight, precisely because medical products are not ordinary consumer products. Consumers often lack the knowledge to make informed choices about when to use a particular medicine, which medicines to use and how to use them. They may 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. Medicines that are not effective or are of poor quality can lead to therapeutic failure, worsening of disease or resistance to the medicines and can cause patients to lose confidence in the health-care system.

The quality, safety and efficacy of originator medicines are in large part determined through extensive pre-clinical and clinical research and trials. For a generic medicine or similar biotherapeutic to be approved, the quality standards must be the same as for originator products, and therapeutic equivalence with originator products has to be shown through appropriate studies.

### (b) Clinical trials

Clinical trials are research studies in which large groups of human participants are enrolled to evaluate the safety and/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. The researchers measure how the subjects' health changes

when compared with no treatment (placebo) or standard treatment. Interventions that can be evaluated in clinical trials may also include surgical procedures, radiologic procedures, 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:

- **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, or 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.
- **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 thousands) by comparing the intervention against the standard of care or placebo, as appropriate. Phase III trials also serve to monitor adverse effects and to collect more information on safety.
- **Phase IV or “post-marketing” 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 (NIH, 2001).<sup>64</sup>

### (c) Research ethics

#### (i) Clinical trial ethics

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

- the benefit-risk ratio
- 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)
- 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 more than 70 years. Following the publication of the Nuremberg Code in 1947, the World Medical Association (WMA) adopted the Declaration of Helsinki in 1964. It has been reviewed regularly in the interim, with the most recent version adopted in 2013. The *International Ethical Guidelines for Biomedical Research Involving Human Subjects*, first published in 1982 by the Council for International Organizations of Medical Sciences, and most recently revised in 2016 in collaboration with the WHO (CIOMS, 2016), constitutes another globally recognized ethical guidance instrument. One essential ethical condition for comparing two treatments for a disease with a randomized controlled trial (in which 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 better than the other, yet, at the same time, there is genuine uncertainty among experts in the field over whether a treatment will be beneficial (equipoise).

Following a resolution of the WHA adopted in 2006,<sup>65</sup> an important tool designed to improve clinical trial transparency was developed by the WHO – the International Clinical Trials Registry Platform, which helps to provide public access to information about clinical trials that are under way around the world (see Chapter III, section B.7).

### *(ii) Health databases and biobanks*

Health databases and biobanks (collections of patients' biological material and associated data) are governed by ethical principles. The WMA has adopted the Declaration of Taipei,<sup>66</sup> which provides additional clinical principles for the application of the Declaration of Helsinki to health databases and biobanks.

Principles outlined in the Declaration of Taipei include:

- The rights to autonomy, privacy and confidentiality, which also entitle individuals to exercise control over the use of their personal data and biological material
- Collection and storage of data and samples must be voluntary, and consent is only valid if the concerned individuals have been adequately informed about certain key aspects of how these data/samples will be used, including information on commercial use

and benefit-sharing, IP issues and the transfer of data or material to other institutions or third countries

- Requirements for consent may be waived to protect the health of the population in the event of a clearly identified, serious and immediate threat where anonymous data will not suffice.

On IP, the Declaration of Taipei finds that "special considerations should be given to the possible exploitation of intellectual property. Protections for ownership of materials, rights and privileges must be considered and contractually defined before collecting and sharing the material. Intellectual property issues should be addressed in a policy which covers the rights of all stakeholders and [is] communicated in a transparent manner".

### *(iii) Bioethics*

UNESCO describes the field of bioethics as follows:

"Stem cell research, genetic testing, cloning: progress in the life sciences is giving human beings new power to improve our health and control the development processes of all living species. Concerns about the social, cultural, legal and ethical implications of such progress have led to one of the most significant debates of the past century. A new word has been coined to encompass these concerns: bioethics."<sup>67</sup>

According to the Universal Declaration on Bioethics and Human Rights, key bioethics principles to be respected include:

- Human dignity and human rights, including that the interests and welfare of the individual should have priority over the sole interest of science or society
- Pluralism, or accommodation of different value systems
- Transparency and access to information
- Benefit-risk ratio, autonomy, prior informed consent, privacy and confidentiality
- Respect for human vulnerability and personal integrity
- Equitable sharing of benefits resulting from scientific research with society as a whole and within the international community, in particular with developing countries
- Protecting future generations: the impact of life sciences on future generations, including on their genetic constitution, should be given due regard
- Protection of the environment, the biosphere and biodiversity.<sup>68</sup>

The diverse issues to be considered are not insulated from one another. Questions in relation to technology

and its legal protection may address a variety of levels, including:

- The ethical aspects of a technology as such (e.g. should research on embryonic stem cells be permitted?)
- The ethical aspects of national authorities granting exclusive IP rights over a technology (e.g. is it contrary to morality to patent a genetically modified mammal?)
- The ethical aspects of an individual, a firm or an institution seeking exclusive IP rights over a technology (e.g. should a publicly funded agency patent its research results? When is it unethical to do so, for instance, in the absence of any necessary consent?)
- The ethical aspects of how an IP right holder should exercise exclusive rights over a technology (e.g. should the holder of a patent over a basic research tool license it in an open or restrictive way? Are public institutions ethically obliged to license medical technology from an explicitly humanitarian perspective?).<sup>69</sup>

In terms of intergovernmental normative work, all three partner organizations of this trilateral study participate in the UN Inter-Agency Committee on Bioethics.<sup>70</sup> Key UN instruments concerning bioethics include the Universal Declaration on the Human Genome and Human Rights (1997),<sup>71</sup> the International Declaration on Human Genetic Data (2003)<sup>72</sup> and the Universal Declaration on Bioethics and Human Rights (2005).<sup>73</sup> The work of the WHO on bioethics includes, among other things, establishment of the Advisory Committee on Developing Global Standards for Governance and Oversight of Human Genome Editing and convening the Global Summit of National Bioethics Committees.<sup>74</sup>

#### (d) Biotherapeutic products

##### *(i) Background*

Biotherapeutic products (also known as biologics, biologicals or biopharmaceutical products) represent one of the fastest-growing pharmaceutical industry sectors. The increasing clinical importance of biologics is reflected in the number of products added to the WHO Model List of Essential Medicines<sup>75</sup> (e.g. bevacizumab in 2013, trastuzumab and rituximab in 2015, and adalimumab and nivolumab in 2019).

Biotherapeutic products are produced by biotechnological processes using biological material and can include blood-derived products and therapeutic recombinant proteins, among others. Often, the term is used for therapeutic recombinant proteins, therapeutic substances that are manufactured by genetically engineering a cell line (that produces and purifies the desired protein from the cell culture).

Currently, the market is dominated by originator products (reference biotherapeutic products, or RBPs), and prices for such products are often high. Similar biotherapeutic products (SBPs, sometimes called biosimilars, follow-on biologics or subsequent-entry biologics) are products that are similar in terms of quality, safety and efficacy to the originator product (the RBP).<sup>76</sup>

Biotherapeutic products can be further divided into compounds with lower molecular weight ("simple" biologics), which are generally smaller proteins that are not antibody based (e.g. insulins), and compounds with higher molecular weight ("large" biologics), such as monoclonal antibodies ("mabs"). Analytical characterization of "simple" SBPs is often easier than of larger SBPs such as mabs, and this has, in some cases, facilitated abbreviated approval pathways.<sup>77</sup>

##### *(ii) Pathways for the registration of biotherapeutic products*

Due to the complexity of the molecules, market authorization for biotherapeutic products in general requires more and larger clinical studies, compared with small-molecule products, to demonstrate that the products are similar from a structural and clinical perspective. For this reason, the WHO has developed specific guidelines for such products<sup>78</sup> and some regulatory authorities, such as the European Medicines Agency (EMA) and the US Food and Drug Administration (FDA), apply specific rules for biotherapeutic products (discussed below).

Similar biotherapeutic products approved by a regulatory authority must have no clinically meaningful differences to the reference product (FDA, 2019b).<sup>79</sup> The efficacy and safety of SBPs cannot be assured by relying on the in vitro test data and simple bioequivalence tests (a single-dose trial in healthy volunteers). Rather, current regulatory policies require that SBPs undergo large, costly clinical trials to demonstrate their similarity with the originator product. These are normally Phase II or III trials (see section 6(b) above), enrolling hundreds of patients and lasting for months. The US Federal Trade Commission (FTC) noted in 2009 that the development of SBPs is likely to cost between US\$ 100 million and US\$ 200 million and take 8–10 years, compared with US\$ 1 million to US\$ 5 million and 3–5 years for small-molecule generics (FTC, 2009). A 2016 report commissioned by Medicines for Europe stated that it can cost around EUR 150 million to EUR 250 million and take up to nine years to develop SBPs (Simon-Kucher, 2016).

Regulatory systems are tasked with defining when such a product can be considered "similar" to, or "interchangeable" with an RBP, and different regulations for different categories of similar biotherapeutic products may be needed.

While the characteristics of a small-molecule medicine are mainly defined by its chemical structure, making such medicines relatively easy to replicate, biotherapeutics consist of complex proteins that often cannot be fully characterized by chemical or physical methods. Slight variations in the production process, including cell line selection and growth medium, can significantly affect the unique properties of biotherapeutic products and may thereby have an impact on the clinical safety and efficacy of the product. The product characteristics and manufacturing process of SBPs should, therefore, ideally deviate as little as possible from the process used for the reference product.

Some medicines regulatory authorities, such as the FDA, EMA<sup>80</sup> and Swissmedic,<sup>81</sup> as well as the WHO,<sup>82</sup> have issued guidelines with respect to the evaluation and/or authorization of SBPs. Guidelines and regulatory pathways are taking shape in many middle-income countries, for example, Colombia, India, Malaysia, Peru and the Russian Federation have all published biosimilar guidelines (Welch, 2016b; GaBI, 2018a). Before the establishment of specific pathways for the registration of SBPs, some countries have approved a number of non-originator biotherapeutic products since the early 2000s (Bosco and Chance, 2013; GaBI, 2018b). These biotherapeutics are different from SBPs approved through demonstrating comparability with the RBP.

### *(iii) What will be the effect of SBPs on prices?*

Due to the complexity of biotherapeutic products and their manufacturing processes, and the need for randomized controlled trials (trials in which patients are randomly allocated to receive either the test substance or a placebo; see also section 6(b) above), developing a biosimilar is much more costly and time consuming than developing generic versions of traditional small-molecule medicines. There is uncertainty as to how much competition can be expected from SBPs and to what extent such competition can lead to price decreases. 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. Early estimates predicted price decreases would be limited to

around 10–40 per cent (Mulcahy et al., 2014; Blackstone and Fuhr, 2013). Substantial price reductions of around 70 per cent have been seen in Denmark, Finland and Norway for similar infliximab, translating to large increases in SBP market share (Chopra and Lopes, 2017; Schafer et al., 2016; Welch, 2016a). Many companies that are well known as originators have entered the SBP market.

The use of biotherapeutic products is limited in many LMICs' health systems due to a range of factors, including the generally high prices of biotherapeutic product, the need (in some cases) for health facilities that can support supervised infusions, and the need (in some cases) for complex diagnostic technology. However, the use of biotherapeutic products in resource-limited health systems is increasing. A 2017 WHO pilot project was launched to prequalify selected biotherapeutic products and SBPs (see also Chapter IV, section A.11(a)). The WHO's Prequalification Team has developed a WHO pilot procedure for prequalification of two biotherapeutic products – rituximab and trastuzumab – and is inviting manufacturers to submit an Expression of Interest (EOI) for product evaluation to the WHO Prequalification Team – Biotherapeutic Products.<sup>83</sup>

The WHO has partnered with the Utrecht Centre for Affordable Biotherapeutics (UCAB) in an initiative to develop an SBP, palivizumab, a treatment that prevents respiratory infections in infants born prematurely. It is estimated that the SBP version can be produced for US\$ 250 per patient, equivalent to about 5–15 per cent of originator prices in high-income countries (Crowe, 2017; Sanchez-Luna et al., 2017).

### (e) Future of regulation

A range of "advanced therapies" or "advanced therapy medicinal products" is being approved by regulators and entering clinical use,<sup>84</sup> including gene therapies, cell therapies and tissue engineering (see Boxes 2.3 and 2.4). Nanoparticles that deliver chemotherapy medicines selectively to cancer cells are in development.<sup>85</sup> These advanced therapies may offer revolutionary treatments for a number of diseases or injuries, such as Alzheimer's disease, sickle cell disease, severe liver conditions, cancer and muscular dystrophy, as well as skin injuries in burn victims. They offer huge potential for research, patients and industry.

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. 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.<sup>86</sup>

### **Box 2.3: CRISPR-Cas9 gene-editing technology**

CRISPR (clustered regularly interspaced short palindromic repeats) is a naturally occurring bacterial defence system, which uses an enzyme to identify and cut the DNA of an invading virus to disable the attack. Researchers have adapted this mechanism to cut DNA at a specific location. For example, CRISPR-Cas9 enables researchers to deploy the Cas9 enzyme to a precise portion of DNA. The Cas9 enzyme then acts as “scissors” to cut the targeted segment and then a customized DNA segment can be inserted into the DNA strand. This technology is considered to be a breakthrough discovery. It provides researchers, for the first time, with a highly flexible, precise, easy-to-use and efficient tool for editing the genomes of living cells, among other uses. More recent developments include the use of CRISPR-Cas13 to edit RNA instead of DNA.<sup>87</sup>

Therapies based on CRISPR are in development for a number of diseases, including sickle cell disease and certain cancers (Mullin, 2017). CRISPR is expected to contribute to the development of other therapies, for instance, increasing the efficacy of CAR T-cell therapy (see Box 2.4) (Eyquem et al., 2017). CRISPR is also being used in the development of LMIC-directed technologies. For example, a CRISPR-based diagnostic system has been developed that is able to detect a range of viruses, including Zika and dengue virus, with a very high degree of sensitivity. It is believed that this system, once developed further, will be easily adaptable to different viruses, rugged in “field” conditions and affordable (Cohen, 2017).

However, CRISPR-based technology is still not fully understood, and potential undesired side effects are being researched.<sup>88</sup> A number of legal, regulatory and ethical questions have been raised, specifically with respect to the application of the technology in clinical germline editing (Lander et al., 2019).

Public discussion of the patent landscape for CRISPR technology has focused on the long-running patent dispute between the Broad Institute of Harvard University and the Massachusetts Institute of Technology on one side and the University of California at Berkeley on the other (Jewell and Balakrishnan, 2017). Studies investigating the patent landscape have found a variety of patent holders, including a hospital, a number of universities, individual researchers and companies, with main patent clusters in China, Europe, Japan, the Republic of Korea and the United States (Ferreira et al., 2018; Martin-Laffon et al., 2019). While the first patents were identified in 2001, increased patent activity has been observed since 2012. By July 2019, 12,000 CRISPR patents had been identified worldwide, falling into 4,600 patent families with more than 740 CRISPR patents granted (Kwon, 2019, referring to data available from [www.ipstudies.ch/crispr-patent-analytics/t](http://www.ipstudies.ch/crispr-patent-analytics/t)). Three main application fields for patent commercialization have been found: (1) CRISPR-Cas9 used in medical applications with a focus on human therapeutics and drug discovery; (2) research tool applications, cell line and animal models; and (3) agriculture and food applications (Ferreira et al., 2018). Aspects of licensing approaches by some patent holders are addressed in Chapter III, sections C.5(g) and D.5(c)–(d).

### **Box 2.4: CAR T-cell therapy**

Chimeric antigen receptor T-cell (CAR T-cell) therapy is a novel type of cell therapy for some people living with some types of blood cancer. T-cells are a type of immune cell. By altering the T-cells of the patient, the therapy boosts their ability to recognize and kill specific cancer cells. CAR T-cell therapy involves collecting a sample of the patient's T-cells and then modifying the cells through gene editing to produce chimeric antigen receptors on their surface, which enable the T-cells to recognize tumour cells more effectively. The CAR T-cells are then reinfused into the patient, where they activate the patient's immune system so that it attacks cancer cells targeting the specific antigen on the tumour cells. Success is not just a function of the engineered cells, but of the patient's own immune system.<sup>89</sup>

CAR T-cell therapies first obtained FDA approval in 2017 for the treatment of advanced leukaemia in some children and adults. It is believed that CAR T-cell therapies may eventually offer curative treatment for some cancers. Significant proportions of patients in early clinical trials, for certain cancers, achieved complete remission (the disappearance of all signs of cancer). However, the majority of CAR T-cell clinical trials currently under way are for the treatment of haematological malignancies; while the use of CAR T-cell therapy in solid tumours has thus far had limited success, it is an area of active development (Pettitt et al., 2018; Shum et al., 2018). Due to the potential for CAR T-cell therapies to cause serious side effects, as part of regulatory approval, a company offering such therapy must manage long-term follow-up studies to fulfil post-marketing requirements and must collect patient safety information for 15 years.<sup>90</sup>

A review of patent activity related to CAR T-cell therapy has found early patent publications in the mid-2000s with publications increasing markedly in 2013 (Jürgens and Clarke, 2019). It has found 1,914 patent documents in 399 patent families worldwide, with the biggest group of applications made through the Patent Cooperation Treaty (PCT), followed by applications with the patent offices in China, the European Patent Office (EPO), the United States and a number of other countries. The analysis revealed that the most cited patent was held by the University of Pennsylvania.<sup>91</sup> It found strong partnership between the University of Pennsylvania and Novartis, evidenced by co-authorship in numerous patent applications. It also concluded from patent applications with co-inventors from the same countries that little international cooperation took place. According to Armstrong (2019), the number of published international patent applications related to CAR T-cell technology increased from 60 in 2014 to 450 in 2018, the main applicants being universities in the United Kingdom and the United States and pharmaceutical companies. Possible patent law issues associated with CAR T-cell therapies include questions related to patentable subject matter and industrial applicability/utility (see Chapter II, section B.1(b)(iii)), patenting material that exists in nature (see Chapter III, section D.4(a)), and exclusions from patentability for diagnostic and therapeutic methods (see Chapter IV, section C.1(a) and Box 4.17). Where such exclusions apply, patent claims may seek patent protection using “active treatment step” and “second/further medical use claims” (Black, 2017; Gainey, 2018; see also Chapter III, section D.4(c)).

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

Also, the increasing use of mobile devices in health brings new regulatory issues that need to be addressed, such as accreditation of applications, liability, interoperability, (cross-border) data flows and patient data confidentiality.<sup>92</sup>

#### (f) Regulatory exclusivities

Regulatory exclusivities are conferred by national or regional law. The period of protection of regulatory exclusivities may overlap with, and is independent of, the term of patent protection (see Figure 2.3). Regulatory exclusivities is an umbrella term that encompasses data exclusivity, which is one way of implementing test data protection (see section B.1(c)) and market exclusivity:

- Data exclusivity provisions prevent regulatory authorities from relying on the reference product test data for approval of a generic medicine for a given period of time.
- Market exclusivity provisions prevent a regulatory authority from granting market approval for a certain period of time. Market exclusivity is distinct from data exclusivity because it prevents a competing firm from obtaining regulatory approval whether or not it is referring to the originator's data (Thomas, 2014). For example, once the data exclusivity period has lapsed, a competitor can rely on the originator test data to submit an application for approval, whereas market exclusivity provisions will still prevent market authorization being granted until the market exclusivity period has also lapsed.

Countries that grant data exclusivity rights generally provide for a fixed period of between five and eight 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 as that where the test data protection is sought. Some WTO members, such as the European Union and the United States, allow an additional period of data exclusivity for new indications and formulations.

In the European Union, originator medicines granted approval by the EMA enjoy ten years of marketing protection, and eight years of data protection, both starting at marketing authorization.<sup>93</sup> This means that the EMA or a national authority could begin assessing the application of a prospective generic competitor at the end of year 8 (relying on reference product data to support

their application), while marketing authorization could only be granted at the end of year 10. The ten-year marketing protection period can be extended to 11 years if the holder of the marketing authorization obtains an authorization for one or more new therapeutic indications during the first eight years that are found to bring significant clinical benefit over existing therapies. This is known as the “8+2+1” system of exclusivities granted in the European Union.<sup>94</sup>

A separate exclusivity is granted in the European Union for drugs designated as orphan drugs (see Chapter III, section B.6). Orphan exclusivity in the European Union confers ten years of market exclusivity from any *similar*<sup>95</sup> product for the same indication as the originator product, and can be extended by two years for the completion of a paediatric investigation plan that sets out paediatric use of an orphan drug.<sup>96</sup> Orphan exclusivity in the European Union runs in parallel to general protection periods granted to all originator medicines (outlined in the paragraph above), and may be shortened from ten to six years, if, at the end of the fifth year, the product no longer meets the criteria for orphan exclusivity.<sup>97</sup>

The US legislature has introduced a range of different types of regulatory exclusivity, including five years' data exclusivity for new chemical entities (Thomas, 2015). As regards biologics, the Biologics Price Competition and Innovation Act provides that similar biotherapeutic products cannot be submitted for approval for four years after the date of first approval of the reference product, nor can they be approved until 12 years after that date if they rely on data submitted by the originator company.<sup>98</sup> The United States awards one year of exclusivity to the first “interchangeable” SBP to enter the market (see section 6(d) above).<sup>99</sup> Each of the exclusivities varies in its eligibility criteria, scope of protection and underlying policy objectives (see Box 2.5 for selected examples). The time frame for these exclusivities can have a significant impact on the time it takes for generics or SBPs to reach the market.

Following the 1997 introduction of paediatric marketing exclusivity,<sup>100</sup> there was a reported increase in paediatric research and in products having their labelling changed to account for paediatric use. However, much of the research conducted for paediatric marketing extensions was conducted on products that treat conditions of public health importance for children (e.g. high blood pressure). It has been reported that some manufacturers have delayed paediatric trials until late in the period of their product's marketing exclusivity (Kesselheim, 2010).

In countries where data exclusivity exists, exceptions and limitations to data exclusivity may apply. US law shortens the period of data exclusivity 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

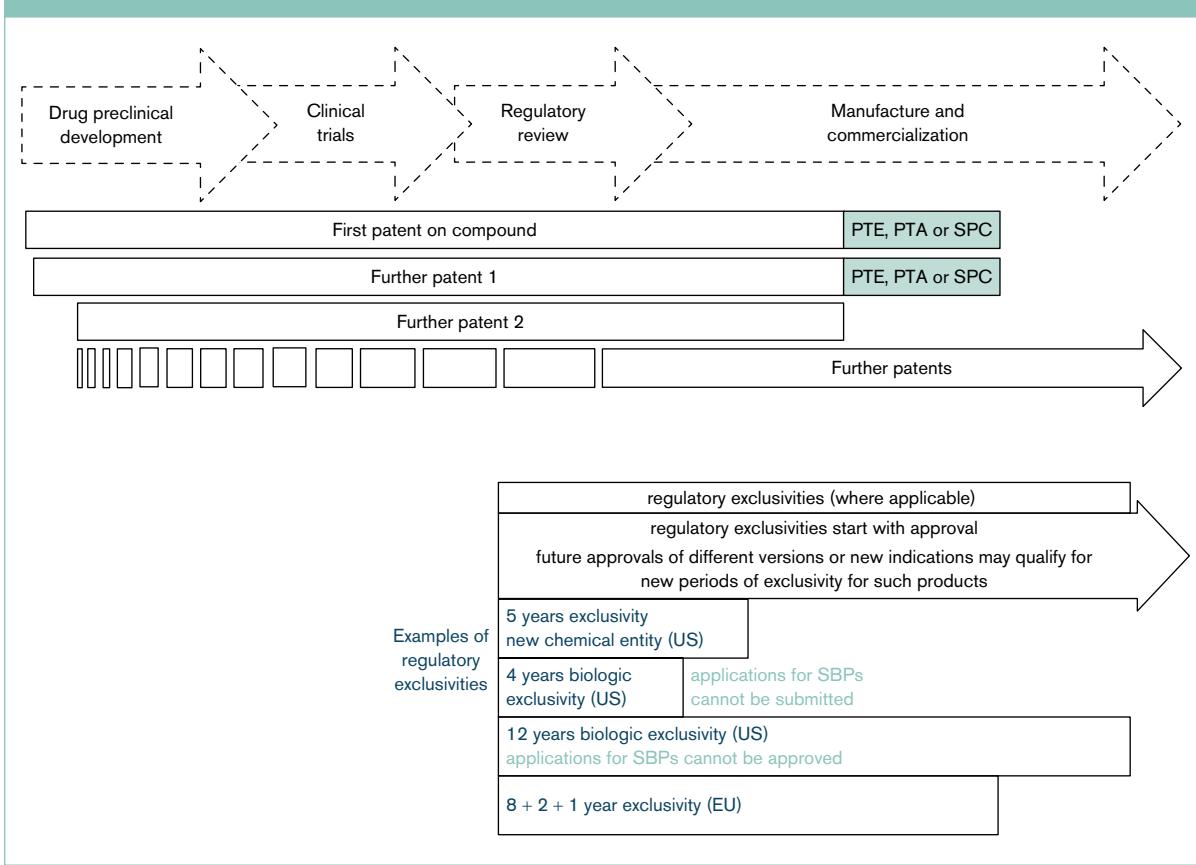
**Box 2.5: Selected types of US regulatory exclusivity**

Type	Eligibility criteria	Scope of protection	Period	Objective
New Chemical Entity (NCE) Exclusivity	Drugs containing NCEs – i.e. the FDA has not previously approved at least one of its active ingredients	This is a general data exclusivity provision for non-biotherapeutics in the United States  No generic application accepted for drugs containing the same active ingredient, unless the sponsor submits a New Drug Application (NDA) and has performed all the required pre-clinical and clinical studies itself	5 years	To encourage development of innovative medicine products that include an entirely new active ingredient
New Clinical Study Exclusivity (for an Original or Supplemental NDA)	NDAs or Supplemental NDAs that contain reports of new clinical studies conducted by the sponsor, which are essential to FDA approval of that application (Supplemental NDAs make changes to product that is already the subject of an NDA)	This is a general data exclusivity provision for non-biotherapeutics in the United States  No generic application may be approved for the same drug, for the same indication  The FDA may still accept generic applications and may issue tentative approval of a generic drug, which will become effective once the exclusivity period has ended  An NDA for the same drug, for the same indication, will still be accepted if the sponsor has performed all the required pre-clinical and clinical studies itself	3 years	To encourage improvements upon drugs that are already known
Orphan Drug Exclusivity	Orphan drugs to treat a rare disease or condition: (1) affecting fewer than 200,000 people in the United States; or (2) for which there is no reasonable expectation that sales of the drug would recover its costs of development	No generic application may be approved for the same drug, for the same indication  Applies even where the sponsor of a subsequent application has performed all the required pre-clinical and clinical studies itself  The FDA may still grant marketing approval for the same drug, for a different indication	7 years	To encourage firms to develop pharmaceuticals to treat rare diseases and conditions
Qualifying Infectious Disease Product Exclusivity	Antibacterial or antifungal drugs intended to treat serious or life-threatening infections	Extends the period of New Chemical Entity, New Clinical Study or Orphan Drug Exclusivity	5 years (starting from end of previous period of exclusivity)	To provide additional incentives for development of antibiotics
Pediatric Exclusivity	NDA holders or applicants who complete pediatric studies requested by the FDA	Extends the period of existing patent or regulatory exclusivity protection	6 months (starting from end of previous period of exclusivity or patent protection)	To improve availability of appropriate pediatric labelling on drug products
Biologics Exclusivity	Biologics	Applications for follow-on biologics will not be accepted  Applications for follow-on biologics may be accepted but will not be approved if the follow-on biologic relies upon data developed by the sponsor of the reference biologic	4 years  12 years	To encourage the development of biologic products

Source: J. R. Thomas, *Pharmaceutical Patent Law*, 3rd edition (2015).

is not being marketed in its territory.<sup>101</sup> Colombia does not provide data exclusivity if the originator product is not marketed in its territory 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.

Data exclusivity has the potential to impede the implementation of compulsory licensing of patents. For example, in 2016, the issuing of a compulsory licence was considered by the Government of Romania for the hepatitis C medicine sofosbuvir, but it was reportedly not pursued because EU data exclusivity would expire only in 2024 (Paun, 2016; 't Hoen et al., 2017).

**Figure 2.3: Illustration of terms of patent protection and regulatory exclusivities**

Source: WHO, WIPO, WTO Secretariats.

**Notes:**

- Timelines are not proportionate, and timing of patent and regulatory elements will vary from case to case. Patent grant and regulatory approval can take a shorter or longer period.
- The word "patent" refers to the patent application filed, the grant of a patent and the maintenance of a patent. The left side of the "patent" bars indicate the date of patent filing. Due to the diversity in time needed for the patent procedure, no indication of patent grant is made in the chart. Granting of a further patent is independent of earlier granted patents and does not extend the patent protection period of any earlier patent.
- The period of patent protection available in national law does not end before 20 years counted from the filing date. Often patents are abandoned, invalidated, not maintained, etc. before the maximum protection period of 20 years is reached.
- The first patent normally covers the compound, and further patents may cover other aspects, such as combinations, uses, etc. as provided in domestic law. The first patent and further patents are not necessarily held by the same entity.
- Some jurisdictions provide for limited patent term extensions (PTEs), limited patent term adjustments (PTAs) or limited additional protection in the form of supplementary protection certificates (SPCs). Not every patent will be extended. PTEs, PTAs and SPCs do not have always have the same duration.

In some countries, exceptions to data exclusivity may cover the protection of the public interest, such as where compulsory licences are issued to protect public health.<sup>102</sup> For example, Chile and Malaysia waive data exclusivity if the product is the subject of a compulsory licence, and Chile, Colombia and Malaysia waive data exclusivity where necessary to protect public health.<sup>103</sup> Another example concerns where it is necessary for exports under compulsory licence under the Special Compulsory Licensing System: Canada and the European Union waive data exclusivity for products produced under compulsory licence for export.<sup>104</sup> Data exclusivity waivers are also provided within the Medicines Patent Pool licensing agreements, as well as in other licensing agreements aimed at enabling generic competition in LMICs.<sup>105</sup>

The awarding of additional exclusivities, such as data exclusivity, generally increases the expectation of revenues for a manufacturer bringing a new product to market and thus, in theory, offers incentives for product development at the expense of delayed generic entry. Some studies are available on the relationship between data exclusivity and other regulatory exclusivities and innovation (Williams, 2017; Goldman et al., 2011; Gaessler and Wagner, 2018; Budish et al., 2015).

### (g) Patent linkage

Normally, different agencies are responsible for granting patents (patent offices) and for approving medicine products for entering the market, each of them operating

independently. Nevertheless, some countries link regulatory approval, normally based on quality, safety and efficacy, to the patent status of the medicine. This is referred to as “patent linkage” and 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 medicine product. A stronger version of patent linkage prohibits the granting of marketing approval for a medicine product by a third party prior to the expiration (or invalidation) of a patent covering that product. An even stronger form of linkage prohibits not only the granting of marketing approval but also the consideration of a generic medicine application during the patent period.

Some stakeholders argue that patent linkage provisions place 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 of the product in the market, if the regulatory agency is unable to begin a review of the generic medicine application during the patent period. On the other hand, proponents of patent linkage argue that it prevents unnecessary infringement and that it increases transparency and predictability through the identification of patents relevant to each pharmaceutical product as part of the marketing approval process.

For explanation and discussion of patent rights and the patent system, see Chapter II, section B.1(b); Chapter III, section D.3–4; and Chapter IV, section C.1–4.

## B. Intellectual property, trade and other policy dimensions

### Key points

- Intellectual property (IP) protection is intended to strengthen market-based incentives to invest resources in product development and the marketing of new technologies.
- The global legal IP framework is defined in particular by the treaties administered by WIPO, and the WTO TRIPS Agreement. Multilateral standards for IP are generally 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. Published patents and patent applications are an important source of technical and legal information.
- 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 international non-proprietary names (INNs) of the products.
- The TRIPS Agreement allows for flexibilities in national implementation. The subsequent Doha Declaration confirmed “the right of WTO members to use, to the full, the provisions in the TRIPS Agreement, which provide flexibility” to protect public health.
- Competition law and policies have an important role to play in enhancing access to health technologies and fostering innovation. Unwarranted restrictions on competition, whether resulting from the abuse of a dominant position resulting from intellectual property rights (IPRs) or other factors, or anti-competitive agreements, can be addressed through competition law enforcement. With regard to innovation, a key concern is merger control, where competition authorities must ensure that mergers do not threaten R&D pipelines.
- 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.
- The WTO Agreement on Government Procurement provides an appropriate framework for rules at the international level that are intended to promote efficient trade and best practices in the area of public procurement. These can contribute to improvements in the accessibility and affordability of medicines and thus towards more efficient and cost-effective health systems.
- Free trade agreements (FTAs) have shaped the framework for access and innovation in many countries.

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

### 1. Intellectual property systems

IPRs 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. IP protection is generally intended to strengthen market-based incentives 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 (see Chapter III, section B.4 for discussion of a range of incentive models for innovation).<sup>106</sup>

In as much 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 exception<sup>107</sup>

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 from patentable subject matter, definition of patentability criteria, exceptions and limitations to 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 global 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 2.6).

The TRIPS Agreement has considerable implications for the application of IP to medical technologies, notably through the implementation of international standards requiring patents to be available for inventions in all areas of technology, including pharmaceutical products, and the requirement to protect undisclosed test data submitted for obtaining marketing approval against unfair commercial use and disclosure. Negotiation of the TRIPS Agreement and its subsequent implementation have seen a continuing focus on IP and health issues (see Box 2.7) and, particularly, the nature and impact of obligations under the TRIPS Agreement on pharmaceutical patents and test data protection.

#### **Box 2.6: 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. It applies to industrial property in the widest sense, including patents, trademarks, service marks, industrial designs, utility models, trade names and the repression of unfair competition. It provides, *inter alia*, 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 trademark 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 trademarks.

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, is 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 exercise of the exclusive rights conferred.
- The registration of a trademark 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, or are liable to create confusion, or are 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.

**Box 2.7: 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 The TRIPS Agreement enters into force, and the WTO is established and is given legal and administrative responsibilities for the TRIPS Agreement.
- 2000 Most TRIPS obligations come into effect for developing-country members, while a transition period is applied in relation to pharmaceutical product patents.
- 2000 WTO panel rules on TRIPS dispute concerning regulatory review (“Bolar”) exceptions to facilitate entry of generic medicines.
- 2001 WHO–WTO Workshop (Høsbjør, Norway) discusses Differential Pricing and Financing of Essential Medicines.
- 2001 Doha Declaration on the TRIPS Agreement and Public Health is adopted, including extension of transition period to 2016 for least-developed country (LDC) members to implement patent and test data protection.
- 2002 WTO General Council adopts waiver of obligation to provide for exclusive marketing rights during transition period for LDCs.
- 2003 “Paragraph 6” mechanism is adopted 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 extends the transition period for LDCs to implement the TRIPS Agreement as a whole until 2013.
- 2013 TRIPS Council extends the transition period for LDCs regarding the implementation of TRIPS until 2021.
- 2015 TRIPS Council extends the transition period for LDCs to implement patent and test data protection in the pharmaceutical sector until 2033. General Council waiver of obligations to provide for mailbox applications and exclusive marketing rights during the transition period.
- 2017 Protocol Amending the TRIPS Agreement (new Article 31bis) enters into force.

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”, “the transfer and dissemination of technology”, the mutual advantage of both “producers and users of technological knowledge”, and also “social and economic welfare”. The principles set out in Article 8 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 adopted at 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 framework of the TRIPS Agreement (discussed further below, after a general review of IP issues).

The multilateral standards for each form of IP are generally minimum standards, which 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 and, where applicable, regional 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 (see Chapter IV, section C.5) and are also motivated by a country’s domestic policy considerations (see section B.5 below).

The principle of non-discrimination forms a cornerstone of the international IP system. “National treatment” provides that countries must not discriminate between their own nationals and 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 was 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.<sup>108</sup> In regard to the non-discrimination principles, the TRIPS Agreement is thus significantly different from other main WTO agreements, in that it normally does not permit countries to discriminate against nationals of their trading partners.

Apart from such general principles, each form of IP is subject to specific standards, reflecting its 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

Since 2000, there has been 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 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 of the patent system is to make investment in innovation attractive and to offer a mechanism that ensures that the knowledge contained in the patent application is accessible to society. Among other obligations, 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, in theory, the under-provision of new inventions. A 2008 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.<sup>109</sup>

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.<sup>110</sup>

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 grant of patents, 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 and the TRIPS Agreement. 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 negotiations of the TRIPS Agreement, 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 manufacturing processes.<sup>111</sup> The duration of patents also varied considerably from country to country.

The TRIPS Agreement is the first multilateral treaty to stipulate the core criteria for patentable subject matter (see also section (iii) below on patentability criteria). The TRIPS Agreement 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. 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. These requirements came into effect progressively, but now apply to all WTO members, except LDCs, for which a transition period was extended until 2033 (see Box 2.7).

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 4bis 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 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 2.8). 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 patent jurisdictions; a number of regional agreements have also harmonized and simplified patent laws within the respective regions.<sup>112</sup>

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 claims may be amended in one country and remain unchanged in another (regarding claims, see also section (vi) below). Consequently, the same PCT application may result in a patent grant in one country, a patent grant with restricted claims 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

#### **Box 2.8: The Patent Cooperation Treaty**

The Patent Cooperation Treaty (PCT)<sup>113</sup> makes it possible to seek patent 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 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 be novel, to involve an inventive step (to be non-obvious) and to be industrially applicable 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 if requested by the applicant. If the applicant decides to continue with the international application, with a view to obtaining national or regional patents, the applicant needs to commence separately the national/regional procedure in each PCT contracting state in which the applicant wishes to obtain patent protection (“enter the national phase”). During this “national phase”, a country’s authorities will apply the substantive rules on eligibility for patents that are defined under national law, which may result in different outcomes from country to country.<sup>114</sup> If the applicant does not initiate the national phase before a specific office within the required time limit, the application loses effect with the same consequences as a withdrawal of a national application.

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.

### *(iii) Basic patent issues*

Patents are territorial rights. In addition, patent protection is limited in time. Patent laws generally provide that patent protection shall not end before the expiration of 20 years counted from the filing date. 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.<sup>115</sup> 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 be abandoned by a failure to respond to patent office notices on time, a failure to pay maintenance fees or filing a written expression of abandonment. Patents may also be invalidated in court or administrative procedures based on grounds established by the domestic law. In countries where no patent application is filed, or where a patent application has been withdrawn or refused, or where a granted patent is no longer in force, a published invention enters into the public domain, provided there is no other patent or other right covering the same technology. The WIPO Committee on Development and Intellectual Property (CDIP) has examined the relationship between patents and the public domain and produced a Study on Patents and the Public Domain.<sup>116</sup>

While a published patent application informs the public of the fact that an application is pending, patent protection begins only with patent grant. Domestic law may provide for provisional protection of published patent applications, where available, usually conditional on patent grant and availability of the publication in the national language. Such provisional protection may take the form of payment of royalties, for example, in European Patent Office (EPO) member states or in the United States. Not all countries provide for provisional protection; for example, the laws of Brazil and India do not provide for provisional protection.<sup>117</sup>

In line with Articles 27 and 29 of the TRIPS Agreement, certain patentability criteria are common to all patent laws: (i) the subject matter claimed in the application must consist of 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); and (v) the invention must be properly disclosed. These requirements apply cumulatively. Failure to satisfy any one criterion leads to rejection of a patent application.<sup>118</sup>

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 with more specific guidance, often basing this guidance on cases previously decided by the responsible courts.<sup>119</sup> Such guidelines can also assist patent examiners when new technologies emerge or where patent applications and the application of patentability criteria raise ethical concerns (see Box 2.9). The EPO has issued examination guidance, for example, for biotechnological inventions,<sup>120</sup> computer-implemented inventions<sup>121</sup> and artificial intelligence and machine learning<sup>122</sup> as part of the EPO Guidelines for Examination.<sup>123</sup>

### **Inventorship, ownership and entitlement to apply**

Every invention is created by 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 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 inventions derived from 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. 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

### **Box 2.9: 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<sup>124</sup> provides a flexible framework for moral assessments to be made, which leaves room for societal and ethical values to be taken into account.<sup>125</sup>

In 2008, the Enlarged Board of Appeal of the EPO ruled that claims were not patentable if directed to products which could only be prepared by a method necessarily involving the destruction of human embryos, even if the said method was not part of the claims.<sup>126</sup> In 2014, the EPO Board of Appeal confirmed the exclusion from patentability for inventions which make use of publicly available human embryonic stem cell lines originally derived by a process resulting in the destruction of human embryos.<sup>127</sup> In 2011, the Court of Justice of the European Union, while not touching upon questions of a medical or ethical nature, ruled that any human ovum capable of commencing the process of development of a human being is a “human embryo” and claims concerning the use and destruction of a human embryo are excluded from patentability.<sup>128</sup> In 2014, the Court of Justice of the European Union (CJEU) held that unfertilized human eggs whose division and development had been stimulated by parthenogenesis but which, in the absence of paternal DNA, were not capable of developing into a human being (“parthenotes”) did not constitute a human embryo and parthenotes were not excluded from patentability.<sup>129</sup> In Australia, stem cells are patentable so long as the material is removed from its natural state and that there is demonstrable use, except in the case of embryonic stem cells, which are specifically excluded from patentability under section 18(2) of the Patent Act 1990 (Commonwealth). Parthenotes may be patented.<sup>130</sup>

Article 27.3(b) of the TRIPS Agreement allows WTO members to exclude from patentability plants and animals and essentially biological processes for their reproduction. This exclusion does not extend to microorganisms and to non-biological and microbiological processes for the reproduction of plants or animals, which must be patentable. There has been no determination in the WTO of the scope of this provision.<sup>131</sup> Some patent systems 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 (this is discussed further in Chapter III, section D.4(a)). A number of countries have expressly elected to exclude patents on any unaltered genetic materials.

include, for example, inventions that would be considered against morality if commercially exploited (see Box 2.9), or certain methods for medical treatment of humans or animals (Article 27.3(a) of the 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 articulate very specific exclusions, such as for first and second medical indications, or expressly allow for the patenting of such claims (see Chapter III, section D.4(c)). The WIPO report on the international patent system has collated information from primary national/regional legislation on exclusions from patentable subject matter.<sup>132</sup>

#### **Novelty**

The criterion of novelty is intended to ensure that patents are only granted on 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 or

before the priority date, if any. National laws define which kind and form of documentation, if any, constitutes prior public disclosure relevant to an assessment of novelty.<sup>133</sup>

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. In such a case, the invention has not been disclosed to the public and would be considered novel for the purpose of patent examination. 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 have been obvious to a person working in the technical area related to the invention with “ordinary skill” or average knowledge (“person skilled in the art”) on the relevant date (being the filing date or priority date of the patent application). While some laws require that this person have “ordinary” or “average” skill, a WIPO study found that no national/regional law explains or defines the term “person skilled in the art”,<sup>134</sup> although it can be deduced that average or ordinary skill is the skill expected to be possessed by a hypothetical person who is an ordinary, duly qualified practitioner in the relevant field.<sup>135</sup> In some countries, administrative guidelines or jurisprudence provide guidance on the meaning of the term.<sup>136</sup>

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 person skilled in the art. For example, a mixture of medicines consists of a painkiller (analgesic) and a tranquilizer (sedative). It was found that, through the addition of the tranquilizer, which intrinsically appeared to have no painkilling effect, the analgesic effect of the painkiller was intensified in a way that could not have been predicted from the known properties of the active substances.<sup>137</sup>

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 (see Chapter III, section D.4(a)). The 2019 WIPO Study on Inventive Step (Part III) has gathered information about how WIPO member states apply the inventive step criterion in the field of organic and inorganic chemistry, including pharmaceutical application.<sup>138</sup>

### **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, in order to comply with the requirement, an applicant has to indicate the ways by which the claimed invention satisfies the possibility of industrial application in the description unless it is clear to a person skilled in the art from the nature of the claimed invention. This general requirement is given a specific form in many countries. For example, the EPO Board of Appeal has decided that the mere fact that a substance can be produced is not sufficient if the inventor cannot describe a concrete use of that product, for example, to relate that product

to a disease or identified condition.<sup>139</sup> In general, the application of this requirement does not pose practical problems in patent examination.

The requirement of industrial applicability has gained importance for the determination of the patentability of inventions in the field of biotechnology – more specifically, of inventions concerning, for example, a sequence or partial sequence of a gene. While product patents granted on gene sequences in general cover all known and unknown uses of a claimed gene sequence, that is, even those uses are protected which are not yet known by the patentee, some jurisdictions require that patent applications specify with respect to the industrial applicability (utility) criterion which function the claimed gene or gene sequence fulfils, or even require that the function be included into the claim (see Chapter III, section D.4(a)). In the latter case, the scope of protection of a product claim will be restricted to the claimed use.

The UK Guidelines for Examining Patent Applications for Biotechnological Inventions<sup>140</sup> explain that the industrial application of genes or protein sequences is not apparent from the invention itself. Based on UK Supreme Court and EPO jurisprudence, the Guidelines state that a practical application and profitable use, as well as a concrete benefit, must be derivable directly from the patent and common general knowledge so that a skilled person was enabled to exploit the claimed invention. The Patent Examination Guidelines issued by the Korean Intellectual Property Office (KIPO)<sup>141</sup> state that, for inventions involving genes, DNA fragments, antisense, vectors, recombinant vectors, transformants, fused cells, proteins, recombinant proteins, monoclonal antibodies, microorganisms, animals, plants, etc., a specific, substantial and credible utility must be stated in the description of the invention. Where the utility is not described or not inferred based on the specification, the invention does not meet the industrial applicability requirement under Article 29(1) of the Patent Act.

### **Disclosure**

Sufficient disclosure of an invention is required in order to grant a patent. Article 29.1 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. The description part of the patent application, in general, allows for the disclosure requirement to be fulfilled. The description should be clear and definite without any ambiguity.<sup>142</sup> In some countries, the applicant may also have to disclose details of patents applied for or granted in other jurisdictions (an option under Article 29.2 of the TRIPS Agreement).

In cases where the application refers to biological material, supplementing a disclosure in writing, the deposit of a sample of this material in an authorized institution can be permitted by patent law. The WIPO Budapest Treaty on the International Recognition of the Deposit for Microorganisms for the Purposes of Patent Procedure<sup>143</sup> provides for a system under which the deposit of a microorganism with any “international depositary authority” is recognized for the purposes of the patent procedure in the contracting states, irrespective of where the international depositary authority is located.<sup>144</sup> The Treaty does not define what is meant by a microorganism. According to the Guide to the Deposit of Microorganisms under the Budapest Treaty, Section D, cell cultures can be deposited with a number of international depositary authorities.<sup>145</sup>

The disclosure requirement is considered one of the important rationales of the patent system as it enables dissemination of information and an increase in the public stocks of knowledge, with an increase in overall social benefits, such as inducing technology transfer.<sup>146</sup> Some argue that disclosure of a patented invention is often not sufficient to “work” the patent, for example, in the field of biotherapeutics (Mandel, 2006; Price and Rai, 2016). One of the fundamental questions raised with respect to the disclosure requirement is the extent to which a patentee must disclose his or her 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. 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, textbooks and scientific journals.<sup>147</sup>

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 to intentionally not fully disclose an invention in a manner inconsistent with the disclosure requirement under the applicable national/regional law. For example, the Supreme Court of Canada<sup>148</sup> 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 more than 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. The Court found that the patentee had chosen to withhold information needed to fully disclose the invention.

#### *(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. Although Article 62 of the TRIPS Agreement states that compliance with reasonable procedures and formalities may be required for the acquisition and maintenance of IP rights, neither the TRIPS Agreement nor the Paris Convention mandates specific patent procedures. As a result, countries have room to manoeuvre in developing an approach to patent procedures that is accommodating of their circumstances (WIPO, 2014a). In general, a patent can be granted following: (i) formality examination only; (ii) formality examination and prior art<sup>149</sup> search; or (iii) formality examination, prior art search and substantive examination.

Under a substantive examination system, a prior art 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.<sup>150</sup> Patent offices have developed a number of mechanisms and practical arrangements to make use of the search and examination results from other patent offices, aiming at improving the overall quality of patents.<sup>151</sup> 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 that are specifically appointed for that purpose by the PCT Union Assembly.<sup>152</sup> These search and examination reports can be used by patent offices to decide on a patent grant. Other cooperation mechanisms exist at a regional<sup>153</sup> and bilateral<sup>154</sup> level. WIPO Centralized Access to Search and Examination (CASE) is an example of a platform for participating patent offices to store, share and retrieve information that is relevant to patent search and examination.

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. The scope of rights in a granted patent may end up being less than what is originally claimed in the application.<sup>155</sup>

Some countries currently employ registration systems as opposed to examination systems. They do not provide for substantive examination and thus do not assess whether a claimed invention fulfils the patentability requirements. The validity of the patents can be challenged before the competent court. Some argue that it is sensible to defer determination of the compliance with the patentability criteria 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.

The flexibility of the international patent system enables countries to move from one system to another. A WIPO guide outlined various options that countries can choose from when designing search and examination of patent applications in accordance with their policies (WIPO, 2014a). It described, for example, the option of limiting substantive examination to certain strategic fields of technology while applications relating to other fields of technology may be subject to formality examination only or to outsourcing, either within or outside the country. With reference to this guide, the 2018 Intellectual Property Policy of the Republic of South Africa<sup>156</sup> announced the introduction of substantive search and examination of patent applications, initially restricted to pharmaceutical patents due to resource constraints.

#### *(v) Review procedures*

Patent systems provide for review procedures to allow third parties to intervene in the patent examination process before the grant of a patent (e.g. before an administrative body, such as an appeal board), or to challenge a patent after its grant (before an administrative body or a court) (see Chapter IV, section C.2). Such procedures complement the office procedures for patent grant and enable the public to contribute to patent quality. The most common mechanisms are opposition systems, re-examination proceedings, administrative revocation and invalidation mechanisms, and third-party submissions.<sup>157</sup>

#### *(vi) Rights conferred by a patent*

The scope of protection conferred by a 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. The rights conferred by a patent, once granted, depend on whether the subject matter is a product patent or a process patent. A product patent confers on its owner the exclusive rights to prevent third parties from making, using, offering for sale, selling or importing the patented invention into the country where the patent rights are granted (Article 28.1(a) of the TRIPS Agreement). A process patent confers on its owner the exclusive rights to prevent third parties from using the process, and from using, offering for sale, selling or importing for these purposes at least the product obtained directly by that process (Article 28.1(b) of the TRIPS Agreement). For example, a process that is patent protected in one country can be used in another country, where the patent is not in force, for production. The products resulting directly from that process, however, must not be imported without the patent owner's consent into the country where the process patent is in force (WTO, 2012).

In addition, Article 34 of the TRIPS Agreement places the burden of proof in civil law infringement cases on the purported patent infringer by determining that a product is deemed to have been produced using a patented process under the following conditions:

- The product obtained by the patented process is new.
- An identical product was produced by the defendant without the consent of the patent holder.
- It is likely that the identical product was made by the patented process.
- The owner of the patent has been unable through reasonable efforts to determine the process actually used.

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, such as marketing of the product or access to the other party's assets) 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 pharmaceutical companies to further develop and/or produce a medical technology where patents are owned by another company or research institution under mutually agreed terms (see also Chapter III, section D.5(c) and Chapter IV, section C.3(b), (c) and (e)).

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", see section A.6(g)).<sup>158</sup>

#### *(vii) Exceptions and limitations to patent rights*

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 restrict the enforcement of patent rights with respect to certain uses of the patented invention, for example, personal and/or non-commercial use. 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, 31 and 31bis 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. The WIPO Standing Committee on the Law of Patents (SCP, see Box 2.10) has undertaken work in the area of exceptions and limitations.<sup>159</sup>

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 (see Chapter III, section D.5(a)). Another common exception is the regulatory review exception (also known as the "Bolar" exception), which allows generic competitors to make limited use of a patented invention before the patent expires, to pursue marketing approval of a competitor product (see 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. Patent owners are, in principle, entitled to receive remuneration. For details on legal requirements regarding the grant of compulsory and government-use licences, see Chapter IV, section C.3(a)(ii).

#### **Box 2.10: WIPO Standing Committee on the Law of Patents**

The SCP serves as a forum to discuss issues, facilitate member coordination and provide guidance concerning the progressive international development of patent law. The SCP is composed of all member states of WIPO and the Paris Union and of accredited observers, for example, intergovernmental and non-governmental organizations. Since 2011, the SCP has focused on topics such as exceptions and limitations to patent rights, technology transfer, quality of patents, including opposition systems, and patents and health.<sup>160</sup> The SCP has produced studies and draft reference documents on exceptions and limitations to patent rights, including those that may be relevant to public health, such as the regulatory review exception,<sup>161</sup> the research exception<sup>162</sup> and compulsory licensing.<sup>163</sup> It also produced a study examining constraints faced by developing countries and LDCs in making full use of patent flexibilities such as exceptions and limitations.<sup>164</sup> The SCP collates information on certain aspects of patent law, which is regularly updated by member states and available on the SCP website.<sup>165</sup>

### *(viii) Patent information*

The patent system requires disclosure of inventions to the public (see section (iii) above) and makes published patents and patent applications an important source of technical and legal information (Bregonje, 2005). Information in patent documents includes bibliographic data about the inventor, patent applicant or patent holder, a description of the claimed invention and related technology developments and a list of claims (regarding this term, see section (vi) above), indicating the scope of protection which is sought by the applicant. Other information is available on patents apart from the patent documents themselves, for example, search and examination reports related to patent applications, patent legal status information and, where the applicable law provides for access to the file, correspondence between the patent office and the applicant. Patent information is a basis for IP and business strategies and decisions,<sup>166</sup> and input into R&D processes. 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.

WIPO Standards<sup>167</sup> are recommendations and guidelines that have been adopted by the Committee on WIPO Standards (CWS).<sup>168</sup> They help IP offices establish and administer their IP data and information practice and publication systems. 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 IP offices, and facilitate retrieval and access to technical information contained in patent documents.<sup>169</sup> WIPO also collects and publishes examples of IP office practices in the WIPO Handbook on Industrial Property Information and Documentation.<sup>170</sup> This has made patent information search easier and more user friendly.

While Article 29.1 of the TRIPS Agreement mandates disclosure of an invention in the patent application, it does not require publication of patent documents *per se*. However, under Article 12 of the Paris Convention, patent offices, as a minimum, must regularly publish the names of the proprietors of granted patents, with a brief designation of the patented inventions, in an official periodical journal. Patent applications are generally published for public access 18 months after their filing dates (or priority dates, as the case may be). Similarly, Article 21 of the PCT generally requires publication of PCT international applications promptly after expiration of 18 months from the priority date.

The form and content of patent publication varies considerably from country to country. Some patent offices publish only patent applications, not granted patents. Other offices do not publish patent applications but publish only granted patents or just 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. On the other hand, countries may opt to publish all documents generated during the process of patent prosecution, including additional useful information, such as search and examination reports, corrections, amendments, translations and legal status information. A 2019 WHA resolution emphasized the importance of transparency in patent status in the context of public health (see Chapter IV, section A.4(f)).<sup>171</sup>

The WIPO Patent Register Portal<sup>172</sup> provides links to online patent registers and gazettes, and to information related to legal status, from more than 200 jurisdictions and patent information collections. It helps identify what information can be retrieved online and how that information can be accessed.

PATENTSCOPE<sup>173</sup> is the WIPO database for patent information. It provides access to published PCT international applications as well as to a number of national and regional patent collections.<sup>174</sup> Besides using advanced search options and offering full text search within documents, the database uses a range of tools to make the technical information more accessible and to help overcome language barriers. For example, the search interface is available in more than 20 languages and offers a multilingual search tool called Cross Lingual Information Retrieval (CLIR),<sup>175</sup> which performs a search in PATENTSCOPE in different languages simultaneously. WIPO Translate<sup>176</sup> is an instant translation tool, designed specifically to translate patent-related texts. WIPO Pearl<sup>177</sup> provides access to scientific and technical terms derived from patent documents across different languages and helps searches for scientific and technical knowledge.

While publication and digitization of patent information have made knowledge more easily accessible and searchable, no database has complete coverage of all patent documents ever published worldwide (WIPO, 2015b). Besides patent office databases (primary sources), commercial entities provide patent information services and additional services, tailored to specific patent information needs. To support the public in finding patent information related to medicines, special databases have been developed that link medicine data and corresponding patent data. Such databases include the Special Gazette for Medicaments published by the Mexican Industrial Property Institute,<sup>178</sup> the Medicines Patents and Licences database (MedsPaL) maintained by the Medicines Patent Pool, and the Patent Information Initiative for Medicines (Pat-INFORMED), an initiative by WIPO and the International Federation of Pharmaceutical Manufacturers and Associations (see Box 2.11 and Table 2.1).

Another method of identifying relevant patent families (see in this section below) is to search the medicine in question in databases maintained by some countries'

**Box 2.11: Selected databases****MedsPaL<sup>179</sup>**

The Medicines Patent Pool has established MedsPaL, a publicly available patents and licences database containing information on the patent status of medicines for treatment of HIV, hepatitis C and TB, and other patented essential medicines, in certain LMICs. Patent families are identified for inclusion as those listed in the FDA Orange Book or Health Canada Patent Register, or those identified by WHO/Unitaid patent landscape searches. MedsPaL obtains patent information from different sources, including directly from patent offices and patent databases as well as directly from industry.

**Pat-INFORMED<sup>180</sup>**

The Patent Information Initiative for Medicines (Pat-INFORMED) is a publicly available patent database containing information on the patent status of medicines across a range of disease areas. Pat-INFORMED reproduces information that is voluntarily submitted by patent holders regarding the key patents on specific medicines as approved in a particular market. Pat-INFORMED relies exclusively on patent information provided by the right holders, and the information provided is not verified by WIPO.

**Table 2.1: Information available in MedsPaL and Pat-INFORMED**

	<b>MedsPaL</b>	<b>Pat-INFORMED</b>
Coverage	Low- and middle-income countries	Global
Types of patent included	Drug product, method of use, intermediates, manufacturing process	Drug product, method of use
Granted patents	Yes	Yes
Pending applications	Yes	No
Expected expiry dates	Yes	No
Oppositions	Yes	No
Licensing information	Yes	No
Data exclusivity	Yes	No
Grant number	Yes	Yes
Priority applications	Yes	No
Ability to directly contact companies with inquiries about patent status	No	Yes
Frequency of updating	Updated every 2 months through an automated process for certain countries; annually for others	At least every 6 months for medicines on the WHO EML, at least annually for others

Sources: Q&A on MedsPaL, available at: <https://medicinespatentpool.org/what-we-do/medspal/>; Pat-INFORMED FAQs, available at: <https://www.wipo.int/pat-informed/en/faqs/>; Pat-INFORMED Terms of Use, available at: [https://www.wipo.int/patinformed/documents/pat\\_informed\\_terms\\_of\\_use.pdf](https://www.wipo.int/patinformed/documents/pat_informed_terms_of_use.pdf).

medicines regulatory authorities (e.g. FDA Orange Book or Health Canada Patent Register; see section B.1(b)(ix) on patent status and legal status information) or to consult published “patent landscapes” (see section B.1(b)(x) on patent landscapes). No source of information is all-encompassing, nor is there a one-stop shop for patent information or legal information, while the accuracy and validity of the information may change rapidly. It is important that relevant authorities maintain and update frequently the information contained in databases to

ensure that it remains current and accurate. It is important to confirm the correctness of information with the competent patent authority or with the right holder should precise information be needed. Therefore, database terms of use will include a legal disclaimer stipulating that there is no warranty for the information.<sup>181</sup>

WIPO initiatives to improve access to information and knowledge are founded in the WIPO Development Agenda,<sup>182</sup> Cluster C: Technology Transfer, Information

and Communication Technologies (ICT) and Access to Knowledge. Such initiatives include:

- Access to Research for Development and Innovation (ARDI):<sup>183</sup> free access to major scientific and technical journals for local, not-for-profit institutions in LDCs, and low-cost access to industrial property offices in developing countries
- Access to Specialized Patent Information (ASPI):<sup>184</sup> free or low-cost access to tools and services for retrieving and analysing patent data for patent offices and academic and research institutions in developing countries
- International Cooperation for Patent Examination (ICE):<sup>185</sup> free expert assistance, training and access to collections of patent documents for developing countries
- Technology and Innovation Support Centers (TISCs):<sup>186</sup> access to technology information and related services to help innovators in developing countries create, protect and manage IP rights
- Digital Access Service (DAS):<sup>187</sup> secure exchange of priority and other similar documents among participating IP offices
- Centralized Access to Search and Examination (CASE):<sup>188</sup> secure sharing of patent search and examination documentation among patent offices.

Such initiatives are particularly important for patent offices in LMICs that are considering patent examination procedures, since they need access to prior art resources as they develop knowledge and practice, for example, on examination of pharmaceutical patent applications, and may want to see results obtained by other patent offices around the world.

A patent family means a number of different patent documents that are either related to each other through one or more common priority documents or are technically equivalent. For instance, a patent applicant may file an initial patent application at one patent office and then subsequent applications in other countries within a specified period of time, claiming the priority (see Box 2.6) of the 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 exists.<sup>189</sup> 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.<sup>190</sup>

The retrieval, analysis and exploitation of patent information are complex matters and require specialized skills. Patent searches serve a variety of purposes, and each requires a proper strategy, for example, a patent examiner doing a prior art search, a scientist seeking solutions to a

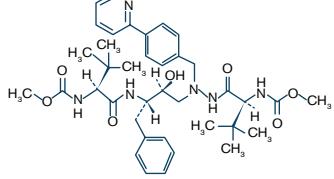
research problem, a procurement officer wanting to identify patent documents related to commercialized medicines, or a generic company assessing business opportunities. Searching patent documents related to pharmaceuticals is further complicated by the fact that a chemical compound can have more than one officially accepted name and can be searched in patent documents by brand name, international non-proprietary name (INN), manufacture name, CAS (Chemical Abstracts Service) Registry Number, International Patent Classification symbol,<sup>191</sup> or text representations of chemical structures, such as International Chemical Identifier (InChI). Examples of search parameters for pharmaceutical substances are illustrated in Table 2.2. An applicant may choose any of these indications as long as the invention is sufficiently disclosed.

Patent examiners and IP professionals use a variety of search parameters to conduct searches, often assisted by commercial database services and new software tools.<sup>192</sup> Search algorithms have been developed to allow the translation of one search query variation (e.g. an INN) to other query variations (e.g. a corresponding molecular name, CAS Registry Number and chemical structure). For example, the European Bioinformatics Institute (EMBL-EBI) makes such a search system available on the Internet.<sup>193</sup> The WIPO Chemical Structure Search<sup>194</sup> in PATENTSCOPE recognizes the names of chemical compounds, including their INN, as well as their structure, from embedded drawings in patent documents. This tool started in 2016 with published PCT applications in English and German (from 1978) and the national collection of the United States (from 1979) and has expanded to other languages and collections since.

#### *(ix) Patent status and legal status information*

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.<sup>195</sup> Patent status and legal status information helps to determine the freedom to operate (FTO) in respect of a project and the extent to which and with whom licences have to be negotiated, but there is in fact no perfect source of information.<sup>196</sup> IP offices provide this information in different formats, inconsistently and in an untimely manner due to differing national and regional patent laws and practices.<sup>197</sup> The WIPO Standard ST.27, adopted in 2017, aims at improving worldwide availability, reliability and comparability of patent legal status data, through promoting an efficient exchange of patent legal status data in a harmonized manner between IP offices, and to facilitate the understanding of end users of patent registers and patent databases about the meaning of certain legal status events across different jurisdictions.

**Table 2.2: Examples of search parameters for pharmaceutical substances**

Parameters	Examples	Explanation
Manufacturer name	BMS-232632	During the R&D stage, a substance is identified by a code (a combination of alphabets and numbers) in the laboratory or in publications.
INN (generic name)	atazanavir	A unique and universally available designated name to identify each pharmaceutical substance.
Brand name	Reyataz®	Once a drug receives marketing approval, it is sold with a proprietary name registered for trademark protection.
IUPAC chemical name	methyl N-[(2S)-1-{[(2S,3S)-3-hydroxy-4-[(2S)-2-[(methoxycarbonyl)amino]-3,3-dimethyl-N-[(4-(pyridin-2-yl)phenyl]methyl]butanehydrazido]-1-phenylbutan-2-yl]carbamoyl}-2,2-dimethylpropyl]carbamate	The International Union of Pure and Applied Chemistry (IUPAC) sets standards for the naming of the chemical elements and compounds in a structured manner.
CAS Registry Number	198904-31-3	Upon publication of chemical literatures and patents, the Chemical Abstracts Service (CAS) assigns a unique numeric identifier for a newly published compound.
International Patent Classification (IPC) code	A61P 31/18	Although the IPC codes do not pin point a particular substance, it is used with other search parameters to narrow down a search result.
Molecular formula	C <sub>38</sub> H <sub>52</sub> N <sub>6</sub> O <sub>7</sub>	A chemical formula that shows the number and kinds of atoms in a molecule.
Chemical structure (graphic formula)		Several commercial services offer patent search databases that allow searching compounds by chemical structure in addition to keywords (names) and classification codes. They use various indexing rules so that searchers can also search chemical compounds described in a Markush structure.

Source: WIPO SCP/21/9.

Note: While there are other organizations that assign identifiers to chemical compounds, the CAS Registry Number is one of the most widely used codes by experts in the field of chemistry.

Patent registers record the most important legal events as required by applicable laws and regulations. The most reliable and authoritative information can usually be obtained from these primary sources. Secondary sources, such as commercial patent databases, often compile legal status data from several primary sources, making it easier to obtain an overview of legal status in multiple jurisdictions. However, these secondary sources are not as up to date as primary sources and may lack some of the data contained in primary sources.<sup>198</sup>

Assessing the patent status of medical products generally requires specific expertise. A product (including products made of combinations of components, e.g. fixed-dose combinations), its manufacturing process and its use can be covered by several patents protecting various technological aspects.

While information about patent applications and grants is public, resources that directly link patents to medicines already on the market are scarce and limited. For medicines commercialized in the United States, some information can be obtained from the FDA Orange Book,<sup>199</sup> which lists FDA-approved medicines and related patent and exclusivity information. The

Orange Book includes those patents, supplied by the manufacturer, "for which a claim of patent infringement could reasonably be asserted against someone manufacturing or selling an unlicensed version of the drug".<sup>200</sup> 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.<sup>201</sup> The Orange Book lists only compound and method-of-treatment patents, and does not include, for example, process patents. In addition, some types of medicines are not listed, for example, most biotherapeutics (see section A.6(d) on biotherapeutic products), for which the FDA maintains a separate list of licensed biotherapeutic products (Purple Book), which provides information on reference product regulatory exclusivity and biosimilarity or interchangeability evaluations, but does not provide information on patents or patent expiry.<sup>202</sup>

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. Unlike the Orange Book, Health Canada's Patent Register generally lists patent information for biotherapeutics.<sup>203</sup>

The Republic of Korea requires the submission of information about patents that are associated with approved medicines within 30 days from market approval and publishes this information in its Green List.<sup>204</sup> The holder of market approval must specify every claim that covers the approved drug product and submit detailed explanation between each claim and the approved medicine.

On the one hand, a patent list for approved medicines is a convenient source of information, making it easy to retrieve patent information. For this reason, many studies start their patent analysis by searching the Orange Book and expanding the search to patent family information.<sup>205</sup> On the other hand, linking patent information to information about regulatory processes has been criticized for impacting access to the market by generic products. For further information on patent linkage, see section A.6(g).

#### *(x) Patent landscapes and medical technologies*

The term “patent landscape” is used in this study to refer to a report based on patent data (referring to patent documents, either applications or granted patents), search and analysis that provides an overview of the patenting activity in a specific technology field. Usually, it is supported by visualizations, including different perspectives and data analysis, depending on the specific project needs. There is no commonly agreed definition of the term “patent landscape” or a predefined content or structure.

The value of a landscape report is the presentation of a technology area in a manner that is easy to understand for a non-expert. The presentation of the empirical findings is enhanced by visualizations, while a combination of different types of data may lead to interesting insights and conclusions. Patent landscapes can therefore be useful for policy discussions, strategic research planning, investments 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 include legal status information 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 (see section (ix) above). Moreover, legal status is always subject to change.

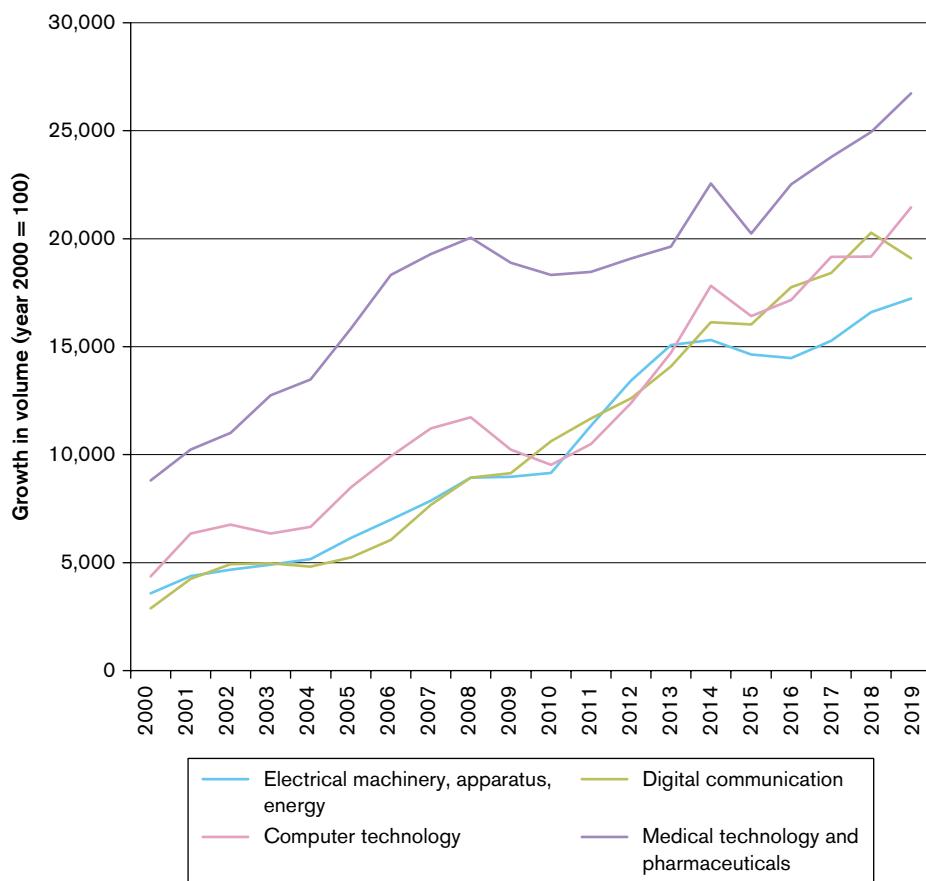
Patent landscape reports are often used as a first step to identify relevant patents, which are further looked into also from a legal status point of view within the framework of a freedom-to-operate (FTO) analysis (see Chapter III, section D.5(f)). An FTO analysis will focus on a limited number of patents and jurisdictions/potential markets of interest, while a patent landscape report will typically include a much broader data set, as its purpose is to provide information about the general landscape rather than questions linked to entry into a market which are FTO specific.

The costs of patent landscape reports can be significant. To enable this information to be shared, WIPO has prepared a list of patent landscape reports in various technical fields,<sup>206</sup> including topics related to public health, such as vaccines for selected infectious diseases,<sup>207</sup> and assistive devices and technologies for the visually and hearing impaired.<sup>208</sup> In addition, WIPO has collected a list of patent landscape reports published by international organizations, national IP offices, NGOs and private-sector entities, which are available in a dedicated, searchable database.<sup>209</sup>

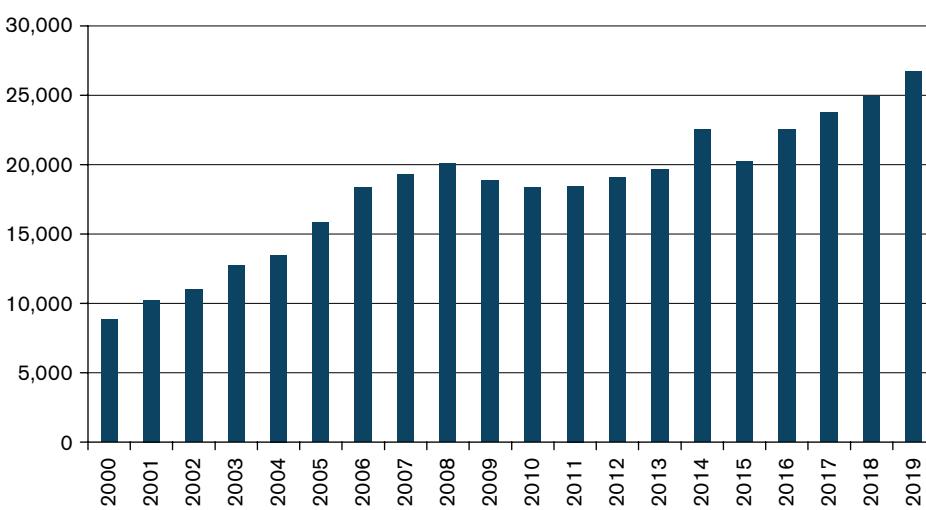
The WHO, Unitaid and civil society organizations have published numerous patent “landscapes” for medicines of high interest to the global health community. These landscapes are overviews of the key patents on a technology and their status by jurisdiction, and, in some cases, analysis of the coverage of claims, put together by patent experts. These include patent landscapes for HIV medicines, pipeline and approved TB medicines, and pipeline and approved hepatitis C medicines.<sup>210</sup>

#### *(xi) Filing trends under the Patent Cooperation Treaty system*

According to WIPO (2019), the area of medical technology accounted for only a relatively small proportion of all applications (6.4 per cent in 2019). However, it should be noted that the term “medical technologies”, as used by WIPO in its annual review of the PCT (WIPO, 2019a), is different from the term used throughout this study. This study also includes data relating to pharmaceuticals (3.7 per cent of all PCT filings in 2019). The PCT filing numbers for both medical technologies and pharmaceuticals accounted for 10.1 per cent of all filings in 2019 and, in this consolidated form, medical technologies and pharmaceuticals represent the field of technology with the highest number of PCT filings between 2000 and 2019 (see Figures 2.4 and 2.5).

**Figure 2.4: Growth of the top four technology fields, 2000–2019**

Source: WIPO Statistics Database.

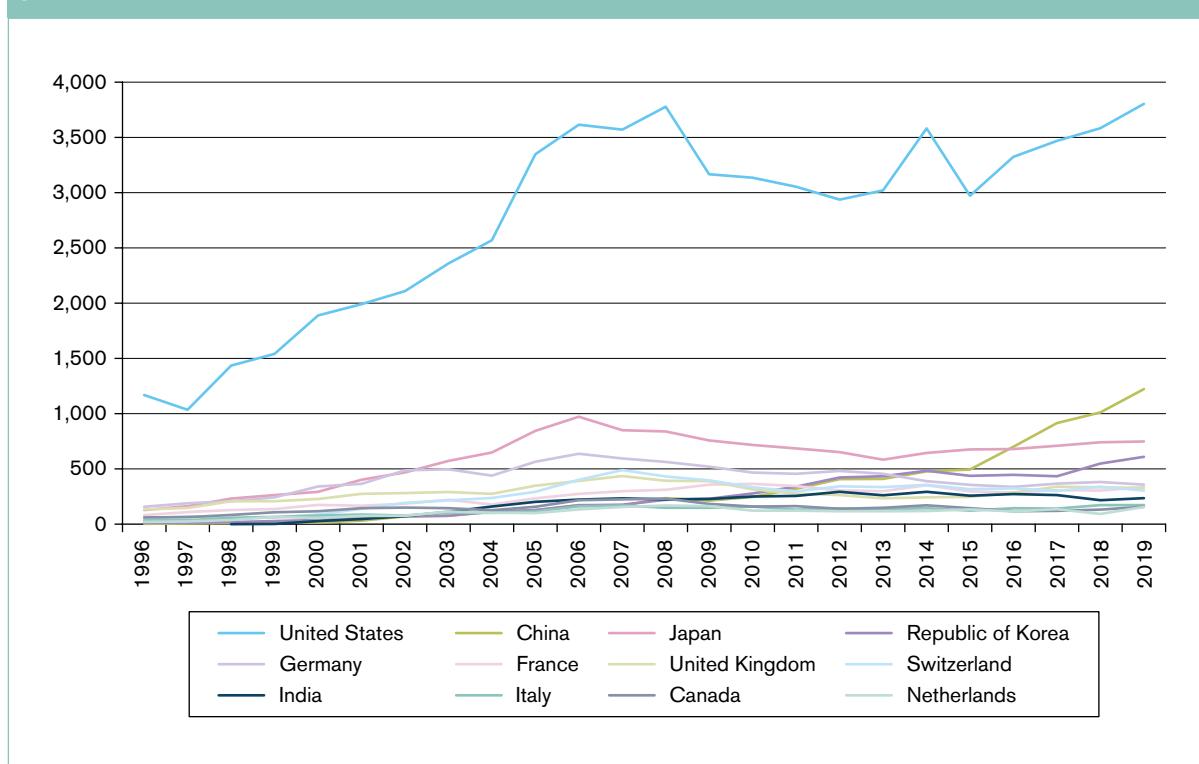
**Figure 2.5: PCT applications in the field of medical technology, including pharmaceuticals, 2000–2019**

Source: WIPO Statistics Database.

According to the WIPO Statistics Database, the annual total number of published PCT applications in the area of medical technologies between 2000 and 2019 remained in a band between 4,497 and 16,953. In the area of pharmaceuticals, the total number of published PCT applications remained in

a band between 3,808 and 9,772 each year from 2000 to 2019. 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 8,805 and 26,725 each year from 2000

**Figure 2.6: Main countries of origin of PCT publications in the field of medical technology, including pharmaceuticals, 2000–2019**



Source: WIPO Statistics Database.

to 2019 (see Figure 2.5). The total numbers increased each year until 2008 and then declined in the two following years, then increased again until 2019, with the exception of 2015. Among the top countries of origin are the United States, China, Japan, the Republic of Korea and a number of Western European countries (see Figure 2.6).

### (c) Protection of test data

Test data protection is closely related to the regulation of medicines, while also being part of the IP system, since it represents a form of protection against unfair competition. As seen in section A.6 above, in order to obtain marketing authorization for any new pharmaceutical product, submission of test data to regulatory agencies is required in countries that undertake an evaluation of the quality, safety and efficacy of medicines. The generated test data are afforded protection against unfair commercial use and against disclosure under international legal standards that are implemented according to the regulations of the particular jurisdiction.

The rationale for awarding test data protection is that considerable effort, in terms of both time and money, is required to produce data, especially with increasingly stricter regulatory requirements. In producing test data, applicants usually have a strong interest in not allowing free-riding by subsequent applicants on their investment in clinical trials. On the other hand, there

are competing public interests to ensure earlier access to generic products, which can be delayed when generics are unable to rely on originator test data. As a result, the way in which test data are protected is one of the more controversial topics in the debate about public health and IP.

It is important to note that “data protection” in other contexts refers to the safeguarding of personal medical data in the interest of privacy (patient confidentiality). That is not the meaning used here.

#### *(i) How test data are protected*

Test data can be protected in different ways, for example, by a regulatory framework of data exclusivity, or reliance on confidentiality or laws on unfair competition. The choice of the protection regime will impact what the regulatory agency can do with data provided by the applicant in the application dossier. The following section sets out the applicable international legal standards, as well as how test data protection is implemented at the domestic level.

#### **International legal standards**

Article 10bis of the Paris Convention (which requires effective protection against unfair competition in general) and Article 39.3 of the TRIPS Agreement contain multilateral standards relating to the protection of test data.

Article 39.3 of the TRIPS Agreement requires WTO members to protect test data against:

- Unfair commercial use: the TRIPS Agreement does not provide a definition of the term “unfair commercial use”, nor does it identify how to achieve this protection. As a result, opinions, as well as national practices, differ on the exact requirements of Article 39.3 of the TRIPS Agreement. Some argue that the most effective way to protect test data is to award a reasonable period of data exclusivity to the originator companies. Others argue that other forms of protection against unfair commercial use are permissible and sufficient. 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.
- Disclosure: this is an obligation not to ordinarily disclose the data submitted for regulatory approval purposes. Regulatory agencies may, however, disclose the data when disclosure is necessary to protect the public or where steps are taken to ensure that there is no unfair commercial use of the data concerned. For example, the EMA has made clinical trial data available, under certain conditions, to avoid duplication of clinical trials, encourage innovative activities to develop new medicines, and allow academics and researchers to reassess clinical trial data (see Box 3.6).

There is no WTO jurisprudence or authoritative WTO guidance on either of these issues. The matter was raised, but not resolved, in consultations between Argentina and the United States 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 Understanding on Rules and Procedures Governing the Settlement of Disputes (DSU) rules.<sup>211</sup> Nor had these issues 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 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 said, there are certain qualifying conditions that apply to the protection of test data:

- The data are 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. There are different views as to whether this condition is applicable to biotherapeutics. Consequently, data protection requirements in this particular industry sector may, or may not, fall within the scope of the TRIPS Agreement.
- 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 2033.

### National implementation

The possibility to protect test data in different ways under the TRIPS Agreement is reflected in the incorporation of this obligation 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 that countries have subscribed to in FTAs (Diependaele et al., 2017; see also Chapter II, section B.5 and Chapter IV, section C.5) or, in a few cases, by legally binding commitments providing expressly for data exclusivity in WTO accession protocols (e.g. China, the Russian Federation and Ukraine).<sup>212</sup> These countries have thus agreed to enter into more detailed obligations than are required under the TRIPS Agreement.

Most high-income countries, and some LMICs, provide for a regime of data exclusivity. Other 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. They do not bar 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.

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) admits a compensation scheme as an alternative to data exclusivity for pharmaceuticals.<sup>213</sup>

### *(ii) Innovation and access dimensions*

From the perspective of the originator companies, reliance on their data by competing generic companies 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. They therefore hold the view that test data protection, especially in the form of data exclusivity, provides an important incentive for the industry to invest in the development of new products and the necessary clinical trials. In addition, originator companies 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, in the absence of other incentive mechanisms, such as grants, market entry awards or advanced market commitments. A similar situation could arise in relation to clinical trials to test the safety and efficacy of known traditional medicines or old medicines that are not patentable, due to lack of novelty (see Box 2.12).

On the other hand, generic pharmaceutical producers will wait for the expiration of any exclusive test data protection period, even though they could, in theory, 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. Applicants for generic medicines want to rely on the originator data so that the generic products can be placed on the market sooner and at lower costs. Reliance on originator data also avoids unethical duplication of clinical trials. Public health advocates therefore highlight that, with regard to developing countries, the additional incentive of data exclusivity 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. The WHO Consultative

Expert Working Group on Research and Development: Financing and Coordination (CEWG) 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, 2012).

### *(iii) Distinction between the protection of patents and of test data*

Patents and test data protection 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 grants legally enforceable rights to the patent owner to protect 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 be held by one party and the regulatory dossier held by another (e.g. a local licensee under the patent).

Patent protection and test data protection run in parallel for the patented medicines that do make it to market (see the example in Figure 2.3). However, patent protection will typically have begun a number of years earlier. This is because patent applications are usually 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 manifest, for example, where a product is either not under patent protection (see an example in Box 2.12), where it has only a short remaining period of patent protection or where the validity of the patent is challenged. In such situations, an exclusivity period may delay the early entry of generics into the market because regulators are obliged not to review/approve products until the exclusivity period expires. For example, in Ukraine, after rejection of key sofosbuvir patents, the originator company challenged the registration of a generic product based on data exclusivity provisions in 2016 leading to deregistration of the generic product. It subsequently reached an agreement with the government on providing the originator product at a reduced price. As of August 2017, the originator agreed to include Ukraine on the list of countries to which its Indian licensees can export their generic production.<sup>214</sup>

### Box 2.12: The example of colchicine

Colchicine is a remedy for gout, known to the Ancient Greeks and used in the United States since at least the 19th century. While the 1938 Federal Food, Drug, and Cosmetic Act required all medicines to be approved by the FDA, those that had been on the market before the Act was in force were allowed to remain on the market, and colchicine was sold as a generic medicine by a number of pharmaceutical companies. In 2006, under the Unapproved Drug Initiative, the FDA required pharmaceutical companies to conduct clinical trials and other studies if they wanted to keep selling colchicine, with the objective of improving the evidence base for the safety and efficacy of the treatment. One pharmaceutical company conducted the requisite trials, leading to FDA approval of its colchicine product in 2009.<sup>215</sup> Under the Hatch-Waxman Act, as the approval was technically for a “new indication” (as previous versions had never been specifically approved for these indications), the pharmaceutical company was granted a three-year regulatory exclusivity for acute gout and a seven-year orphan drug exclusivity for another indication, familial Mediterranean fever (a rare genetic disorder) (see Chapter II, section A.6(f)). Other colchicine products previously on the market were required to phase out production. The price of colchicine increased from \$0.09 to \$4.85 per tablet (Brett, 2010; Kesselheim and Solomon, 2010). Additionally, the company was granted method-of-use patents that were expected to expire in the United States around 2028. However, the FDA approved a competitor product in 2014, and several other generic versions have been approved since then.<sup>216</sup>

In addition, test data protection is granted automatically, while obtaining and maintaining patents requires effort and investment. Patents may be revoked. Test data protection does not require maintenance fees to be paid, unlike patents. Compulsory licences under the TRIPS Agreement concern use of patented technology, but not test data. The laws of some countries nevertheless provide for waivers to test data protection for products manufactured under compulsory licences ('t Hoen et al., 2017). While it may be possible to invent around patents, especially patents on formulations, methods of manufacture and chemical intermediaries, it is more difficult for a generic competitor to generate its own clinical trial data. Given these characteristics, some argue that the pharmaceutical industry places more importance on data and other regulatory exclusivities than on patents (Roth, 2012; Diependaele et al., 2017).

#### (iv) Open access to test data

Open access to test data is desirable from the public health perspective, in particular, to avoid duplication of clinical trials, encourage innovative activities to develop new medicines and allow researchers to evaluate clinical trial data. That said, the question arises how the legitimate public policy objective of open access to test data and the requirement to protect such data against unfair commercial use and disclosure pursuant to Article 39.3 of the TRIPS Agreement can both be met.

For example, as set out in Box 3.6, the European Union has put in place a policy and legal framework regarding public access to clinical trial data.<sup>217</sup> It provides, among other things, that an EU database be set up and maintained by the EMA with a view to ensuring an appropriate level of transparency in clinical trials. Arguably, in the European Union, the public disclosure of test data does not affect the protection under Article 39.3 of the TRIPS Agreement,

as they are covered by a regime of data exclusivity of up to eight years, during which no competitor can rely on the data in order to obtain marketing authorization. The impact of the European Union's open access policy on the protection of test data in third countries, however, seems to be unclear.<sup>218</sup> Once published in the database, the data would no longer have to be considered as “undisclosed” within the meaning of Article 39.3 of the TRIPS Agreement and would therefore not have to be protected by other WTO members. However, the EMA's Terms of Use specify that the clinical reports may only be used for general information and non-commercial purposes, requesting the user of the data to agree not to refer to the data in support of an application for marketing authorization in third countries. There is no liability provision in the event of non-respect of the Terms of Use.

The EU General Court, in its judgment of 25 September 2018, ruled that Article 39.3 of the TRIPS Agreement does not mean “that protection granted to intellectual property rights must be given absolute precedence over the principle of disclosure of the information submitted in the context of a marketing authorisation application for an orphan medicinal product”.<sup>219</sup> The Court concluded that “clinical study reports cannot therefore be considered to enjoy a general presumption of confidentiality on the implicit ground that they are, as a matter of principle and in their entirety, clearly covered by the exception relating to the protection of the commercial interests of marketing authorisation applicants”.<sup>220</sup>

#### (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. Trademarks work better in helping consumers assess quality when the goods are not “search” goods, for which the quality is readily discernible before purchase (e.g. red and firm tomatoes), but are “experience” goods, which the consumer has to purchase in order to know its attributes (e.g. cough syrup). Brand advertising expenditures are consequently higher for experience goods than for search goods.<sup>221</sup>

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, or 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 both originator and generic companies to distinguish the product they are responsible for manufacturing and distributing. These are sometimes termed “brand names”. The WHO approves generic names, called international non-proprietary names (INNs)

for pharmaceutical substances (see section 1(d)(ii)), which are universally recognized as unique names that identify particular active pharmaceutical ingredients. Trademarks are linked to a product and are used by both originator and, in most cases, generic companies to create trust and brand loyalty between the company, the prescribing practitioner and the patient, potentially allowing the trademark owners to charge higher prices. The often-used term “brand name” medicine to describe an originator product is inaccurate because both originator and generic companies use brand names to market and distinguish their products.

Trademarks are protected under the laws of each country or region, and not globally. International standards for protection of trademarks are set out in the Paris Convention and the TRIPS Agreement. 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 using the Madrid System for the International Registration of Marks (Madrid System) (see Box 2.13).<sup>222</sup> 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 the unauthorized use of signs that are identical or similar to the registered trademark on 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. However, defences to infringement exist, including trademark fair use. Trademarks have a defined initial

#### **Box 2.13: The Madrid System for the International Registration of Marks**

Pharmaceutical companies pursue high numbers of registrations under the Madrid System. International registrations for pharmaceuticals and other medicinal preparations<sup>223</sup> account for 10 per cent of all international registrations filed yearly. They increased threefold, from 2,810 of 24,414 in 2000 to 6,216 of 61,139 in 2018.<sup>224</sup> The Madrid System offers an option for trademark holders to obtain and maintain trademark protection in export markets. By filing one international application, a trademark holder may obtain protection in the contracting parties,<sup>225</sup> provided that the holder has a “basic mark”, that is, a trademark application or registration with the Trademark Office of a Contracting Party (“Office of origin”). The International Bureau of WIPO carries out a formality examination, with matters of substance being left to each designated contracting party to determine in accordance with their national or regional 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 considered to be the same as if it had been registered by the Office concerned.

The Madrid System simplifies the management of the mark by providing for one international registration with one renewal date, and this one registration may contain protection in many designated contracting parties. It is also possible to further extend the trademark protection to additional contracting parties and to manage centrally the renewal and recording of changes of the international registration. During the first five years from the date of the international registration, the international registration depends on the basic mark: if the basic mark is cancelled, the international registration will be cancelled to the same effect. Should this happen, the trademark owner would have the opportunity of transforming the international registration into national and regional rights, to ensure continued protection of the trademark.

term of protection and can be renewed indefinitely,<sup>226</sup> provided they remain in use and maintain their distinctive character and trademark holders see a need to renew them. Rights to a trademark can be lost through cancellation or removed from the registry if the trademark is not renewed or the renewal fees due are 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.

#### *(ii) Trademarks and international non-proprietary names (INNs) for active pharmaceutical ingredients*

In contrast with trademarks, which are proprietary private rights, INNs are generic names for active pharmaceutical ingredients<sup>227</sup> and biotherapeutic products.<sup>228</sup> Lists of proposed and recommended INNs are also available on the WHO INN website and, with searchable capabilities, on the WHO INN MedNet. Moreover, a web service, the INN Global Data Hub, allows authorized users to query the INN database. The WHO has a constitutional mandate to “develop, establish and promote international standards with respect to food, biological, pharmaceutical and similar products”. The setting of INNs and their publication are administered by the WHO INN Programme, a core normative programme of the WHO, initiated in 1950. The WHO Secretariat and the WHO INN Expert Group collaborate closely with national nomenclature committees, drug regulatory authorities, pharmacopeias 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 “non-proprietary”. An INN can be used by any manufacturer or supplier for their product provided that it is used accurately. For example, “ibuprofen” is an INN and can be used by any manufacturer or supplier 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 adrenoreceptor 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.<sup>229</sup> 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 among other grounds on a similarity between a proposed INN and a trademark. On the other hand, trademarks that include an established INN stem infringe the INN system. The WHA has requested member states to discourage the use of names derived from them, and particularly names including established stems, as trademarks (WHA46.19). 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 INN website and WHO INN MedNet.<sup>230</sup> The WHO INN Global Data Hub allows those with appropriate credentials to search for the INNs online.

WIPO and the WHO started cooperating in November 1999, to provide timely and accurate information on INNs to trademark offices of their members. In view of the improvements in communication technology in both organizations, in 2018, the two organizations concluded a cooperation agreement that enables integration of the INN data contained in the WHO INN database into the WIPO Global Brand Database. Trademark examiners in WIPO member states may now search the Global Brand Database for INNs in an accessible format and by using different filters that facilitate the textual comparison between INNs and verbal marks. With the help of this new tool, they will be able to fulfil the public interest in keeping these names free and available for use by pharmacists and medical practitioners around the world, thus preventing medication errors. At the other end of the spectrum, information on existing trademarks that have been properly granted for use on pharmaceutical technologies is key to avoiding counterfeiting in this crucial area. INN experts can also use the trademark data in the Global Brand Database to avoid proposing or recommending new INNs that may cause confusion with existing trademarks, therefore contributing to enhancing pharmacovigilance and more reliable medicines.<sup>231</sup>

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 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. Article 20 of the TRIPS Agreement allows members to apply special requirements on the use of a trademark, provided that such requirements do not unjustifiably encumber the use of the trademark in the course of trade.

#### *(iii) Trademarks and unfair competition*

Inaccurate or misleading labelling of products can also be considered a form of unfair competition (see section B.2(d)). It is covered by Article 10bis of the Paris Convention,<sup>232</sup> which is designed to safeguard against deceptive or misleading labelling.

#### *(iv) 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 FDA and the EMA to introduce assessments of proprietary nomenclature in the interest of public health and safety.<sup>233</sup> 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.<sup>234</sup> For example, from January to September 2018, the EMA accepted 182 proposed (invented) names and rejected 150 such names.<sup>235</sup>

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. Concerns regarding INNs (see section B.1(d)(ii)), such as similarity with the INN or inclusion of an INN stem, are also taken into account.

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 4.3 per cent of all trademark applications in 2016 (WIPO, 2017b). Such volumes of applications can lead to a situation where there are many unused trademark registrations in existence (see section (v) below).

#### *(v) Trademark cluttering*

The volume of applications for trademark protection can result in trademark registers containing a significant number of unused trademarks. This is sometimes termed trademark cluttering. This can increase the costs of creating and registering new trademarks for other applicants, including producers of generic medicines. Considering the increased demand for trademarks and given the reliance on trademarks, which are not time-limited in the same way as patents, such cluttering of the trademark register can have a serious effect. Some national and regional legislation contains provisions that make the trademark liable for revocation on the basis of non-use. For example, while in the European Union registrations can be renewed indefinitely for consecutive ten-year periods, the European Union also allows for the application for revocation of a trademark on the basis of non-use if the trademark has not been used in the five years since registration. In some jurisdictions, including Cambodia, the Philippines and the United States, the trademark holder has to declare actual use or non-use throughout the life cycle of the trademark.

#### *(vi) Non-traditional marks*

Non-traditional marks may consist of signs, such as sound, colour, shape, aspects of packaging and texture. At the international level, these marks were first recognized in Rule 3 of the Regulations to the Singapore Treaty on the Law of Trademarks (2006)<sup>236</sup> and appear in numerous FTAs; however, they are not mentioned specifically in the TRIPS Agreement (although the list of possible signs

that can be registered as trademarks is non-exhaustive). Non-traditional marks are protected in some, but not all, jurisdictions, and they are particularly relevant in the area of pharmaceuticals, where protections have been granted by IP offices and the courts to the colour of drugs, for example, the colour blue, Pantone 284 U, for originator sildenafil, with the name of the company appearing thereon,<sup>237</sup> to the shape of drugs (heart shaped for dextroamphetamine)<sup>238</sup> and to the three-dimensional shape of a medical device (the plastic shell of an inhaler).<sup>239</sup> Pharmaceutical companies rely on non-traditional marks in the same way they rely on trademarks: to make their products unique in the marketplace and to enable patient confidence. Non-traditional marks have been at the centre of litigation, with action being taken against competitors who copy distinctive physical features of a medicine. However, non-traditional marks can have an impact on access to medicine, by increasing transaction costs and by blocking market entry of a generic medicine that would have the same physical characteristics as its reference product (Scaria and Mammen, 2018). Patients may be reluctant to take a generic drug that has different physical attributes (Kesselheim, et al., 2013). The effectiveness of a generic could also, in theory, be undermined by the non-traditional mark, if the physical characteristics of the medicine are important to its efficacy. A study has shown that patients react best when the colour corresponds with the intended results of the medication – for example, a pink colour for antacids (Srivastava and More, 2010). A particular flavour, for example, can be necessary to make a medicine palatable to children.

#### *(vii) Standardized packaging*

Standardized packaging or “plain packaging” involves regulators requiring features of packaging to comply with certain parameters. A well-known example of standardized packaging is tobacco plain packaging, with Australian legislation, the first of its kind in relation to tobacco products, setting out the physical features, colour and brand display requirements of tobacco products.<sup>240</sup> The WTO panel in *Australia – Tobacco Plain Packaging* (see section B.6 below) did not find that this legislation unjustifiably encumbers the use of trademarks in the course of trade within the meaning of Article 20 of the TRIPS Agreement.<sup>241</sup> In the pharmaceutical sector, standardized packaging mandates identifiers that do not enable consumer preference for particular medicines. In the European Union, regulatory frameworks provide guidelines on the labelling and packaging of medicines relating to the colour and size of packaging.<sup>242</sup> Following a review that found 2–3 per cent of hospital admissions in Australia are related to medication errors,<sup>243</sup> the Australian Therapeutic Goods Administration has proposed giving the brand and active ingredient the same prominence on pharmaceutical packaging.<sup>244</sup> In Chile, law requires that the INN be printed on the package directly under the

brand name, using the same font and colour in capital letters, and that the text size for the INN must be at least 50 per cent of the brand name size.<sup>245</sup>

#### *(e) Copyright*

Copyright protects every original expression in the literary, scientific or artistic domains, as provided by the Berne Convention for the Protection of Literary and Artistic Works, and as incorporated by reference into the TRIPS Agreement. The list of works protected by copyright in the treaties is not exhaustive and can include literary works, computer programs, databases, films and musical compositions. Copyright protection does not extend to ideas, procedures, methods of operation or mathematical concepts as such. Copyright grants economic rights, which can be licensed or assigned, to derive financial reward to the owner of the work and to encourage the creation of additional works for the benefit of society and the general public. Copyright is an automatic right and, in most cases, it can be obtained without registration or formalities. The Berne Convention minimum standard for the duration of copyright is generally the life of the author of the copyright work plus 50 years; however, longer periods of protection can be provided at the national level.

Copyright, like other forms of IP, has to consider the balance between the rights of authors and owners and the larger public interest. Copyright provides exceptions and limitations that allow access to those works under certain special cases. Both copyright, on the one hand, and exceptions and limitations to copyright, on the other hand, are of particular importance when considering the question of access to medical technology and innovation.

#### *(i) Copyright and pharmaceutical package inserts*

For pharmaceutical products, a key issue in relation to copyright is whether protection covers the accompanying package inserts or information leaflets. Copyright protection extends to expressions and not to ideas, procedures, methods of operation or mathematical concepts as such. Generic producers are free to use the factual information provided in an insert, because copyright does not extend to the information as such, only to the way it is expressed as an original work; 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.<sup>246</sup> A similar finding was initially 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 product text, in any manner, including a direct reproduction, is not an infringement of copyright. A subsequent Federal Court decision confirmed that generic pharmaceutical companies are able to reproduce product information that has been approved by the Therapeutic Goods Administration in a range of circumstances, without infringing copyright.<sup>247</sup>

#### *(ii) Exceptions and limitations – text and data mining*

Text and data mining (TDM) has been defined as "automated analytical techniques" that work by "copying existing electronic information, for instance articles in scientific journals and other works, and analysing the data they contain for patterns, trends and other useful information".<sup>248</sup> TDM can be an invaluable technique for researchers to develop new technologies in health care. For example, a drug discovery company may apply technology to analyse thousands of molecules that might serve as drug candidates and predict their suitability for blocking the mechanism of a pathogen, or to mine large data sets of genetic information and medical records to identify linkages between genetic mutations and disease. New research techniques and diagnostic methods that involve TDM can be developed, thanks to the application of balanced copyright flexibilities for the development of medical innovations.

Flexibilities can be based on fair use clauses, in particular, non-expressive use (Sag, 2009), or on specific statutory TDM exceptions. In 2009, Japan was the first country in the world to permit TDM as a specific exception to copyright. In 2018, Japan extended this exception to the use of raw data, specifically permitting electronic and incidental copies of works and allowing for use of copyright works for data verification. TDM exceptions appear, for example, in the copyright legislation of the European Union,<sup>249</sup> United Kingdom,<sup>250</sup> France<sup>251</sup> and Germany.<sup>252</sup>

#### *(iii) Licensing schemes*

Waivers or licences may be available to obtain access to information such as research data that may be copyright protected. Increasingly, research funders, including national governments, require that data produced in the course of research they fund be made available to other researchers. However, acquiring these licences can be time consuming and costly for researchers and their institutions and, as a result, the process can inhibit the speed at which new medical technologies are developed and subsequently reach the market. Licensing schemes,

such as creative commons and open data commons licensing, can ensure that medical research data, for example, can be shared more readily. The WHO Hinari Access to Research for Health Programme is a voluntary licensing initiative that provides free access to copyright works, such as biomedical and health literature, by health workers and researchers in LMICs.<sup>253</sup>

#### *(iv) Orphan works access licensing schemes*

Orphan works are works for which the copyright holders are unknown or cannot be located. The process of identifying and locating the owner of the right can be extremely costly and time consuming for the prospective user of the work, and might eventually yield no results. For example, the Mahidol-Oxford Tropical Medicine Research Unit wanted to make available to its researchers research papers from an early-20th-century malaria therapy experiment in which patients were intentionally infected with malaria. As the research papers were considered orphan works, published in long-defunct journals, it could not. The articles (and the pictures and diagrams within them) could not be copied to make them available online, nor could they be data mined to find patterns and associations which could assist researchers. To enable access to this information, and other information like this, an orphan works licensing scheme was developed in the United Kingdom to grant licences for the use of orphan works for both commercial and non-commercial purposes, subject to certain conditions.<sup>254</sup> According to section 77 of the Copyright Act of Canada, if a copyright owner is not located after a reasonable search, a user may apply to the Copyright Board of Canada for a licence to use the work.. An EU Orphan Works Directive permits certain uses of orphan works<sup>255</sup> and the European Union Intellectual Property Office (EUIPO) has established an online database that provides information about orphan works contained in the collections of EU members.<sup>256</sup> The Committee on WIPO Standards (CWS) approved the inclusion of data dictionary and XML components for copyright orphan works in WIPO Standard ST.96.

#### *(v) Software licensing and eHealth*

Increasingly, electronic and digital processes are used in health-care practice (eHealth or health informatics). eHealth can include electronic health records, e-prescribing, diagnostic tools and health applications on mobile phones to collect health data, provide health-care information or for the real-time monitoring of patient vital statistics. In 2005, the WHO recognized the importance of eHealth and its ability to rapidly transform the delivery of health services and systems around the world, especially in LMICs.<sup>257</sup> The WHO Global Observatory for eHealth provides member states with strategic information and guidance on effective practices and standards in eHealth. Copyright law (and, to a lesser

extent, patent law) can protect the specific graphic user interface and functionality that make mobile apps easy to use, supporting access to health care by a broad cross-section of users.<sup>258</sup> As a result, while the IP system can support the investment in eHealth initiatives, licensing models are also integral to the widespread use of eHealth services, for example, health information platforms whose effectiveness depends on uptake. Product development can also be enhanced by flexible licensing, reducing costs and shortening development periods. Licensing practice will need to develop approaches to issues of ownership and privacy of electronic health records used as training data for machine learning, or artificial intelligence (e.g. databases of radiological images) (see Box 2.14).<sup>259</sup> Open source models, such as those widely used in software development, may be an effective option.

## (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 (see Chapter IV, section C.3(h)). Infringements are thus normally pursued by the right holders in civil actions. However, where public interests are at stake, IP infringements can be remedied through criminal measures, for example, when a trader, without permission, knowingly and on a commercial scale, manufactures, distributes or sells goods marked with another company's trademark, particularly in the areas of pharmaceuticals and foods. That said, the enforcement of IPRs is clearly distinct from the regulation of

### **Box 2.14: Artificial intelligence and health**

Artificial intelligence (AI)<sup>260</sup> emerged in the middle of the 20th century and, while definitions vary, it can be broadly categorized as computer algorithms simulating human cognitive functions and capabilities, such as perceiving the environment, gaining information to take action and then improving these actions based on machine learning. Artificial neural networks, for example, have been used in drug discovery for screening compounds in the automated design of new classes of medicines and in finding novel uses for known medicines. One area in which AI has shown high effectiveness is the interpretation of imaging, such as computed tomography (CT) and magnetic resonance imaging (MRI) scans (Topol, 2019). AI is already being used in the design and analysis of clinical trials. Some expect that computer modelling and AI may enable reductions in the costs and time needed to carry out clinical trials (Harrer et al., 2019).

Twelve per cent of all AI patent applications refer to the field of life and medical sciences,<sup>261</sup> and AI is already having a significant impact on the medical landscape, with the potential to improve the future quality of health care. At present, AI is, among other things, being used to enable patient data management and personalized medicine. In particular, AI can improve the working methods of doctors and help complement traditional medical tools and techniques, improving the accuracy and speed of diagnosis.<sup>262</sup> For example, a deep learning model based on mammogram images created by a team of US researchers was able to predict whether a woman will develop breast cancer within five years, reducing false positives and unnecessary surgeries (Conner-Simons, 2017). Software applications may help doctors and patients manage conditions through customized monitoring and follow-up care. Guidelines are being developed to assist policy-makers in this area. For example, the International Telecommunication Union (ITU) is working in partnership with the WHO to establish a standardized assessment framework for the evaluation of AI-based methods for health, diagnosis, triage or treatment decisions.<sup>263</sup> The assessment framework will help identify key issues related to ethical, business, legal, technical, or other constraints that arise when using AI in the health field and develop a pragmatic method to solve them.<sup>264</sup>

Researchers are also making use of AI for data mining and machine learning, to make the development of new medicines quicker as data can be synthesized and analysed more easily (see section B.1(e)(ii) on text and data mining). There are, for example, initiatives that use AI to predict chemical reactions, in which AI is simulating different combinations and their expected effect and properties.<sup>265</sup>

Software applications use AI and blockchain technology in order to support the maintenance of traceable supply chain security (Lock, 2019; Mok, 2018). AI uses machine-learning processes and compares unique product identifiers, such as a chemical signature or image patterns, with corresponding reference data, with the goal to recognize and authenticate substandard and falsified (SF) products in an automated manner. At the same time, AI uses the data recognized to maintain and improve the database and hence to train and improve the system itself.<sup>266</sup>

Investment at the national and regional levels in AI technology is increasing.<sup>267</sup> However, ethical issues, including accountability and liability for AI decisions and actions, as well as ownership and data privacy concerns, will remain of interest for policy-making. From the perspective of IP, discussions are looking at issues such as how AI-related IP rights are managed, access and ownership of data, and how patentability criteria will be interpreted and applied to AI in different jurisdictions.<sup>268</sup> This places a focus on the way that health-care providers that hold "big data" manage data-sharing with AI developers (Geis et al., 2019; UNESCO and IBC, 2017).

medicines for safety, quality and efficacy purposes, including any remedies against substandard and falsified (SF) products (see Chapter IV, section A.12).

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

The motivation to combat SF products differs in the public health context and the IP context. From the perspective of public health, the fight against SF products is exclusively motivated by the threat to public health and related concerns about consumer protection. From an IP perspective, commercially using a sign that is identical to, or cannot be distinguished in its essential aspects from, a registered trademark without the authorization of its owner is the key condition to consider a product as counterfeit. In this context, the primary objectives are to preserve the interest of the trademark owner in enforcing their rights and to prevent consumers from being misled about the origin of the goods that bear the trademark, but also to protect the public interest by fighting infringements that take place on 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 SF products have some similarities, with customs controls and criminal law figuring among the most frequently used means to combat these products. The enforcement of IPRs can thus have implications for the broader public health considerations. In international trade, a trademark plays an important role as a trade identifier and is an indication of trade source, which can and does help to identify fake products. Counterfeitors use trademarks without authorization by the right holder to give the impression that a product is a genuine product, thus falsely representing its identity and source. Therefore, IP enforcement measures to combat trademark counterfeiting can have positive side effects, potentially supporting efforts to keep dangerous products out of the market. This is illustrated by the fact that pharmaceuticals are regularly reported to figure among the top commodities suspended by customs authorities for IPR infringement.<sup>269</sup>

*(ii) Enforcement provisions of the TRIPS Agreement*

The TRIPS Agreement is the only comprehensive multilateral legal framework for the enforcement of IPRs. It contains a set of minimum standards that safeguard the rights of IP owners (see Chapter IV, section C.3(h)). These standards include civil court procedures and remedies that should be made available, such as injunctions, damages and orders for the disposal of IP-infringing goods. These remedies must be available for all the IPRs covered by the TRIPS Agreement, including patents, undisclosed information (such as test data), trademarks

and copyright. Administrative procedures, such as actions before administrative authorities, are optional and must 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, which may include 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 clarifies 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.<sup>270</sup>

*(iii) The WIPO Advisory Committee on Enforcement*

The WIPO Advisory Committee on Enforcement (ACE) is a forum for policy dialogue on questions of IP enforcement and building respect for IP, with a mandate for technical assistance and coordination while specifically excluding norm setting. Since 2016, the Committee has discussed topical issues relating to awareness-raising, IP enforcement policies and regimes, capacity-building activities and legislative assistance on the basis of written contributions of experts.<sup>271</sup> Issues have included the role of intermediaries in preventing counterfeiting and piracy, online infringements and new technologies in IP enforcement, IP enforcement coordination, effective IP dispute resolution mechanisms and the environmentally safe disposal and destruction of IP-infringing goods.

*(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 created 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 made exclusively 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.<sup>272</sup>

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”.<sup>273</sup>

Based on the Agreement between the World Intellectual Property Organization and the World Trade Organization of 22 December 1995,<sup>274</sup> 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 (see Box 2.15).<sup>275</sup>

- 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 the WHO GSPA-PHI and the Roadmap for Access to Medicines, Vaccines and Other Health Products 2019–2023 (see Box 2.16) and in a number of recommendations contained in the WIPO Development Agenda (Chapter I, section B.2). Following the request of the Committee on Development and Intellectual Property (CDIP), WIPO prepared studies on patent-related flexibilities in the multilateral legal framework and their legislative implementation at the national and regional levels. These studies present a non-exhaustive number of flexibilities, with annexes and tables reflecting corresponding legal provisions and practices in a number of countries. The studies show a diverse approach to the implementation of TRIPS flexibilities in national laws.<sup>276</sup>

Since 2011, the WIPO Standing Committee on the Law of Patents (SCP) has reviewed legislation by member states and has identified that many countries provide for exceptions and limitations to patent rights relating to: (i) private and/or non-commercial use; (ii) experimental use and/or scientific research; (iii) extemporaneous preparation of medicines; (iv) prior use; (v) use of articles on foreign vessels, aircraft and land vehicles; (vi) acts for obtaining regulatory approval from authorities; (vii) exhaustion of patent rights; (viii) compulsory licensing and/or government use; and (ix) certain use of patented inventions by farmers and breeders.<sup>277</sup> A WIPO study has examined the constraints faced by developing countries and LDCs in making full use of patent flexibilities and their impacts on access to affordable, especially essential, medicines for public health purposes in those countries. Countries continue to report that they face constraints in making full use of flexibilities such as compulsory licensing, including political and economic pressure from some industrialized countries, the complexity of practical implementation, insufficient institutional capacity and lack of coordination between patent offices, ministries of health and trade, and drug regulatory authorities.<sup>278</sup>

### *(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 certain options on patentability and scope of rights 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, 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 NGOs and AIDS activists. During the court process, 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 in Høsbjør, Norway, on differential pricing and financing of essential drugs. Following the publication of the report on that workshop,<sup>279</sup> 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.<sup>280</sup> This was followed in June 2001 by a detailed written proposal prepared by a

#### **Box 2.15: Definition of flexibilities according to WIPO**

According to the WIPO CDIP report,<sup>281</sup> 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, as it:

- Highlights the idea of using various options as a means of implementation
- 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
- Refers to the reason for flexibilities, which is to accommodate national interest
- 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
- Regarding the scope of the right
- By enforcing and using the right.

WIPO established a database of flexibilities in the IP system. This database allows searches for implementation of flexibilities in national IP laws in selected jurisdictions.<sup>282</sup>

#### **Box 2.16: TRIPS flexibilities highlighted in the GSPA-PHI and Road Map for Access to Medicines, Vaccines and Other Health Products, 2019–2023**

The GSPA-PHI (see section A.4(c) and Box 2.2) includes explicitly actions relating 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 the impact on public health into account when considering the adoption or implementation of such obligations (Element 5.2b). Member states should also take flexibilities into account 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)<sup>283</sup>
- Voluntary patent pools of upstream and downstream technologies (Element 4.3a)
- For countries with manufacturing capacities, consider taking measures to implement the WTO Paragraph 6 System (Element 5.2d)<sup>284</sup>
- Develop effective and sustainable mechanisms in LDCs in order to improve access to existing needs, acknowledging the transitional period until 2016 (Element 6.1b)<sup>285</sup>
- Regulatory review exception, also known as “Bolar”-type exception (Element 6.3a).<sup>286</sup>

The WHO Road Map for Access to Medicines, Vaccines and Other Health Products, 2019–2023, lists the following deliverables with regard to TRIPS flexibilities:<sup>287</sup>

- Provide information on country experiences promoting public health approaches in the implementation of health-related provisions of the TRIPS Agreement, including relevant TRIPS flexibilities and intellectual property management
- Provide technical support (as appropriate, upon request, in collaboration with other competent international organizations), in order to promote access to pharmaceutical products.

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.<sup>288</sup>
- 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 these types of emergency, the Doha Declaration cites “public health crises, including those relating to HIV/AIDS, TB, 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.<sup>289</sup> 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 another country. Countries are thus free to determine whether or not they want to allow parallel importation of patented goods, including medical products.

The panel in *Australia – Tobacco Plain Packaging* considered that paragraph 5 constitutes a “subsequent agreement” of WTO members within the meaning of Article 31(3)(a) of the Vienna Convention on the Law of Treaties, and thus expresses an agreement among members on the approach to be followed in interpreting the provisions of the TRIPS Agreement.<sup>290</sup>

Paragraph 6 of the Doha Declaration prompted the commencement of work that 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.<sup>291</sup> Article 31bis of the TRIPS Agreement implemented that decision, and it entered into force on 23 January 2017.

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). The initial agreed transition period deadline of 1 January 2016 was extended to 1 January 2033.<sup>292</sup>

### *(iv) Implementation of the Doha Declaration*

Unlike the TRIPS Agreement itself, the Doha Declaration does not oblige any specific legislative enactment. The

Doha Declaration has been referenced in the work of other international organizations, notably in many WHO resolutions, the WIPO Development Agenda and UN General Assembly resolutions.

#### *(v) Least-developed country transition periods*

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. Transition periods have expired for developed and developing-country WTO members. Based on the Doha Declaration and subsequent TRIPS Council Decisions, LDCs continue to benefit from an extended transition period until 1 January 2033 with regard to pharmaceutical patents and test data protection for pharmaceutical products (including enforcement procedures and remedies).<sup>293</sup>

The WTO General Council also approved a waiver for LDCs from the transitional obligations under Article 70.8 and Article 70.9 of the TRIPS Agreement until 1 January 2033.<sup>294</sup> As a result of the waiver for Article 70.8, LDCs are not obliged to allow for the filing of patent applications for pharmaceutical inventions during the transition period. Nor are they under an obligation 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, which covers all TRIPS obligations except the non-discrimination principles until 1 July 2021.<sup>295</sup> Further extensions of the LDC transition periods are possible upon duly motivated request by LDC members.

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 decisions, 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”.<sup>296</sup> Under Rwanda’s previous patent legislation, pharmaceutical products were patentable subject matter. The 2018 Revised Policy on Intellectual Property in Rwanda<sup>297</sup> expressed the desire to create an environment that enabled more local manufacturing of pharmaceuticals, including an enabling IP environment for investments in pharmaceuticals in Rwanda. That

notwithstanding, the policy proposed that Rwanda, as an LDC that wanted to ensure access to affordable medicines for the most vulnerable, continued “the exceptions in the patenting regime for, among others: a) pharmaceutical patents, b) new medical uses of known substances, c) research exception, d) marketing approval (“Bolar” exception), e) clinical test data exception”. 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 with 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.<sup>298</sup> While some LDCs exclude pharmaceutical products from patent protection during the transition period, others, such as LDCs that are members of the Organisation africaine de la propriété intellectuelle (African Intellectual Property Organization) (OAPI), have until now foregone this option because the Bangui Agreement provides for the granting of pharmaceutical patents.<sup>299</sup> However, a revision of the Bangui Agreement adopted in Bamako, Mali, in December 2015 will exempt LDC members of OAPI from the obligation to provide for the protection and enforcement of patents and undisclosed information until 2033.<sup>300</sup> For the Bamako Act to enter into force, 12 ratifications by OAPI members are required; in October 2019, nine ratifications had been deposited.

#### **(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 Marrakesh Agreement Establishing the World Trade Organization (WTO Agreement).<sup>301</sup> The terms of accession are thus a matter of negotiation. These negotiations take place between the acceding member and existing members that 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 an 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 (see section A.6(f)).<sup>302</sup>

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.<sup>303</sup> 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 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”.<sup>304</sup> 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.<sup>305</sup> LDCs that acceded to the WTO since its establishment in 1995 include Cambodia and Nepal (2004), Cape Verde (2008), Samoa and Vanuatu (2012), Lao People’s Democratic Republic (2013), Yemen (2014), and Afghanistan and Liberia (2016) (see Box 2.17). Typically, acceding LDCs undertook a commitment to fully implement the TRIPS Agreement as of the date determined in their respective accession protocols. However, at the time of writing, the TRIPS Council, while preparing for the review of Samoa’s implementing legislation, has not yet initiated the review of any of these countries’ implementing legislation.

## 2. Competition law and 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 law and 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).

#### **Box 2.17: The example of Cambodia: an LDC's terms of accession to the WTO**

Cambodia was the first 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 as of 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<sup>306</sup>. 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 then 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)”.<sup>307</sup>

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.<sup>308</sup>

Second, the enforcement of competition law also helps to correct anti-competitive behaviour that may take place in the different business sectors involved in developing and supplying medical technology to patients who need them. It aims to discipline 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 through refusal to deal by companies with market power with, or imposition of, overly restrictive conditions in medical technology licensing; (ii) preventing generic competition through patent settlement agreements that were considered anti-competitive; (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. Recently, excessive pricing in the pharmaceutical sector has also been identified as behaviour that may merit competition authority scrutiny.<sup>309</sup> These practices can be addressed on a case-by-case basis through competition law enforcement (see Chapter IV, section D.2).

### (b) The interface between competition law and policy, and IP protection

In the area of innovation, the aims and effects of IP protection and competition policy are complementary: both are aimed at fostering innovation by creating incentives to develop new products and services.<sup>310</sup> 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 enhanced by IPRs. Competition policy also helps to maintain the innovative potential of the industry by keeping the market structure open and providing countermeasures to anti-competitive behaviour.

As competitors are excluded from using the patented or otherwise protected medical technology, IPRs provide an incentive for them to come up with alternative or superior products. IPRs, when used to exclude competitors, may provide a commercial advantage to an innovator who can be the first on the market (this is called the “first mover” advantage) (Bond and Lean, 1977), and initial profits can encourage competing originators to enter those markets by developing competing products. 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 medical technologies then compete in the same market.

#### *(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.<sup>311</sup> 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.<sup>312</sup>

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 that 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 also 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 grant-back conditions, conditions preventing challenges to validity, and coercive package licensing.<sup>313</sup>

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 Patents 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.<sup>314</sup> Generally speaking, no special principles of competition

law apply to IP, but the anti-competitive use of IP rights is subject to 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. For example, a January 2012 decision by the Competition Authority, which had fined a pharmaceutical company for exclusionary abuse of dominant position, was confirmed by the State Council of Italy. The State Council highlighted that the simple enforcement of IPRs was not sufficient to constitute an abuse of a dominant position, but the strategy employed by the company did so.<sup>315</sup>

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 unlawful restrictions of competition. There has been growing interest in ensuring an appropriate balance between IP and competition law and policy across a range of jurisdictions.

#### (c) Preserving innovation: merger control in the pharmaceutical sector

There has been an increasing number of mergers in the pharmaceutical sector, including between originator and generic companies with potential new medicine pipelines (UNCTAD, 2015b). To ensure that consolidation does not significantly impede effective competition, competition agencies in various jurisdictions conduct merger control activities. They may make mergers subject to divestiture of certain branches of research in order to prevent the abandonment of research for potentially competing future medical technology (see Box 2.18 for European Commission merger control activities).<sup>316</sup>

#### Box 2.18: Merger control in the European Union<sup>317</sup>

In recent years, the European Commission has prevented transactions that could compromise R&D efforts to launch new medicines or to extend the therapeutic use of existing medicines. The Commission intervened to protect innovation competition in a number of cases that, for example, threatened to thwart advanced R&D projects for life-saving cancer medicines or for pipeline insomnia medicines at an early stage of development. The potential competition concerns identified related mainly to the risk of: (i) depriving patients and national health-care systems of some medicinal products; and (ii) diminishing innovation in relation to certain treatments developed at a European or even global level, with the potential to result in price increases for some medicines in one or several member countries. In most cases, the Commission cleared all these transactions only after the companies offered remedies to ensure that pipeline projects were not dropped and found a new operator to drive them forward.

#### (d) Unfair competition

Unfair competition is covered by Article 10bis of the Paris Convention.<sup>318</sup> It requires countries of the Paris Union to assure to nationals of such countries effective protection against unfair competition, that is, against acts of competition that are contrary to honest practices in commercial matters. The TRIPS Agreement extends this obligation to all WTO members (Article 2.1 of the TRIPS Agreement). In particular, they shall prohibit certain acts that create confusion, discredit competitors through false allegations and mislead the public as to the nature, the manufacturing process, the characteristics, the suitability for their purpose, or the quantity, of the goods.

Protection against unfair competition serves to protect competitors as well as consumers, together with the public interest. When determining honesty in business dealings, all these factors have to be taken into account. This approach is consistent with Article 7 of the TRIPS Agreement, which reflects the intention of establishing and maintaining a balance between the societal objectives mentioned therein.<sup>319</sup> Consequently, a determination of what amounts to an act that is contrary to honest practices in commercial matters may, depending on the circumstances, reflect a balancing of these interests.<sup>320</sup>

The rules on the prevention of unfair competition and those on the control of anti-competitive practices are interrelated in that both aim at ensuring the efficient operation of markets but do so in different ways. The first set of rules is aimed at protecting competitors and consumers against acts of competition that are contrary to what would be regarded as truthful and fair within a certain market. The latter set of rules is aimed at ensuring competition in the marketplace that is free from private restraints and abuses of market power.

Countries have implemented protection against unfair competition in their domestic laws in diverse ways. Some have passed special legislation on the topic, while others rely on general consumer protection and similar laws.

### 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 the country's national health system. 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 all WTO agreements, including the GATT in relation to trade in goods, the General Agreement on Trade in Services (GATS) in relation to trade in services, and the TRIPS Agreement in relation to IP. In the case of the GATT and GATS, important exceptions apply, notably as regards special and differential treatment in favour of developing countries, and with respect to regional integration agreements.

The WTO also guarantees its members the right to protect public health. Since its inception in 1947, the 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). The GATS contains a similar exception with regard to trade in services in its Article XIV(b). These general exceptions can justify a measure that would be otherwise inconsistent with WTO obligations and commitments, provided that the health measures, and the ways in which they are applied, satisfy certain conditions, such as that they are not applied in a manner that constitutes an unjustifiable discrimination or a disguised restriction to international trade. 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 (for tariffs on health-related products see Chapter IV, section D.1(b)). 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 21.3 per cent *ad valorem* (calculated on the value of the imports), but they actually applied tariffs on average at 2.5 per cent *ad valorem* in the year 2016.<sup>321</sup>

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 WTO Pharmaceutical Agreement in 1994 (see Chapter IV, section D.1(b) and Box 4.29). 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* in 2016. Developing countries have lowered their applied tariffs rates on medicines from 6.7 per cent to 2.5 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 4.4 per cent to 2.2 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 identified the various costs associated with the prices of medicines in different countries. For some countries, the data include information on tariffs and exemptions.<sup>322</sup>

## (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, including the Agreement on the Application of Sanitary and Phytosanitary Measures (SPS Agreement) and Agreement on Technical Barriers to Trade (TBT Agreement), 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 discriminatory or unnecessary trade barriers. While all

these measures can affect trade in pharmaceuticals, the following two have a direct link to public health outcomes.

### *(i) Sanitary and phytosanitary measures*

The SPS Agreement contains specific rules for countries that 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 permitted to adopt SPS measures that result in higher levels of health protection, or measures for which international standards do not exist, provided that those measures are scientifically justified.

The SPS Committee oversees the implementation of the SPS Agreement and facilitates the exchange of information among members regarding regulatory procedures and the use of risk assessments in the development of SPS measures, among other things. In addition, the Committee provides a forum for members to discuss specific trade concerns in relation to the SPS measures of another member (see Box 2.19).

### *(ii) Technical barriers to trade*

The TBT Agreement applies to technical product requirements that are not covered by the SPS Agreement. The TBT Agreement helps support the alignment of divergent national regulations to international standards, which, in turn, promotes regulatory cooperation and convergence among national systems. The TBT Agreement strongly encourages such regulatory alignment by requiring that members should normally use relevant international standards as the basis for their regulatory measures (i.e. technical regulations, conformity assessment procedures and domestic standards). When trade frictions arise due to differences in regulatory systems or approaches, the TBT Committee of the WTO provides a forum for members to discuss and solve problems. The TBT Committee also serves as an incubator for best practices on how to regulate, that is, a place where members can share experiences, including on good regulatory practices (such as internal coordination, analysis of regulatory and non-regulatory alternatives, and transparency and public consultation).

**Box 2.19: Antimicrobial resistance in the SPS Committee**

Since 2018, the issue of antimicrobial resistance (AMR) has been raised in the SPS Committee meetings, within the context of the sharing of information on SPS-related legislation, and also as a specific trade concern.

In July 2018,<sup>323</sup> the European Union informed the Committee of its new Regulation on Veterinary Medicinal Products, which takes effect by the end of 2021. One of the key objectives of the Regulation is to address the public health risk of AMR, following a “One Health” approach. The Regulation provides for actions against AMR, including through prudent use of antibiotics, and reserving certain antimicrobials for treatment of infections in humans only and banning their use in animals for growth promotion. It was part of a package that also included a new regulation on medicated feed, which contained measures aimed at fighting the misuse of antimicrobials, including a ban on their use in medicated feed for prophylaxis, and limits on treatment duration. Regarding the EU Regulation on Veterinary Medicinal Products, certain WTO members raised concerns that foreign producers had to abide by EU production methodology requirements related to antibiotic use restrictions in livestock, despite the differences in the prevailing sanitary conditions, as well as different regional conditions and disease prevalence in third countries.<sup>324</sup> Members queried the scientific basis of the measures and were concerned about the unnecessary restrictive impact on international trade. They cautioned against any unilateral approach, expressing a preference for multilateral efforts taken to collaboratively set standards to address AMR by FAO, the OIE and the WHO, including through the Codex Task Force on Antimicrobial Resistance. The European Union replied that the ban on using antibiotics as feed additives had been in force in the European Union since 2006 and was based on a scientific opinion. It was in line with the growing international recognition of the need to phase out the use of antimicrobials as growth promoters, some of which were critically important for human medicine. The new Regulation imposed stricter requirements on operators in the European Union than on operators in non-EU countries. The new import requirements should be considered as part of the overall fight against the global spread of AMR, and not as trade barriers.<sup>325</sup>

The Agreement covers both instruments 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 and packaging requirements for foods and medicines, as well as, for example, 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 Agreement also contains similar obligations to conformity assessment procedures and standards. The protection of human health or safety is listed in the Agreement 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 discriminate or unnecessarily restrict trade. Under the TBT Agreement, only unnecessarily trade-restrictive regulations are thus prohibited, while regulations that are, for example, necessary to protect human health are allowed, even if they strongly restrict trade. Regulatory harmonization, that is, the alignment of national regulations with international standards, is another fundamental pillar of the TBT Agreement. The Agreement strongly encourages such regulatory alignment by requiring members to use relevant international standards (i.e. technical regulations, conformity assessment procedures and domestic standards) as the basis for their regulatory measures. The Agreement also provides for flexibility by

relieving members of such obligation when they consider that an international standard would be ineffective or inappropriate for the fulfilment of legitimate objectives pursued by the measure in question. Finally, the Agreement expressly refers to an additional important benefit of harmonization through international standards by recognizing in its Preamble “the contribution which international standardization can make to the transfer of technology from developed to developing countries”.

### (c) Trade in services

Trade in health services has been growing, thanks to the increased mobility of individuals (whether patients or health services providers) and the growing role of the private sector in the provision of health services (i.e. establishment of transnational corporations), as well as the communications revolution, which has brought an explosion in the number of mobile applications and health-related connected devices. Also, 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 health services to foreign services and services providers may therefore affect access to medical technologies.

### (i) The multilateral legal framework

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

- Mode 1: cross-border supply (e.g. telemedicine-health)
- 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 opening an overseas subsidiary or investing in an existing facility abroad)
- Mode 4: presence of natural persons (e.g. a physician moving abroad to work in a foreign-owned clinic).

### (ii) The scope of GATS commitments in health-related sectors

The GATS grants WTO members full flexibility when it comes to deciding whether to include binding commitments for the opening of health-related sectors and which 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.<sup>326</sup> Other services complement and facilitate access to health services and medical technologies, such as: insurance services; 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. However, many public-sector health services lie outside the scope of the GATS, since its disciplines do not cover services “supplied in the exercise of governmental authority” (i.e. those supplied neither “on a commercial basis” nor “in competition with one or more service suppliers”).

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 the GATS. Apart from health insurance services, there are, therefore, fewer legally binding commitments under the GATS to liberalize health services *per se* than there are for any other sector (see Table 2.3). This may be due to the major role played by public entities in providing public health services, coupled with political sensitivities. 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

**Table 2.3: Number of GATS commitments (as of 2020)**

Medical and dental services	52
Nurses, midwives, etc.	22
Hospital services	49
Other human health services (ambulances, etc.)	25
Social services	15
Other health-related and social services	6

Source: WTO Secretariat

Note: The schedule of commitments of the European Union (25) is counted as one, but includes commitments of its 25 member states as of 2004. Bulgaria, Romania and Croatia have separate schedules of commitments.

event, that committing to open a service sector to foreign competition does not affect a government’s capacity to regulate the sector.

Across the 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 also observed across other service sectors).

Bindings with respect to 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 jurisdiction 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 jurisdiction.

Nearly half the commitments relating to the supply of health services through commercial presence appear to be bound without limitations at the sectoral level, a result that seems to be above average for all sectors.<sup>327</sup> Most commitments under this mode, however, are subject to limitations, for example, limits on foreign equity and requirements for joint venture or residency. Some members apply economic needs tests – criteria such as population density, existing medical facilities, degree of specialization, type of medical equipment, and distance from a facility or availability of transport infrastructure are considered before new hospitals or clinics are authorized.

Unlike the other modes of supply, commitments on health services supplied through health professionals working abroad have been undertaken on a “horizontal” basis by the vast majority of members. This means that they equally apply to all services sectors for which a member has undertaken binding commitments. 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 (Adlung, 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. However, it is important to note that there has been an increase in the number of commitments in health services with the accession of new members to the WTO.

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

According to Global Health Observatory (GHO) data, health expenditure represented US\$ 7.5 trillion or 10 per cent of global gross domestic product (GDP) in 2016. It is expected that an additional 40 million jobs will be created in the health sector by 2030 (WHO, 2016e). Available statistics show that, in the OECD area, the health-sector workforce increased by 48 per cent between 2000 and 2014, which is 3.5 times more than the increase in total employment. However, this increasing demand is challenging, and trade in services clearly has a role to play to respond to some foreseen shortages in certain jurisdictions. Empirical evidence regarding the share of health services in international trade is limited, due to the lack of reporting of detailed official statistics by many countries. However, estimates derived from an experimental data set produced by the WTO Secretariat show that health services account for US\$ 50 billion. The establishment of foreign-controlled medical institutions is the predominant method of providing such services (71 per cent), followed by health treatment received abroad (23 per cent), cross-border supply, such as telemedicine (5 per cent) and temporary presence of health professionals/workers (1 per cent).

Health services are globalizing, through increased cross-border movement of health-care workers and patients, as well as technological developments and decreasing telecommunications costs, which are contributing to the development of eHealth across a range of activities (e.g. teleradiology, telediagnosis, telepathology, teleconsultation and telesurgery).

However, it is almost 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 bindings under trade

agreements from those of other policy and regulatory measures. However, studies suggest that the effects of GATS commitments – where these exist – on trade patterns have most likely been insignificant. GATS commitments do not entail additional liberalization, but (at best) bind existing levels of market access. Consequently, the commercialization of health services has occurred irrespective of GATS obligations, and the main effect of the GATS seems to have been to make national policies more predictable (Adlung, 2010). The coverage of health services in FTAs is discussed in Chapter IV.

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

An increasing challenge in the context of health services is linked to demographic changes (i.e. ageing population), which is driving the growth in demand for medical and care-related services. Opening of trade in health services should not be seen as an end in itself, but, rather, as a tool to generate distinct benefits if properly used in a broader policy context. From a public health perspective, increasing trade in health services bears both opportunities for improving health service delivery (e.g. accessibility in remote areas, alleviating human resource constraints, additional resources) and risks for equity (e.g. serving only certain segments of the population, large initial investments for telecommunications networks, attracting investment). The concern is often expressed that opening (trade in) 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.

Publicly owned and operated health facilities thus require an appropriate regulatory framework 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 the GATS or any other trade agreement. The mobility 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. Demand for foreign health workers has increased in high-income countries because of insufficient numbers of health professionals being trained locally, and due to ageing populations in these countries. When considering the mobility of health professionals, recognition of qualifications is also a requisite for the supply of services in foreign markets. Governments wishing to contain “brain drain” remain free to do so, as such measures are not subject to GATS disciplines, particularly those that relate to the temporary mobility of foreign health workers.

The limited scope of this commitment, both its definition and specific commitments, means that the GATS has probably traditionally played an insignificant role in the international migration of health personnel, but could help to fill an increasing resources gap in the future.

#### 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 a well-designed framework for government procurement can be expected to have on the health sector. It sets out the rules established for that purpose by the plurilateral Agreement on Government Procurement (GPA) under the WTO (as amended in 2012), and the size of procurement markets in health-related sectors covered by that Agreement.

(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 (Savedoff, 2011). Available surveys show that, in many LMICs, availability remains far from adequate and prices remain many times higher than international reference prices (IRPs) (see Chapter IV, section A.3). 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 Chapter IV, section A.8.

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

The GPA provides an appropriate framework for rules at the international level that 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 (48 as at 5 May 2019) are bound by its rules.

In addition to its role as a binding international agreement, the GPA has served as a model in several bilateral and regional trade agreements that embody government procurement commitments. It is also broadly consistent with the United Nations Commission on International Trade Law (UNCITRAL) Model Law on Procurement of Goods, Construction and Services, including the 2011 revision, which has inspired the national legislation of many countries, and it reinforces other international instruments such as World Bank guidelines and the work of the OECD on prevention of corruption. As a consequence, the basic disciplines of the GPA are relevant to substantially more procurement and potentially more countries than its current membership would suggest.<sup>328</sup>

(i) *GPA coverage*

The GPA has important application vis-à-vis the public health 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,<sup>329</sup> including medicines and pharmaceutical products (see Table 2.4).

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 covered in a GPA party 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 2.4). 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).

**Table 2.4: Coverage in the health sector by parties to the WTO GPA**

<b>Party to the WTO GPA as of 5 May 2019</b>	<b>Coverage of health-related entities at the central government level</b>	<b>Coverage of health-related entities at the sub-central government level</b>	<b>Coverage of goods (pharmaceutical products are generally considered to be goods)</b>	<b>Coverage of health-related services</b>
Armenia <sup>a</sup>	✓		✓	✓
Australia <sup>d</sup>	✓	✓	✓	X
Canada	✓	✓	✓	X
European Union, including its member states <sup>330</sup>	✓	✓	✓	X
Hong Kong, China	✓	N/A	✓	X
Iceland <sup>b</sup>			✓	X
Israel <sup>c</sup>	✓	X	✓	X
Japan	✓	X	✓	X
Korea, Republic of	✓	X	✓	X
Liechtenstein <sup>b</sup>			✓	X
Moldova, Republic of <sup>a</sup>	✓		✓	X
Montenegro <sup>a</sup>	✓		✓	X
Netherlands, with respect to Aruba	✓	N/A	✓	X
New Zealand <sup>e</sup>	✓	✓	✓	X
Norway <sup>a</sup>	✓		✓	X
Singapore	✓	N/A	✓	X
Switzerland	✓	✓	✓	X
Chinese Taipei	✓	✓	✓	X
Ukraine <sup>b</sup>			✓	✓
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 levels of government and accordingly have scheduled no commitments in this regard: Hong Kong, China; Netherlands with respect to Aruba; and Singapore.

<sup>a</sup> In Annex 2 of Armenia, Republic of Moldova, Montenegro and Norway, health-related entities are neither expressly covered nor excluded.

<sup>b</sup> Health-related entities (Annex 1 and Annex 2) are neither expressly covered nor excluded.

<sup>c</sup> Israel 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, hemodialysis 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.

<sup>d</sup> In its GPA coverage, Australia expressly excluded health services (Annex 5) and procurement of blood and blood-related products, including plasma derived products (Annex 4).

<sup>e</sup> In addition to explicitly covering sub-central health-related entities, Annex 2 of New Zealand also clarifies that procurement undertaken by the listed district health boards through their agent Health Alliance Limited is covered. Procurement of public health services is expressly excluded from New Zealand's coverage (Annex 5).

As is made clear in the revised GPA text, 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 its 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. New Zealand expressly covers its district health boards.<sup>331</sup>

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, Ukraine and the United States are the only GPA parties currently covering them. New Zealand expressly excludes procurement of public health services. Overall, the GPA thus 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. As a result of several rounds of negotiations and the addition of new members, the GPA parties have opened procurement activities worth an estimated US\$ 1.8 trillion annually to international competition (i.e. to suppliers from GPA parties offering goods, services or construction services). 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 useful source of information regarding the magnitude of the market access commitments under the GPA.<sup>332</sup>

These official sources make clear that the size of government procurement markets in health-related sectors covered by the GPA is substantial.<sup>333</sup> 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 2010 was US\$ 49 billion for hospitals and US\$ 47 billion for health.<sup>334</sup> In addition, the United States reports that the value of goods and services covered by the GPA and procured by the Department of Health and Human Services in 2010 was estimated to be around US\$ 10 billion. The European Union also notes in its statistical report for 2013 that its covered entities had procured an estimated EUR 28 billion of medical and laboratory devices, pharmaceuticals and related medical consumables covered by the GPA.<sup>335</sup> Japan reports that

the value of contracts covered by the GPA awarded by the Ministry of Health, Labour and Welfare in 2010 was estimated at US\$ 1.8 billion.<sup>336</sup>

## 5. Free trade agreements

The terms "regional trade agreement" (RTA), "free trade agreement" (FTA), "bilateral trade agreement" (BTA) and "preferential trade agreement" often overlap. The WTO defines any reciprocal trade agreement between or among two or more partners, not necessarily belonging to the same region, as a regional trade agreement. This study uses the term "free trade agreement" as a synonym.

FTAs are discussed here in general terms; they are covered with more specific reference to access to medicines aspects in Chapter IV, section C.5.

#### (a) 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 Figure 4.9), 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).

Early agreements focused on trade in goods and the elimination of tariff duties and other restrictions between parties to an agreement that were applied at the border. As border measures were reduced or even eliminated, FTAs evolved to cover a wide range of domestic regulatory policy areas, such as services and IP. Modern FTAs include parties, or regions, with different levels of development. Negotiations covering a wide range of trade-related disciplines started with the Uruguay Round, where broader coverage was a deliberate strategy to allow all negotiating parties to benefit in terms of trade, in order to compensate for real or perceived trade losses. The resultant trade openness from the FTAs has fostered harmonization of national practices, international governance and the rule of law, which transcend national borders. In the area of IP law and policy, this trend might entail changes in national laws, which, in turn, can directly affect access to, and innovation in, medicines and medical technologies.

Motivations to negotiate and implement FTAs may include:

- Neutralizing "beggar-thy-neighbour" trade policies that seek benefits for one country at the expense of others
- Increasing market size

- Enhancing policy predictability
- Signalling openness to investors
- Fostering the expansion of international production networks (WTO, 2011).

The *World Trade Report 2011* concludes that, for LMICs, having policies in common with high-income countries 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 pressured to adopt common rules that are inappropriate for their national context, or which could be used by high-income countries to protect vested interests.

Increasing market size can be one goal of establishing an FTA, as it enables companies to exploit economies of scale and gain a relative advantage over competitors in third countries. In addition, preferential access to a larger market may increase a country’s attractiveness as a destination for foreign direct investment (FDI). Both aims are potentially of particular value 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) The non-discrimination principles and FTAs

The key feature of FTAs is the preferential treatment for its parties, which is not automatically extended to third parties. Article XXIV of the GATT 1994 and Article V of the GATS provide for broad exceptions to the principles of non-discrimination and allow WTO members to negotiate and implement FTAs. However, the TRIPS Agreement does not provide for such an exception. In concrete terms, if two WTO members agree on higher standards of IP protection than those 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. This can have important implications for access to medicines and medical technologies, as well as for the innovation of new products.

For example, if two countries agreed to provide patent term extensions for one another’s patent holders, the MFN treatment 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 reduce or eliminate tariffs on pharmaceuticals or chemical ingredients imported from one another as part of an FTA or customs union, they would not need to reduce or eliminate 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(a), 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 can affect trade in pharmaceuticals and can have an impact on prices for medical technologies (see Chapter IV, section C.5).

Moreover, in areas that usually operate through the use of national regulations, such as IP, services and competition policy (WTO, 2011), in any event, it would be costly in practice to tailor regulations in order to favour nationals originating from preferential partner economies, 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.

#### (d) Investor–state dispute settlement

Another important element of a number of FTAs is investor–state dispute settlement (ISDS) mechanisms, which allow private entities to sue national governments for alleged violation of FTA provisions in a tribunal established to resolve the dispute (see Chapter IV, section C.5(b)).

#### (e) Commitments in other areas

A thorough analysis of the potential effects of FTAs on innovation in, and access to, medical technologies must take into account the commitments and standards agreed in all key policy areas that directly relate to the pharmaceutical sector, such as tariffs for inputs and finished products for wholesale or retail, government procurement and competition law.

Due to the low average applied tariff across products and countries (see Chapter IV, section D.1(a)), there is not usually much room left for exchanging preferential tariff concessions in trade agreements. Therefore, 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 convergence of regulatory regimes. Modern FTAs contain specific, stand-alone FTA chapters on regulatory issues. For example, around 64 per cent of FTAs include a dedicated competition chapter (Anderson et al., 2018).

Alternatively, as is often the case for the competition sector, they can become an integral part of chapters, for example, on IPRs or government procurement (WTO, 2011).

## 6. Resolving trade disputes at the WTO

Health has been touched upon in numerous WTO disputes.<sup>337</sup> The WTO Appellate Body in *EC – Asbestos* considered that the preservation of human life and health through the elimination, or reduction, of the well-known, and life-threatening, health risks posed by asbestos fibres was a “value [that] is both vital and important in the highest degree”.<sup>338</sup> Similarly, in *Brazil – Retreaded Tyres*, the Appellate Body agreed with the panel that “few interests are more ‘vital’ and ‘important’ than protecting human beings from health risks”.<sup>339</sup> At issue in that dispute were Brazil’s measures aimed at reducing exposure to risks, including dengue fever and malaria, arising from the accumulation of waste tyres.

In the area of the TRIPS Agreement, the panel report in *Canada – Pharmaceutical Patents* illustrates the policy space available to members to use permissible exceptions to seek appropriate balance between the interests of patent holders and users. The panel found that Canada’s regulatory review provision was permissible under the so-called “three-step test” under Article 30 of the TRIPS Agreement,<sup>340</sup> but that its stockpiling provision was not justified under Article 30, especially because there were no limitations on the quantity of production for stockpiling or market destination of the products manufactured under this provision.<sup>341</sup>

In 2018, the intersection between public health, IP and trade was addressed in comprehensive panel reports in *Australia – Tobacco Plain Packaging*.<sup>342</sup> At issue were Australia’s tobacco plain packaging (TPP) measures requiring that tobacco products and their retail packaging appear in a uniform manner.<sup>343</sup> The Panel Reports discuss, *inter alia*, certain aspects of coherence in domestic and international law and policy.

In these disputes, the complainants challenged the TPP measures as being *unnecessary* within the meaning of Article 2.2 of the TBT Agreement and *unjustifiable* within the meaning of Article 20 of the TRIPS Agreement. The complainants did not dispute the harmful consequences of tobacco consumption and acknowledged the importance of effective tobacco-control measures to reduce the public health burden resulting from tobacco use. Their key argument was, however, that the TPP measures were not capable of contributing to their public health objective. Having examined an extensive amount

of evidence provided by the parties, the panel concluded that the TPP measures, as applied in combination with other tobacco-control measures maintained by Australia, are capable of contributing, and do in fact contribute, to their objective of improving public health by reducing the use of, and exposure to, tobacco products.

The panel recognized the importance of use of trademarks to distinguish products in the marketplace, on the one hand, and the exceptional gravity of the domestic and global health problems at issue, involving a high level of preventable morbidity and mortality, on the other hand, and considered these factors in the light of the TPP measures’ contribution to improving public health. The panel found that the complainants had not demonstrated that the trademark-related requirements of the TPP measures unjustifiably encumber the use of trademarks in the course of trade within the meaning of Article 20 of the TRIPS Agreement. In its analysis, the panel noted that Australia, while having been the first country to implement TPP, had pursued its relevant domestic public health objective in line with the emerging multilateral public health policies in the area of tobacco control as reflected in the WHO Framework Convention on Tobacco Control (FCTC) and the work under its auspices, including the Article 11 and Article 13 FCTC Guidelines.<sup>344</sup>

The panel similarly found that the complainants had not demonstrated that the TPP measures are more trade restrictive than necessary to fulfil a legitimate objective, within the meaning of Article 2.2 of the TBT Agreement.<sup>345</sup> In that context, the panel noted that, while Australia had not demonstrated that the Guidelines constituted a “standard” under Annex 1.2 of the TBT Agreement with respect to TPP, they provided important guidance to FCTC parties in addressing packaging, and, as relevant, implementing plain packaging as an element of a comprehensive scheme of effective tobacco-control policies.<sup>346</sup>

The panel rejected the complainants’ claims that the TPP restrictions on the use of figurative elements of trademarks, geographical indications and marks of origin were contrary to certain other provisions of the TRIPS Agreement, including those incorporated by reference from the Paris Convention (1967).<sup>347</sup> In discussing the interpretation of the provisions of the pre-existing treaties incorporated by reference into the TRIPS Agreement, the panel recalled that it is a general principle of interpretation to adopt the meaning that reconciles the texts of different treaties and avoids a conflict between them. Accordingly, one should avoid interpreting a provision of the Paris Convention (1967) as incorporated by reference into the TRIPS Agreement to mean something different than that within the context of the Paris Convention (1967) except where this was explicitly provided for.<sup>348</sup>

## 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”.
- Special challenges in the area of health technologies include the long product development times, the necessarily stringent regulatory burden, the relatively high risk of failure and the comparatively low marginal costs of production.
- The pharmaceutical sector stands out in terms of its dependence on patents to capture returns on research and development (R&D).
- Several policy options exist within and outside the patent system to attenuate the negative price and welfare effects of patents, especially on pharmaceuticals.

The past decades have seen more systematic efforts to use the tools of economic analysis to support discussions on health policy. The WHO Commission on Macroeconomics and Health (WHO, 2001a) was a major milestone along this road. This 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, private entities may not 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, where investments can be recouped only through sales, 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, 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.

The patent system can result in a net social benefit. While patents may increase costs to society in the short term by restricting competition, it is hoped that they generate greater and more dynamic benefits as a result of encouraging more innovation in the long term. The requirement to disclose the invention in patent applications helps to disseminate scientific and technical information that could otherwise be kept secret. In these circumstances, society 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 once introduced into the market, it has been relatively easy for other companies to reverse engineer new pharmaceutical compounds and market generic versions at much lower prices. Several studies have shown that when an array of different choices is 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 many other countries (WIPO, 2009). However, the advent of biologics is changing the industrial organization of the industry, as biotherapeutics are not as easy to reverse

engineer as traditional small-molecule innovations. As a result, trade secrecy surrounding the production process has turned into an important protection mechanism for biotherapeutics (Price and Rai, 2015, 2016). While biologic innovator companies regularly seek product patent protection, details of the manufacturing processes that are not covered by those patents may be kept as trade secrets. It has been observed that this combination of protection by patents and trade secrets can complicate achieving sufficiently similar production processes for similar biotherapeutic products (SBPs). In addition, it has been argued that, due to the 12-year regulatory exclusivity period for biotherapeutic products in the United States, companies might rely rather on trade secrets than patent protection, which would lead to a lack of disclosure (Price and Rai, 2016). On the other hand, the view has been held that, in the future, technological advances may further enable reverse engineering even for biological therapeutic products and would reduce the value of trade secrets for manufacturing processes (Weires, 2019).

The period of commercialization of a medicine under patent protection is typically much shorter than the patent term (period between grant and expiry). It has been estimated that the effective patent term of a new medicine, which is the balance remaining in the patent term after obtaining the relevant regulatory approvals, is an average of 8 to 13.5 years in the US market, depending on the source (US Congress, Office of Technology Assessment, 1993; Grabowski and Kyle, 2007; Aitken and Kleinrock, 2017).

The pharmaceutical sector has a higher accounting rate of profit compared with most other industries, which, according to the US Government Accountability Office, was just over two times the average profit margins for the 500 largest companies in industries other than pharmaceuticals and software in 2015.<sup>349</sup> The majority of spending on biomedical R&D is undertaken in only a few countries, while medical innovation benefits patients around the world, when and where it is accessible and affordable (Viergever and Hendriks, 2016). This raises the question of how the R&D expenditures should be equitably shared among countries.

According to the National Science Foundation, US pharmaceutical companies invested three times as much in R&D, relative to their sales, than the average US manufacturing firm in 2015.<sup>350</sup> Moreover, most of the investments made in R&D performed by pharmaceutical companies in the United States come from the relevant companies themselves, rather than from outside funding sources, including the US federal government.<sup>351</sup>

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. One study found that the extent of price reduction after patent expiry varied greatly between products and countries

and concluded that future research should gather more country-specific data (Vondeling et al., 2018). 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). On the other hand, a study using Indian pharmaceutical market data on central nervous system medicines, from 2003 to 2008, showed little evidence of substantial increases in average pharmaceutical prices in this market, but statistically significant price increases of about 12 per cent in one segment of this market, namely, products protected by a compound patent (as opposed to secondary patents) (Duggan and Goyal, 2012). However, these findings are limited by narrow inclusion criteria and failure to account for “mailbox” patents,<sup>352</sup> wherein the Indian post-TRIPS amendments to the Patents Act included a clause that allowed Indian generic companies to continue to manufacture medicines for which patents were granted in India with applications filed since 1995, upon payment of a royalty to the patent holder. Further studies done with data after 2015 will shed light on more systematic effects on prices, as the mailbox patents will have expired.

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.<sup>353</sup>

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)(ii)). However, compulsory licences may have limited effectiveness for more complex technologies such as biotherapeutics, as they do not oblige the patent owners to cooperate in divulging trade secrets about production processes, transferring the additional know-how and/or transferring materials that might be required.

Permitting parallel imports does not automatically result in lower prices. The reason is that 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 marketing 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 A.4(g)). 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. One alternative 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 parallel importation by design limits the ability to segment markets and employ price differentiation, among countries in which parallel importation is possible and practised.

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 price discrimination to occur, three conditions would need to be fulfilled:

- 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 (Watal, 2001; see also Chapter IV, section A.4(g)).

However, in practice, there is little evidence that pharmaceutical companies engage in differential pricing based on per capita income (Scherer and Watal, 2002; Watal and Dai, 2019 – see Box 2.20). Flynn et al. (2009) showed that, in the case that income distribution in the local economy is unequal, the firm will maximize its revenue by selling a restricted quantity to the wealthy at a high price, resulting in relatively similar prices between countries of different per capita income levels. Danzon et al. (2015) found evidence that income inequality does contribute to relatively high drug prices. Besides, they

found that, in such markets, prices of originator products are only slightly reduced, even after generic entry.

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, companies tend to launch products later where there is price regulation. The picture is mixed for the other countries. Lanjouw concluded that, for LMICs with a high capacity to manufacture generic versions of 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 ability to pay, 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 Kyle and Qian (2014), who examined the effects of patent protection on availability of new medicines and found that patents do encourage launches of these molecules in local markets. Cockburn et al. (2016) also conclude that, while originator companies tend to launch later where there is price regulation, longer and more extensive patent rights accelerate product launch across all countries. Following these studies, a WTO working paper (Watal and Dai, 2019) studies both the question of availability and affordability with respect to innovative medicines in a post-TRIPS era (see Box 2.20).

#### **Box 2.20: Product patents and access to innovative medicines in a post-TRIPS era**

Watal and Dai (2019)<sup>354</sup> investigated two questions: (1) How does the introduction of product patents for pharmaceuticals affect the likelihood of pharmaceutical firms launching new and innovative medicines in those markets? (2) For innovative medicines,<sup>355</sup> how much do patent owners or generic pharmaceutical firms adjust their prices to local income levels?

Using launch data from 1980 to 2017 covering 70 markets, the study finds that introduction of product patent for pharmaceuticals in the patent law has a positive effect on the likelihood of earlier launch, especially for innovative pharmaceuticals. However, this effect is quite limited in low-income markets. Also, innovative pharmaceuticals are launched sooner than non-innovative ones, irrespective of the patent regime in the local market.

Using a panel data set of originator and generic prices from 2007 to 2017, the study finds evidence of some differential pricing for both originator and generic products. Overall, originators differentiate by about 11 per cent and generics by about 26 per cent. Differential pricing is larger for pharmaceuticals to treat infectious diseases, particularly for HIV/AIDS medicines, than for those to treat NCDs. However, pharmaceutical prices are far from being fully adjusted to local income levels in either case. It is clear that competition, especially that within a particular medicine market as opposed to the market of medicines that treat similar medical conditions, can effectively drive down prices in both originator and generic markets.

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 the date of first approval in that country. For example, Chile has implemented such a system following the US–Chile FTA (Fink, 2011).<sup>356</sup> 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 (AMCs), and it has spawned new business models such as product development partnerships (PDPs).<sup>357</sup>

## D. Genetic resources, traditional knowledge and traditional medicine

### Key points

- 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 in the prevention, diagnosis, improvement or treatment of physical and mental illnesses.
- 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.
- The commercial exploitation of genetic resources (GRs) and traditional knowledge (TK) by other than the TK holders raises questions of legal protection of TK against unauthorized use.
- Documentation of traditional medical knowledge, such as databases and national inventories, can be used as evidence of prior art in patent procedures.
- The essential effect of the Convention on Biological Diversity (CBD) and the Nagoya Protocol is to confirm national sovereignty over GRs and to establish a right of prior informed consent (PIC) over access to, and use of, GRs and associated TK. The three main objectives of the CBD are the conservation of biological diversity, the sustainable use of its components and the fair and equitable sharing of the benefits arising out of the utilization of GRs.
- The WHO Pandemic Influenza Preparedness (PIP) Framework governs the sharing of influenza viruses (and related materials) between research centres and commercial entities.

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 in the prevention, diagnosis, improvement or treatment of physical and mental illnesses.<sup>358</sup> It is used as a comprehensive term to refer to both traditional medicine systems, such as traditional Chinese medicine (TCM), Ayurvedic medicine and Unani medicine, and 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).<sup>359</sup>

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.<sup>360</sup> Traditional medicine is used widely throughout the world, but especially in developing countries. As of 2018, 88 per cent of WHO member states acknowledged use of traditional and complementary medicine (T&CM) (WHO, 2019f).

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 that the total value of exports of Chinese *Materia Medica* is more than US\$ 39 billion, and the annual growth rate is about 0.5 per cent from 2014 to 2018.<sup>361</sup>

The goals for the WHO Traditional Medicine Strategy 2014–2023 are to support member states in:

- harnessing the potential contribution of T&CM to health, wellness, people-centred health care and universal health coverage
- promoting safe and effective use of T&CM through the regulation, research and integration of T&CM products, practices and practitioners into the health system, as appropriate.<sup>362</sup>

In the GSPA-PHI, the WHO identified traditional medicine as one of the areas to be addressed in its Quick Start programme. The programme aimed “to support research

and development and to promote standard-setting for Traditional Medicine products in developing countries".<sup>363</sup> The relevance of integrating T&CM into health systems to strengthen global efforts targeting health challenges has been acknowledged by the World Health Assembly Resolution on Global Action on Patient Safety and the UN Political Declaration on UHC, both adopted in 2019.

## 2. Traditional medical knowledge in 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, 2015a).<sup>364</sup> 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).

In general, traditional medicine systems may be categorized as follows:

- Codified systems, which have been disclosed in writing in ancient scriptures; these include the systems of Ayurveda, Mongolian traditional medicine, Siddha medicine, traditional Chinese medicine, Thai traditional medicine, Tibetan medicine and Unani medicine
- Non-codified traditional medical 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<sup>365</sup> 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, traditional knowledge and traditional cultural expressions, as well as the manifestations of their sciences, technologies and cultures".

## 3. Traditional medicines regulation

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. 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, natural health products, health foods or functional foods. As of 2018, 124 member states (64 per cent) reported that they have laws and/or regulations on herbal medicines (WHO, 2019f).

As part of implementing the WHO Traditional Medicine Strategy 2014–2023, a comprehensive regulatory package is promoted and supported by the WHO, which includes the regulation of products, practices and practitioners of traditional, complementary and integrative medicine. As of 2018, 109 member states reported the presence of a legal framework for T&CMs, and 78 member states reported regulation of T&CM providers (WHO, 2019f). In this regard, the WHO is developing several categories of standards, norms and technical documents, such as a series of benchmarks for training in T&CM, a series of benchmarks for the practice of T&CM, a series on terminology in T&CM, and a traditional medicine chapter in the international classification of diseases.<sup>366</sup>

Growth in international trade in traditional medical products has sparked discussions on the trade impact of regulations. WTO members have notified and discussed regulations dealing with such products in the WTO TBT Committee (see section B.3(b)(ii) above). Since 1995, more than 80 measures regulating traditional medical products were notified to the TBT Committee.<sup>367</sup> The growth that could be observed in such notifications reflects an increasing prevalence of regulation of these products.<sup>368</sup> The main objectives of these measures cited by members are the need to protect human health or safety, and the prevention of deceptive practices and consumer protection.

WTO members have raised a small number of specific trade concerns in the TBT Committee dealing with measures on traditional medical products. The purpose is to discuss concerns pertaining to specific laws, regulations or procedures that affect their trade, usually in response to notifications.

For example, in 2010, China, Ecuador and India argued that EU Directives 2001/83/EC and 2004/24/EC on Traditional Herbal Medicinal Products<sup>369</sup> introduced unnecessary barriers to trade in traditional medical products.<sup>370</sup> The European Union explained that the 2004 Directive provided a simplified registration procedure for traditional herbal medicines, for example, by exempting the manufacturer from providing a number of tests and clinical trials that were otherwise required under the normal authorization procedure.<sup>371</sup>

#### 4. Concerns about misappropriation of traditional knowledge and genetic resources

One problem confronting TK holders is the commercial exploitation of their knowledge by others. This raises questions of legal protection of TK against unauthorized use. Research is continuing on traditional medicines and traditional medical knowledge in various 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.<sup>372</sup> Current malaria treatments contain synthetic derivatives of artemisinin, which is derived from a plant, sweet wormwood, *Artemisia annua*. This is an ancient Chinese medicine still used in modern practice, which 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). Many of the issues highlighted in this debate concern genetic materials used as the basis for medical research, and traditional medical knowledge that is used either directly to produce new products or 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 (CIPIH) has stated that it sees a need to guard against misappropriation of genetic resources (GRs)

and TK to ensure that the benefits derived from TK are fairly shared with the communities that discovered those resources and their possible medical uses, and to promote the use of such knowledge for the benefit of public health (WHO, 2006a).

Access to GRs and associated TK is primarily regulated by the Convention on Biological Diversity (CBD), which came into force in 1993, 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), which came into force in 2014.<sup>373</sup> 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 GRs and associated TK.

The essential effect of the CBD and Nagoya Protocol is to confirm national sovereignty over GRs and to establish a right of prior informed consent (PIC), approval and involvement over access to, and use of, GRs and associated TK. The three main objectives of the CBD are the conservation of biological diversity, the sustainable use of its components, and the fair and equitable sharing of the benefits arising out of the utilization of GRs (see Box 2.21).

How to apply PIC and access and benefit-sharing (ABS) has sparked a wide-ranging debate. For the area of vaccines development, the WHO Pandemic Influenza Preparedness Framework for the Sharing of Influenza Viruses and Access to Vaccines and other Benefits (PIP Framework) has established Standard Material Transfer Agreements to implement ABS considerations for the exchange of viruses in that Framework (for the political debate on ABS aspects regarding the sharing of viruses, see Chapter III, section E).<sup>374</sup> With regard to IP, however, the policy issues can be distilled into two broad themes:

- Whether patents and other IPRs can and should be obtained over inventions derived from GRs and associated TK. In particular, what mechanisms, if any, should be put in place to ensure that patents are not erroneously granted over TK and GRs and that patent holders comply with the principles of PIC and ABS. Strategies to ensure that third parties do not gain illegitimate or unfounded IPRs over TK subject matter and related GRs are known as "defensive protection", such as measures to pre-empt or invalidate patents that claim pre-existing TK as inventions.
- How to recognize and give legal and practical effect to positive IPRs that owners or custodians of GRs and associated TK 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 taking due account of TK in patent examination have led to initiatives at international and national levels to avoid grant of erroneous patents, on traditional medicines in particular. A leading example is the Traditional Knowledge Digital Library (TKDL), a collaborative project in India between the Council of Scientific and Industrial Research (CSIR), Ministry of Science and Technology and Ministry of Health and Family Welfare. An interdisciplinary team of Indian medicine experts, patent examiners, IT experts, scientists and technical officers has 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. Thus, the TKDL provides information on traditional medical knowledge in five international languages and formats that are understandable by patent examiners at international patent offices. The aim is to prevent the grant of erroneous patents,<sup>375</sup> while, at the same

time, not publishing TK in a way that would facilitate its misappropriation. The GSPA-PHI urges governments and concerned communities to facilitate access to traditional medicinal knowledge information for use as prior art<sup>376</sup> in the patent examination procedures, where appropriate, through the inclusion of such information in digital libraries (Element 5.1f). The WTO TRIPS Council<sup>377</sup> and the WIPO Intergovernmental Committee on Intellectual Property and Genetic Resources, Traditional Knowledge and Folklore (IGC) have discussed how to preclude erroneous patents using GRs and associated TK through the use of databases.<sup>378</sup>

## 5. New approaches to IP protection of traditional medical knowledge

Parties to the CBD, members of WIPO and of the WTO have considered the concept of a disclosure requirement

### **Box 2.21: 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)**

The Convention on Biological Diversity (CBD) and Nagoya Protocol cover both GRs and TK associated with them. While the Convention confirms the sovereign rights of states over their natural resources, the Nagoya Protocol has established a transparent legal framework that aims to ensure that the benefits of utilization and/or commercialization of GRs and associated TK are shared in a fair and equitable way with their country of origin.

Access to GRs under the Nagoya Protocol is subject to two basic requirements: PIC and mutually agreed terms (MAT). Those who wish to access GRs need the PIC of the competent authority in the country of origin or source according to Article 6.1 of the Nagoya Protocol and MAT have to be reached. For instance, a research institute wishing to access a GR that is from another jurisdiction must meet the obligations set by that jurisdiction's ABS legislation. In practice, this could mean establishing contact with the relevant National Focal Point on ABS or other competent authority responsible for granting access to the specific GR, and applying for the necessary permits and entering into a bilateral agreement on MAT that specify the terms and conditions for, in particular, the equitable sharing of benefits. Parties to the agreed utilization of a GR must make sure that due diligence is exercised, ensuring that anyone using GRs in their jurisdiction follows proper PIC and MAT procedures.<sup>379</sup>

Different approaches have been formulated to managing IPR in accordance with the ABS principles of the Nagoya Protocol. Argentina's model MAT for the CBD generally stipulate that the Government exclusively retains all IPRs related to the material used and its derivatives. At the other end of the spectrum is the Australian model MAT for the CBD, which grants to the user IPRs arising from R&D activity using the material. Under the Swiss model agreement, if commercialization is sought of the fruits of R&D, new PIC and MAT have to be negotiated, and the user has the opportunity to file an application for an IPR within an agreed period of time, after which the provider exercises his or her right to publish the research, thereby placing it in the public domain. Annex 1(j) to the Nagoya Protocol contemplates the possibility of joint ownership of relevant IPRs. Within the PIP Framework, the Standard Material Transfer Agreement (SMTA) 1, which governs the sharing of PIP biological materials within the WHO Global Influenza Surveillance and Response System (GISRS), prohibits the user from obtaining IPR on the material, while SMTA 2, which governs sharing of PIP biological materials outside the GISRS, does not (see Chapter III, section E.3).

The use of digital sequence information on GRs with respect to the objectives of the CBD is being discussed by the parties to the CBD and Nagoya Protocol.<sup>380</sup> The term "digital sequence information" has not been defined in the context of the CBD. A similar discussion is taking place in the context of the PIP Framework (see Chapter III, section E.3–4). That debate uses the term "genetic sequence data" and understands both terms as meaning information related to genetic sequencing.<sup>381</sup> The WHO considers that digital sequence information from pathogens is a global public health good that should be widely available to all and that benefits derived from using such sequence information should be shared equitably with all, without impeding the rapid, timely and broad sharing of sequences for disease control, prevention and preparedness.<sup>382</sup>

in the patent system, put forward by its proponents as a means of ensuring that patents on inventions derived from TK and GRs are consonant with the principles of PIC and ABS. 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 and GRs used in claimed inventions and to document compliance with PIC and ABS requirements. A number of countries have implemented such provisions in their national laws, but there is no agreed international standard. An alliance of WTO members has proposed a revision to the TRIPS Agreement to make such provisions mandatory,<sup>383</sup> but other countries continue to question the usefulness and effectiveness of this kind of disclosure mechanism.<sup>384</sup> *Key Questions on Patent Disclosure Requirements for Genetic Resources and Traditional Knowledge* (WIPO, 2017b) offers a comprehensive overview of key legal and operational questions on disclosure requirements.

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: (i) preserving the living cultural and social context of TK, and maintaining the customary framework for developing, passing on and governing access to TK; and (ii) 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.

In the WIPO IGC, member states are working on the development of an international legal instrument for the effective protection of TK and on ways to address IP aspects of access to, and benefit-sharing of, GRs, including patent disclosure requirements. Two draft texts are available for member states to discuss.<sup>385</sup> The work of the IGC on TK<sup>386</sup> is concentrating on positive protection and the IP aspect of protection – the recognition and exercise of rights to preclude others from illegitimate or unauthorized 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.

At the WTO TRIPS Council, members have continuously discussed the protection of TK, including measures taken at the national level and the need to put an international framework for the protection of TK in place. Previously, the African Group had proposed a formal decision to establish a system of TK protection, but this discussion has not led to any conclusions.<sup>387</sup>

#### (a) Why protect traditional knowledge?

The IGC has considered the policy objectives for international protection,<sup>388</sup> including to:

- Prevent unauthorized use of 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 MAT and promote equitable benefit-sharing (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 terms “indigenous peoples” or “local communities” and consider that individuals or families maintain TK.

#### (c) What is it to be protected from?

TK holders 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, such as in the Pelargonium case (Wendland and Jiao, 2018).

**(d) How can traditional knowledge be protected?**

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 used successfully to protect against some forms of misuse and misappropriation of aspects of TK. *Protect and Promote Your Culture: A Practical Guide to Intellectual Property for Indigenous Peoples and Local Communities* (WIPO, 2017c) explains how to use IP tools to protect and promote 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. 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 obtain 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 *Documenting Traditional Knowledge – A Toolkit* (WIPO, 2017a) to help holders of TK, in particular, indigenous peoples and local communities, protect their interests should they decide to document their TK. 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 The right to health is recognized in international instruments, such as the WHO Constitution, the Universal Declaration of Human Rights (Article 25) and the International Covenant on Economic, Social and Cultural Rights (Article 12).
- 2 See Sustainable Development Knowledge Platform at <https://sustainabledevelopment.un.org/sdgs>, in particular SDGs 1, 3 and 17.
- 3 UN document E/C.12/2000/4.
- 4 Ibid.
- 5 Report of the Special Rapporteur on the right to health (2006), A/61/338, para. 49.
- 6 UN document E/C.12/GC/17.
- 7 UN document E/C.12/GC/24.
- 8 Commission on Human Rights resolution 2002/31, see <https://www.ohchr.org/EN/Issues/Health/Pages/SRRightHealthIndex.aspx>.
- 9 See <https://www.ohchr.org/EN/Issues/Health/Pages/SRRightHealthIndex.aspx>.
- 10 See <https://www.ohchr.org/EN/Issues/Health/Pages/AnnualReports.aspx>.
- 11 UN documents A/HRC/RES/32/15, A/HRC/RES/23/14 and A/HRC/41/L.13.
- 12 UN documents A/HRC/RES/32/15 and A/HRC/41/L.13.
- 13 UN document A/RES/S-26/2.
- 14 UN document A/RES/70/266.
- 15 See Sustainable Development Knowledge Platform at <https://sustainabledevelopment.un.org/sdgs>.
- 16 See <https://www.un.org/millenniumgoals/>.
- 17 All submissions to the UNHLP are available at: <http://www.unsgaccessmeds.org/reports-documents>.
- 18 WTO document IP/C/75. Council for Trade-Related Aspects of Intellectual Property Rights – Annual report (2016) of the Council for TRIPS; WHO document A70/20. Addressing the global shortage of, and access to, medicines and vaccines; UN Human Rights Council. 34th session of the Human Rights Council (27 February to 24 March 2017). Panel discussion on good practices and key challenges relevant to access to medicines as one of the fundamental elements of the right of everyone to the enjoyment of the highest attainable standard of physical and mental health.
- 19 See, in particular, TRIPS Council meetings of 8–9 November 2016, WTO documents IP/C/M/83 and Add.1, and TRIPS Council meetings of 1–2 March 2017, WTO documents IP/C/M/85 and Add.1.
- 20 See WIPO documents SCP/25/6, SCP/26/8, SCP/27/10, SCP/28/12 and SCP/29/8, available at: [https://www.wipo.int/meetings/en/topic.jsp?group\\_id=61](https://www.wipo.int/meetings/en/topic.jsp?group_id=61).
- 21 UN documents WHA70/2017/REC/3, WHA71/2018/REC/3, EB140/2017/REC/2 and EB144/2019/REC/2.
- 22 General Assembly resolution A/RES/71/159.
- 23 WHA, Resolution WHA49.14: Revised drug strategy.
- 24 WHA, Resolution WHA52.19: Revised drug strategy.
- 25 WHA, Resolution WHA60.30: Public health, innovation and intellectual property.
- 26 WHA, Resolution WHA56.27: Intellectual property rights, innovation and public health.
- 27 WHA, Resolution WHA56.30: Global health-sector strategy for HIV/AIDS.
- 28 WHA, Resolution WHA59.26: International trade and health.
- 29 WHA, Resolution WHA60.30: Public health, innovation and intellectual property.
- 30 For a list of relevant publications from the WHO and other intergovernmental organizations, see <https://www.who.int/phi/publications/en/>.
- 31 WHA, Resolution WHA56.27: Intellectual property rights, innovation and public health.
- 32 WHA, Resolution WHA61.21: Global strategy and plan of action on public health, innovation and intellectual property; WHA, Resolution WHA62.16: Global strategy and plan of action on public health, innovation and intellectual property.
- 33 WHA, Resolution WHA61.21: Global strategy and plan of action on public health, innovation and intellectual property, Annex, para. 7.
- 34 See Chapter III, section C.4.
- 35 WHA, Resolution WHA61.21: Global strategy and plan of action on public health, innovation and intellectual property, Annex, para. 14(e).
- 36 Ibid., Annex Element 5.1(h).
- 37 WHA, Resolution WHA61.21: Global strategy and plan of action on public health, innovation and intellectual property, para. 4(5).
- 38 See Chapter I, section B.4.
- 39 See WHA Resolutions WHA62.16, EB136(17), and WHA68.18.
- 40 WHA, Decision: WHA71(9): Global strategy and plan of action on public health, innovation and intellectual property: overall programme review.
- 41 WHA, Resolution WHA64.5: Pandemic influenza preparedness: sharing of influenza viruses and access to vaccines and other benefits. See also Chapter III, section E.
- 42 UN document A/RES/66/2. See also WHA, Decision WHA65(8): Prevention and control of non-communicable diseases: follow-up to the High-level Meeting of the United Nations General Assembly on the Prevention and Control of Non-communicable Diseases.
- 43 See <https://www.gardp.org/>.
- 44 See <https://www.who.int/research-observatory/en/>.
- 45 See [https://www.who.int/medicines/access/fair\\_pricing/en/](https://www.who.int/medicines/access/fair_pricing/en/).
- 46 See [https://www.who.int/phi/implementation/tech\\_transfer/en/](https://www.who.int/phi/implementation/tech_transfer/en/).

- 47 "Antimicrobial resistance – a global epidemic, Background paper for the Technical Symposium on Antimicrobial Resistance: How to Foster Innovation, Access and Appropriate Use of Antibiotics? Prepared by the Secretariats of WHO, WIPO and WTO", available at: [https://www.wipo.int/edocs/mdocs/mdocs/en/wipo\\_who\\_wto\\_ip\\_ge\\_16/wipo\\_who\\_wto\\_ip\\_ge\\_16\\_inf\\_2.pdf](https://www.wipo.int/edocs/mdocs/mdocs/en/wipo_who_wto_ip_ge_16/wipo_who_wto_ip_ge_16_inf_2.pdf).
- 48 See <https://www.who.int/antimicrobial-resistance/interagency-coordination-group/final-report/en/>.
- 49 WHA, Resolution WHA68.7: Global action plan on antimicrobial resistance.
- 50 See WHO Document A72/18 at paras. 37–41, available at: [http://apps.who.int/gb/ebwha/pdf\\_files/WHA72/A72\\_18-en.pdf](http://apps.who.int/gb/ebwha/pdf_files/WHA72/A72_18-en.pdf); see also <http://www.fao.org/antimicrobial-resistance/en/>, <https://www.oie.int/en/our-scientific-expertise/veterinary-products/antimicrobials/> and [https://www.who.int/foodsafety/areas\\_work/antimicrobial-resistance/tripartite/en/](https://www.who.int/foodsafety/areas_work/antimicrobial-resistance/tripartite/en/).
- 51 UN document A/RES/71/3.
- 52 Ibid., para. 15.
- 53 The IACG developed six discussion papers, which cover the topics: (i) Antimicrobial resistance: Invest in innovation and research, and boost R&D and access; (ii) Antimicrobial resistance: national action plans; (iii) Surveillance and monitoring for antimicrobial use and resistance; (iv) Future global governance for antimicrobial resistance; (v) Optimize use of antimicrobials; and (vi) Meeting the challenge of antimicrobial resistance: from communication to collective action. The discussion papers are available at: <https://www.who.int/antimicrobial-resistance/interagency-coordination-group/public-consultation-discussion-papers/en/>.
- 54 UN document A/73/869.
- 55 UN document A/RES/74/2.
- 56 See [https://www.wipo.int/meetings/en/2016/wipo\\_wto\\_who\\_technical\\_symposium.html](https://www.wipo.int/meetings/en/2016/wipo_wto_who_technical_symposium.html); "Antimicrobial resistance – a global epidemic, Background paper for the Technical Symposium on Antimicrobial Resistance: How to Foster Innovation, Access and Appropriate Use of Antibiotics? Prepared by the Secretariats of WHO, WIPO and WTO", available at: [https://www.wipo.int/edocs/mdocs/mdocs/en/wipo\\_who\\_wto\\_ip\\_ge\\_16/wipo\\_who\\_wto\\_ip\\_ge\\_16\\_inf\\_2.pdf](https://www.wipo.int/edocs/mdocs/mdocs/en/wipo_who_wto_ip_ge_16/wipo_who_wto_ip_ge_16_inf_2.pdf).
- 57 See, for example, WTO Workshop on Trade and Public Health, organized in close collaboration with WHO and WIPO, 8 to 12 October 2018, [https://www.wto.org/english/news\\_e/news18\\_e/tra\\_15oct18\\_e.htm](https://www.wto.org/english/news_e/news18_e/tra_15oct18_e.htm).
- 58 See [https://apps.who.int/iris/bitstream/handle/10665/193736/9789241509763\\_eng.pdf?sequence=1](https://apps.who.int/iris/bitstream/handle/10665/193736/9789241509763_eng.pdf?sequence=1).
- 59 See <https://www.who.int/antimicrobial-resistance/en/>.
- 60 See WHO Library of national action plans, available at: <https://www.who.int/antimicrobial-resistance/national-action-plans/library/en/>.
- 61 See, for example, WHO. Marketing authorization of pharmaceutical products with special reference to multisource (generic) products: a manual for National Medicines Regulatory Authorities (NMRAs) – 2nd edition, available at: [https://apps.who.int/iris/bitstream/handle/10665/44576/9789241501453\\_eng.pdf?sequence=1](https://apps.who.int/iris/bitstream/handle/10665/44576/9789241501453_eng.pdf?sequence=1); WHO Global Benchmarking Tool, available at: [https://www.who.int/medicines/regulation/benchmarking\\_tool/en/](https://www.who.int/medicines/regulation/benchmarking_tool/en/); WHO Global Benchmarking Tool (GBT) for Evaluation of National Regulatory System of Medical Products. National Regulatory System (RS): Indicators and Fact Sheets, available at: [https://www.who.int/medicines/areas/regulation/01\\_GBT\\_RS\\_RevVI.pdf?ua=1](https://www.who.int/medicines/areas/regulation/01_GBT_RS_RevVI.pdf?ua=1).
- 62 See also [http://www.who.int/medical\\_devices/safety/en/](http://www.who.int/medical_devices/safety/en/).
- 63 See Regulation (EU) 2017/745 and Regulation (EU) 2017/746; BBC News, "Q&A: PIP breast implants health scare", 10 December 2013, available at: <https://www.bbc.com/news/health-16391522>.
- 64 See also <https://www.who.int/clinical-trials-registry-platform/about/glossary>. For information on the role of clinical trials in the drug development process, see Chapter III, section B.7.
- 65 WHA, Resolution WHA58.34: Ministerial Summit on Health Research.
- 66 World Medical Association, WMA Declaration of Taipei on Ethical Considerations regarding Health Databases and Biobanks, available at: <https://www.wma.net/policies-post/wma-declaration-of-taipei-on-ethical-considerations-regarding-health-databases-and-biobanks/>.
- 67 UNESCO, About the Bioethics Programme, available at: <http://www.unesco.org/new/en/social-and-human-sciences/themes/bioethics/about-bioethics/>.
- 68 UNESCO, Universal Declaration on Bioethics and Human Rights. 19 October 2005, available at: [http://portal.unesco.org/en/ev.php?URL\\_ID=31058&URL\\_DO=DO\\_TOPIC&URL\\_SECTION=201.html](http://portal.unesco.org/en/ev.php?URL_ID=31058&URL_DO=DO_TOPIC&URL_SECTION=201.html).
- 69 WIPO, *Intellectual Property and Bioethics – An Overview: Consultation Draft*, available at: [https://www.wipo.int/edocs/pubdocs/en/intproperty/932/wipo\\_pub\\_b932ipb.pdf](https://www.wipo.int/edocs/pubdocs/en/intproperty/932/wipo_pub_b932ipb.pdf); see also WIPO Life Sciences Symposium, 4 September 2007, available at: [https://www.wipo.int/meetings/en/details.jsp?meeting\\_id=14142](https://www.wipo.int/meetings/en/details.jsp?meeting_id=14142).
- 70 See <https://www.who.int/ethics/about/unintercomm/en/>.
- 71 Available at: <http://www.unesco.org/new/en/social-and-human-sciences/themes/bioethics/human-genome-and-human-rights/>.
- 72 Available at: <http://www.unesco.org/new/en/social-and-human-sciences/themes/bioethics/human-genetic-data/>.
- 73 Available at: <http://www.unesco.org/new/en/social-and-human-sciences/themes/bioethics/bioethics-and-human-rights/>.
- 74 WHO expert advisory committee on Developing global standards for governance and oversight of Human Genome editing, see <https://www.who.int/ethics/topics/human-genome-editing/committee-members/en/>; The Global Summit of National Bioethics Committees, see <https://www.who.int/ethics/partnerships/globalsummit/en/>.
- 75 The WHO Model Lists of Essential Medicines are available at: <https://www.who.int/medicines/publications/essentialmedicines/en/>.
- 76 World Health Organization, Expert Committee on Biological Standardization, Geneva, 19 to 23 October 2009, "Guidelines on Evaluation of Similar Biotherapeutic Products (SBPs)", available at: [https://www.who.int/biologicals/publications/trs/areas/biological\\_therapeutics/TRS\\_977\\_Annex\\_2.pdf?ua=1](https://www.who.int/biologicals/publications/trs/areas/biological_therapeutics/TRS_977_Annex_2.pdf?ua=1).

- 77 See, for example, Berkowitz, S. A., Engen, J. R., Mazzeo J. R. and Jones, G. B. (2012), “Analytical tools for characterizing biopharmaceuticals and the implications for biosimilars”, *Nature Reviews. Drug Discovery* 11(7): 527–540.
- 78 See <https://www.who.int/biologicals/biotherapeutics/biotherapeutic-products/en/>.
- 79 See also European Medicines Agency, Biosimilar medicines: Overview, available at: <https://www.ema.europa.eu/en/human-regulatory/overview/biosimilar-medicines-overview>.
- 80 See European Medicines Agency, Multidisciplinary: biosimilar, available at: <https://www.ema.europa.eu/en/human-regulatory/research-development/scientific-guidelines/multidisciplinary/multidisciplinary-biosimilar>.
- 81 See [https://www.swissmedic.ch/swissmedic/en/home/humanarzneimittel/authorisations/information/anpassung\\_wlbiosimilar.html](https://www.swissmedic.ch/swissmedic/en/home/humanarzneimittel/authorisations/information/anpassung_wlbiosimilar.html).
- 82 See [https://www.who.int/biologicals/biotherapeutics/similar\\_biotherapeutic\\_products/en/](https://www.who.int/biologicals/biotherapeutics/similar_biotherapeutic_products/en/).
- 83 See WHO Pilot procedure for prequalification of biotherapeutic products and similar biotherapeutic products, available at: [https://www.who.int/medicines/regulation/biotherapeutic\\_products/en/](https://www.who.int/medicines/regulation/biotherapeutic_products/en/).
- 84 The range of products included in the advanced therapy medicinal products category varies slightly between regulators, see <https://eur-lex.europa.eu/legal-content/EN/TXT/?qid=1560343808209&uri=CELEX:32007R1394> and <https://www.fda.gov/BiologicsBloodVaccines/CellularGeneTherapyProducts/ucm537670.htm>.
- 85 See National Cancer Institute, Treatment and Therapy, available at: <https://www.cancer.gov/nano/cancer-nanotechnology/treatment>.
- 86 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, section A.4–9.
- 87 UNEP, 2019, p. 12.
- 88 See, for example, Heidi Ledford (2018), “CRISPR gene editing produces unwanted DNA deletions”, *Nature*, online version, 16 July 2018, available at: <https://www.nature.com/articles/d41586-018-05736-3>; Wellcome Trust Sanger Institute (2018), “Genome damage from CRISPR/Cas9 gene editing higher than thought”, 16 July 2018, available at: <https://phys.org/news/2018-07-genome-crisprcas9-gene-higher-thought.html>.
- 89 Manuel Juan Otero (Head of Section, Hospital Clinic of Barcelona), presentation to Cutting-Edge Health Technologies: Opportunities and Challenges, Joint Technical Symposium by the WHO, WIPO, WTO, Geneva, 31 October 2019, available at: [https://www.wto.org/english/tratop\\_e/trips\\_e/who\\_wipo\\_wto\\_e.htm](https://www.wto.org/english/tratop_e/trips_e/who_wipo_wto_e.htm); WIPO, 2019b, p. 143; WIPO document SCP/30/5.
- 90 US FDA, BLA Approval Letter, 30 August 2017, available at: <https://www.fda.gov/media/106989/download>.
- 91 WO/2012/079000; Jürgens and Clarke, 2019.
- 92 See discussion on “Supporting new data infrastructure and regulatory processes” in Cornell University, INSEAD and WIPO (2019).
- 93 Directive 2001/83/EC of the European Parliament and of the Council on the Community Code Relating to Medicinal Products for Human Use, Articles 10(1) and (5); Regulation (EC) No 726/2004, Article 14(11), see also WT/TPR/S/284/Rev.2, para. 3.295.
- 94 See Frias, Z. (2013), “Data Exclusivity, Market Protection and Paediatric Rewards”, presentation to European Medicines Agency Workshop for Micro, Small and Medium Sized Enterprises, 26 April 2013, available at: [https://www.ema.europa.eu/en/documents/presentation/presentation-data-exclusivity-market-protection-paediatric-rewards-zaide-frias\\_en.pdf](https://www.ema.europa.eu/en/documents/presentation/presentation-data-exclusivity-market-protection-paediatric-rewards-zaide-frias_en.pdf).
- 95 The concept of “similarity” in this context is different from the concept of “similarity” in biotherapeutic products (see Chapter II, section A.6(d)). A system of tests is provided in guidelines to determine what constitute “similar” orphan products, see 19.9.2008 C(2008) 4077 final. European Commission, *Communication from the Commission: Guideline on aspects of the application of Article 8(1) and (3) of Regulation (EC) No 141/2000: Assessing similarity of medicinal products versus authorised orphan medicinal products benefiting from market exclusivity and applying derogations from that market exclusivity*, available at: [https://ec.europa.eu/health/sites/health/files/files/orphanmp/doc/c\\_2008\\_4077\\_en.pdf](https://ec.europa.eu/health/sites/health/files/files/orphanmp/doc/c_2008_4077_en.pdf).
- 96 Regulation (EC) No 1901/2006 of the European Parliament and of the Council of 12 December 2006 on medicinal products for paediatric use and amending Regulation (EEC) No 1768/92, Directive 2001/20/EC, Directive 2001/83/EC and Regulation (EC) No 726/2004 (OJ L 378, 27.12.2006, p. 1) provides in its Article 37 that for medicinal products designated as orphan medicinal products, if specified criteria in the paediatric Regulation are met, the ten-year period referred to in Article 8(1) of Regulation (EC) No 141/2000 shall be extended to twelve years (two-year extension as reward for compliance with paediatric investigation plan).
- 97 See Guideline on review of the period of market exclusivity of orphan medicinal products, available at: <https://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:C:2008:242:0008:0011:EN:PDF>.
- 98 US FDA, Guidance for Industry: Reference Product Exclusivity for Biological Products Filed Under Section 351(a) of the PHS Act, August 2014, available at: <https://www.fda.gov/downloads/drugs/guidancecomplianceregulatoryinformation/guidances/ucm407844.pdf>.
- 99 42 U.S.C. §262(k)(6).
- 100 21 U.S.C. §355A(b) (1997).
- 101 See C.08.004.1(5) of the Food and Drug Regulations; Guidance Document: Data Protection under C.08.004.1 of the Food and Drug Regulations, available at: <https://www.canada.ca/en/health-canada/services/drugs-health-products/drug-products/applications-submissions/guidance-documents/guidance-document-data-protection-under-08-004-1-food-drug-regulations.html#a25>.
- 102 't Hoen et al., 2017. This is explained in Chapter IV, section C.3(a)(ii).
- 103 See: s. 5 of Malaysia 2011 Directive of Data Exclusivity; Article 91 of Chilean Law 19.996 as amended in 2012; and Article 4 of Colombian Decree 2085 or 2002; 't Hoen et al., 2017.
- 104 This is explained in Chapter IV, section C.3(a)(iii).
- 105 See Medicines Patent Pool, Frequently Asked Questions (FAQs), 1 June 2018, “6. Why do companies work with the MPP?” (“Licenses include data exclusivity waivers [...]”), available at: <https://medicinespatentpool.org/uploads/2018/04/MPP-FAQ-EN.2018.06.06.pdf>.

- 106 For a review the economics of IP in the field of medical technologies, see Chapter II, section C.
- 107 For an explanation of the research exception, see Chapter III, section D.5(a).
- 108 This effect of “multilateralizing” the scope of bilateral deals on IP is discussed in Chapter II, section B.5(b).
- 109 WIPO document SCP/12/3 Rev. 2.
- 110 Ibid.
- 111 WIPO document MTN.GNG/NG11/W/24/Rev.1.
- 112 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).
- 113 See <https://www.wipo.int/treaties/en/registration/pct>.
- 114 Article 27 of the PCT.
- 115 WTO document WT/DS170.
- 116 See WIPO documents CDIP/8/INF/3, CDIP/12/INF/2REV, and member states' comments to the study in document CDIP/12/INF/2 REV. ADD.
- 117 Information on provisional protection of published international patent applications in PCT Contracting States is available at the PCT Applicants Guide (in the table, under International Phase, General Information), at <https://www.wipo.int/pct/en/guide/index.html>.
- 118 The WHO, WIPO, WTO joint technical workshop on patentability criteria of 27 October 2015 provided participants with practical insights into how the main substantive patentability criteria are applied in practice at country level and how different definitions and interpretations can impact public health. The presentations given are available from the website of the workshop at [https://www.wto.org/english/tratop\\_e/trips\\_e/trilat\\_workshop15\\_e.htm](https://www.wto.org/english/tratop_e/trips_e/trilat_workshop15_e.htm).
- 119 See Chapter IV, section C.1(b).
- 120 See [https://www.epo.org/law-practice/legal-texts/html/guidelines/e/g\\_ii\\_5.htm](https://www.epo.org/law-practice/legal-texts/html/guidelines/e/g_ii_5.htm).
- 121 See <https://www.epo.org/law-practice/legal-texts/html/guidelines/e/j.htm>.
- 122 See [https://www.epo.org/law-practice/legal-texts/html/guidelines/e/g\\_ii\\_3\\_3\\_1.htm](https://www.epo.org/law-practice/legal-texts/html/guidelines/e/g_ii_3_3_1.htm).
- 123 See <https://www.epo.org/law-practice/legal-texts/html/guidelines/e/index.htm>.
- 124 Article 27.2 reads “Members may exclude from patentability inventions, the prevention within their territory of the commercial exploitation of which is necessary to protect *ordre public* or morality, including to protect human, animal or plant life or health or to avoid serious prejudice to the environment, provided that such exclusion is not made merely because the exploitation is prohibited by their law.”
- 125 For example, under Article 53 of the European Patent Convention (EPC), patents shall not be granted on inventions whose publication or exploitation would be contrary to *ordre public* or morality (paragraph (a)). Rule 29 of the Implementing Regulations to 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.
- 126 See G.0002/06 (Use of embryos/WARF) of 25 November 2008, OJ 2009, 306, available at: <https://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: <https://www.epo.org/law-practice/case-law-appeals/recent/t041374ex1.html>.
- 127 See T 2221/10 (Culturing Stem Cells/TECHNION) of 4 February 2014, available at: <https://www.epo.org/law-practice/case-law-appeals/recent/t102221eu1.html>.
- 128 See C-34/10 (*Oliver Brüstle v. Greenpeace eV.*) of 18 October 2011, available at: <http://curia.europa.eu/juris/liste.jsf?language=en&num=C-34/10>.
- 129 See C-364/13 (*International Stem Cell Corporation v. Comptroller General of Patents, Designs and Trade Marks*) of 18 December 2014, available at: <http://curia.europa.eu/juris/document/document.jsf?text=&docid=160936&pageIndex=0&doclang=EN&mode=lst&dir=&occ=first&part=1&cid=344078>.
- 130 International Stem Cell Corporation [2016] APO 52.
- 131 The WTO TRIPS Council has reviewed the Scope of Article 27.3(b) since 1999, see WTO document IP/C/W/369/Rev.1. A 2010 WIPO Study (WIPO document SCP/15/3, Annex 3: Denis Borges Barbosa and Karin Grau-Kuntz, Exclusions from Patentable Subject Matter and Exceptions and Limitations to the Rights, Biotechnology) has looked in detail at how countries have implemented biotechnology-related provisions in patent law. Updated information on the exclusion from the patentable subject matter is available at: [https://www.wipo.int/scp/en/annex\\_ii.html](https://www.wipo.int/scp/en/annex_ii.html).
- 132 Certain Aspects of National/Regional Patent Laws: Revised Annex II of document SCP/12/3 Rev.2: Report on the International Patent System, available at: [https://www.wipo.int/scp/en/annex\\_ii.html](https://www.wipo.int/scp/en/annex_ii.html).
- 133 Information on how national and regional law defines novelty is published in WIPO document SCP/12/3 Rev.2, Report on the International Patent System, Annex II, Certain Aspects of National/Regional Patent Laws Revised, which is regularly updated and available at: [https://www.wipo.int/scp/en/annex\\_ii.html](https://www.wipo.int/scp/en/annex_ii.html).
- 134 WIPO SCP/22/3, paras. 13–14.
- 135 WIPO SCP/22/3, para. 23.
- 136 WIPO SCP/22/3, para. 14.
- 137 Example quoted from the PCT International Search and Preliminary Examination Guidelines, para. 13.4(d), available at: <https://www.wipo.int/export/sites/www/pct/en/texts/pdf/ispe.pdf>.
- 138 WIPO document SCP/30/4, available at: [https://www.wipo.int/meetings/en/doc\\_details.jsp?doc\\_id=435831](https://www.wipo.int/meetings/en/doc_details.jsp?doc_id=435831).
- 139 EPO Board of Appeal, BDP1 Phosphatase/MAX-PLANCK, T 0870/04, of 11 May 2005, available at: <https://www.epo.org/law-practice/case-law-appeals/recent/t040870eu1.html>.
- 140 See <https://www.gov.uk/government/publications/examining-patent-applications-for-biotechnological-inventions>.
- 141 KIPO, Patent Examination Guidelines, Part IX, Examination Criteria by Technology, Chapter 1, Biotechnological Inventions, 2017, available at: [https://www.kipo.go.kr/en/HtmIApp?c=92006&catmenu=ek03\\_06\\_01](https://www.kipo.go.kr/en/HtmIApp?c=92006&catmenu=ek03_06_01).

- 142 WIPO document SCP/22/4, para. 11.
- 143 See <https://www.wipo.int/treaties/en/registration/budapest/>.
- 144 Information on how national and regional law defines sufficiency of disclosure is published in WIPO document SCP/12/3 Rev.2, Report on the International Patent System, Annex II, Certain Aspects of National/Regional Patent Laws, which is regularly updated and available at: [https://www.wipo.int/export/sites/www/scp/en/national\\_laws/disclosure.pdf](https://www.wipo.int/export/sites/www/scp/en/national_laws/disclosure.pdf).
- 145 For example, according to the Guide to the Deposit of Microorganisms under the Budapest Treaty, Section D, available at: <https://www.wipo.int/treaties/en/registration/budapest/guide/index.html>, human cell cultures can be deposited with international depositary authorities in Australia, Belgium, China, France, Germany, Italy, Japan, Mexico, the Republic of Korea, the Russian Federation, Switzerland, the United Kingdom, and the United States.
- 146 WIPO document SCP/22/4, para. 8.
- 147 WIPO document SCP/13/5.
- 148 Supreme Court of Canada Decision of 8 November 2012, 2012 SCC, 60, *Teva Canada Ltd. V. Pfizer Canada Inc.*, available at: <https://scc-csc.lexum.com/scc-csc/scc-csc/en/item/12679/index.do>.
- 149 "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, para. 210).
- 150 WIPO documents SCP/12/3 and CDIP/7/3.
- 151 See International Worksharing and Collaborative Activities for Search and Examination of Patent Applications, available at: <https://www.wipo.int/patents/en/topics/worksharing>.
- 152 By 1 July 2020, 23 International Searching and International Preliminary Examining Authorities have been appointed, see [https://www.wipo.int/pct/en/access/isa\\_ipca\\_agreements.html](https://www.wipo.int/pct/en/access/isa_ipca_agreements.html).
- 153 ASEAN Patent Examination Co-operation Program (ASPEC); PROSUR, a system for technical co-operation between participating countries of Latin America; and the Vancouver Group, a collaboration between the IP Offices of Australia, Canada and the United Kingdom; The five IP offices (IP5: i.e. the European Patent Office (EPO), Japan Patent Office (JPO), Korean Intellectual Property Office (KIPO), National Intellectual Property Administration of the People's Republic of China (CNIPA) and United States Patent and Trademark Office (USPTO)) have established a mechanism to improve the efficiency of the examination process for patents worldwide, see: <http://www.fiveipoffices.org/index.html>. The IP5 offices handle about 80 per cent of the world's patent applications and 95 per cent of all work carried out under the PCT.
- 154 Examples include the SHARE pilot work-sharing initiative project between the Korean Intellectual Property Office and the United States Patent and Trademark Office and bilateral Patent Prosecution Highway agreements.
- 155 Patent grant and review procedures from an access-to-medicines perspective are addressed further in Chapter IV, section C.1–2.
- 156 See [https://www.gov.za/sites/default/files/gcis\\_document/201808/ippolicy2018-phasei.pdf](https://www.gov.za/sites/default/files/gcis_document/201808/ippolicy2018-phasei.pdf), p. 5.
- 157 For further information on opposition systems and other administrative revocation and invalidation mechanisms, see Opposition and Administrative Revocation Mechanisms, available at: [https://www.wipo.int/scp/en/revocation\\_mechanisms/](https://www.wipo.int/scp/en/revocation_mechanisms/), and WIPO document SCP/18/4. Review procedures from an access-to-medicines perspective are addressed in Chapter IV, section C.2.
- 158 For further information, see Chapter IV, section C.5(a)(vi).
- 159 See WIPO documents SCP/13/3, SCP/15/3, SCP/16/3, SCP/17/3, SCP/18/3, SCP/20/3, SCP/20/4, SCP/20/5, SCP/20/6, SCP/20/7, SCP/21/3, SCP/21/4 Rev., SCP/21/5 Rev., SCP/21/6, SCP/21/7, SCP/23/3, SCP/25/3, SCP/25/3 Add., SCP/27/3, SCP/28/3, SCP/28/3 Add., available at: [https://www.wipo.int/patents/en/topics/exceptions\\_limitations.html](https://www.wipo.int/patents/en/topics/exceptions_limitations.html). Exceptions and limitations and flexibilities in the patent system from an innovation and access-to-medicines perspective are addressed in Chapter II, section B.1(b)(vii); Chapter III, section D.5(a)–(b); and Chapter IV, section C.3(a), respectively.
- 160 For detailed information, see Topics and issues: patents and health, available at: [https://www.wipo.int/patents/en/topics/public\\_health.html](https://www.wipo.int/patents/en/topics/public_health.html).
- 161 Draft Reference Document on Exception Regarding Acts for Obtaining Regulatory Approval from Authorities (Second Draft), WIPO document SCP/28/3, available at: [https://www.wipo.int/meetings/en/doc\\_details.jsp?doc\\_id=406783](https://www.wipo.int/meetings/en/doc_details.jsp?doc_id=406783).
- 162 Draft Reference Document on Research Exception, Document SCP/29/3, available at: [https://www.wipo.int/meetings/en/doc\\_details.jsp?doc\\_id=420102](https://www.wipo.int/meetings/en/doc_details.jsp?doc_id=420102).
- 163 Draft Reference Document on the Exception Regarding Compulsory Licensing, Document SCP/30/3, available at: [https://www.wipo.int/meetings/en/doc\\_details.jsp?doc\\_id=437425](https://www.wipo.int/meetings/en/doc_details.jsp?doc_id=437425).
- 164 WIPO documents SCP/26/5, SCP/27/5.
- 165 See [https://www.wipo.int/scp/en/annex\\_ii.html](https://www.wipo.int/scp/en/annex_ii.html).
- 166 An overview of freedom-to-operate issues is provided in Chapter III, Section D.5(f).
- 167 See <https://www.wipo.int/standards/en/>.
- 168 See <https://www.wipo.int/cws/en/index.html>.
- 169 For a list of WIPO Standards, Recommendations and Guidelines, see [https://www.wipo.int/standards/en/part\\_03\\_standards.html](https://www.wipo.int/standards/en/part_03_standards.html).
- 170 See [https://www.wipo.int/standards/en/part\\_07.html](https://www.wipo.int/standards/en/part_07.html).
- 171 WHA document A72.8. Improving the transparency of markets for medicines, vaccines, and other health products, available at: [https://apps.who.int/gb/ebwha/pdf\\_files/WHA72/A72\\_R8-en.pdf](https://apps.who.int/gb/ebwha/pdf_files/WHA72/A72_R8-en.pdf).
- 172 See [https://www.wipo.int/patent\\_register\\_portal/en/index.html](https://www.wipo.int/patent_register_portal/en/index.html).
- 173 See <http://www.wipo.int/patentscope/en/>.
- 174 As at May 2020, more than 60 collections of national and regional offices, see: [https://patentscope.wipo.int/search/en/help/data\\_coverage.jsf?new=true](https://patentscope.wipo.int/search/en/help/data_coverage.jsf?new=true).
- 175 See <https://patentscope.wipo.int/search/en/clir/clir.jsp?new=true>.
- 176 See <https://patentscope.wipo.int/translate/translate.jsp?interfaceLanguage=en>.

- 177 See <https://www.wipo.int/reference/en/wipopearl>.
- 178 Gaceta de medicamentos, available at: <https://www.gob.mx/impi/documentos/gaceta-de-medicamentos?state=published>.
- 179 See <https://www.medspal.org/>.
- 180 See <https://www.wipo.int/pat-informed/en/>.
- 181 See Pat-INFORMED Terms of Use/Disclaimer, available at: <https://www.wipo.int/patinformed/>.
- 182 See <https://www.wipo.int/ip-development/en/agenda/recommendations.html>.
- 183 See <https://www.wipo.int/ardi>.
- 184 See <https://www.wipo.int/aspi>.
- 185 See <https://www.wipo.int/patentscope/en/data/developing-countries.html>.
- 186 See <https://www.wipo.int/tisc>.
- 187 See <https://www.wipo.int/das>.
- 188 See <https://www.wipo.int/case>.
- 189 For more information, see WIPO Handbook on Industrial Property Information and Documentation, Glossary of Terms (available at: <https://www.wipo.int/export/sites/www/standards/en/pdf/08-01-01.pdf>); and, for example, the EPO patent family definitions (available at: <https://www.epo.org/searching-for-patents/helpful-resources/first-time-here/patent-families.html>).
- 190 See Trippé (2015); WIPO Handbook on Industrial Property Information and Documentation, available at: <https://www.wipo.int/standards/en/#handbook>; Martinez (2010).
- 191 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 <https://www.wipo.int/classifications/ ipc/en/>.
- 192 WIPO document SCP/28/5.
- 193 SureChEMBL can be accessed free of charge at <https://www.surechembl.org/search/>.
- 194 See [https://www.wipo.int/patentscope/en/news/pctdb/2016/news\\_0008.html](https://www.wipo.int/patentscope/en/news/pctdb/2016/news_0008.html).
- 195 An overview of freedom-to-operate issues is provided in Chapter III, section D.5(f).
- 196 Ibid.
- 197 See WIPO Standard ST.27, available at: <https://www.wipo.int/export/sites/www/standards/en/pdf/03-27-01.pdf>.
- 198 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. In total, 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 [https://www.wipo.int/patentscope/en/programs/legal\\_status/index.html](https://www.wipo.int/patentscope/en/programs/legal_status/index.html).
- 199 The book's full title is the *Approved Drug Products with Therapeutic Equivalence Evaluations*; it is available at: <https://www.fda.gov/drugs/drug-approvals-and-databases/approved-drug-products-therapeutic-equivalence-evaluations-orange-book>.
- 200 See <https://www.accessdata.fda.gov/scripts/cder/ob/index.cfm> and 21 U.S.C. §355. New drugs. (b)(1), available at: <https://www.law.cornell.edu/uscode/text/21/355>.
- 201 See <https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/CFRSearch.cfm?fr=314.53>.
- 202 See <https://www.fda.gov/drugs/biosimilars/purple-book-lists-licensed-biological-products-reference-product-exclusivity-and-biosimilarity-or>.
- 203 See <http://pr-rdb.hc-sc.gc.ca/pr-rdb/index-eng.jsp>.
- 204 See <https://nedrug.mfds.go.kr/pbp/CCBAK01> (in Korean); "Searching in databases – Korea" at <https://www.epo.org/searching-for-patents/helpful-resources/asian/korea/search.html>; <http://koreaniplaw.blogspot.com/search/label/Green%20List>.
- 205 See, for example, the WIPO Patent Landscape reports on ritonavir, available at: <https://www.wipo.int/publications/en/details.jsp?id=230&plang=EN>, and on atazanavir, available at: <https://www.wipo.int/publications/en/details.jsp?id=265&plang=EN>.
- 206 See [https://www.wipo.int/patentscope/en/programs/patent\\_landscapes/](https://www.wipo.int/patentscope/en/programs/patent_landscapes/).
- 207 See [https://www.wipo.int/edocs/pubdocs/en/patents/946/wipo\\_pub\\_946\\_3.pdf](https://www.wipo.int/edocs/pubdocs/en/patents/946/wipo_pub_946_3.pdf).
- 208 See [https://www.wipo.int/edocs/pubdocs/en/wipo\\_pub\\_949\\_1.pdf](https://www.wipo.int/edocs/pubdocs/en/wipo_pub_949_1.pdf).
- 209 See [https://www.wipo.int/patentscope/en/programs/patent\\_landscapes/plrdb.html](https://www.wipo.int/patentscope/en/programs/patent_landscapes/plrdb.html).
- 210 See, for example, Unitaid (2014a); Unitaid and Medicines Patent Pool (2015).
- 211 The Uruguay Round Understanding on Rules and Procedures Governing the Settlement of Disputes; see WTO documents WT/DS171/3 and WT/DS196/4.
- 212 See WTO documents WT/MIN(01)/3, para. 284 (China); WT/ACC/RUS/70, WT/MIN(11)/2, para. 1295 (the Russian Federation); WT/ACC/UKR/152, para. 433 (Ukraine).
- 213 For the text of the Agreement, see <https://www.efta.int/free-trade/free-trade-agreements/korea>.
- 214 WHO, 2018e, p. 11.
- 215 See Drugs@FDA: FDA-Approved Drugs. Colcrys, available at: <http://www.accessdata.fda.gov/scripts/cder/daf/index.cfm?event=overview.process&varApplNo=022352>.
- 216 See Wasserman (2016); Drugs@FDA: FDA-Approved Drug Products. Colchicine, available at: <https://www.accessdata.fda.gov/scripts/cder/daf/index.cfm>.
- 217 Regulation (EU) No. 536/2014 of the European Parliament and of the Council of 16 April 2014 on Clinical Trials on Medicinal Products for Human Beings, OJEU L 158/1, 27 May 2014. For more details on the EU's regime, see also the WTO Secretariat Report on the EU's Trade Policy, WTO document WT/TPR/S/357/Rev.1, paras. 3.330–3.334.

- 218 WTO Secretariat Report on the EU's Trade Policy, WTO document WT/TPR/S/317, paras.3.302–3.303. See also the discussion of the impact of open access to data on their use by competitors in third countries, in Judgment of the General Court (Second Chamber), 25 September 2018, in *Amicus Therapeutics UK Ltd and Amicus Therapeutics, Inc. v. European Medicines Agency (EMA)*, para. 84, available at: <http://curia.europa.eu/juris/document/document.jsf?text=&docid=206064&pageIndex=0&doclang=en&mode=lst&dir=&occ=first&part=1&cid=4729437>.
- 219 Ibid., para. 55.
- 220 Ibid., paras. 77 and 85. This decision was appealed and the Advocate General's opinion was delivered on 11 September 2019; see: <http://curia.europa.eu/juris/document/document.jsf?docid=217636&doclang=EN>.
- 221 The economics of TRIPS, A series of primers on economic questions concerning Trade Related Aspects of Intellectual Property Rights, available at: [https://www.wto.org/english/tratop\\_e/trips\\_e/trips\\_econprimer1\\_e.pdf](https://www.wto.org/english/tratop_e/trips_e/trips_econprimer1_e.pdf).
- 222 See [www.wipo.int/madrid/en/](http://www.wipo.int/madrid/en/).
- 223 The Nice Classification (NCL), established by the Nice Agreement (1957), is an international classification of goods and services applied for the registration of marks. Class 5 of the Nice Classification includes mainly pharmaceuticals and other preparations for medical or veterinary purposes. For further information, see <https://www.wipo.int/classifications/nice/en/>.
- 224 WIPO IP Statistics Database: <https://www3.wipo.int/ipstats/pmhindex.htm?tab=madrid>. These figures relate to goods and services specified in Madrid System registrations by office of origin under Class 5 of the Nice Classification, see <https://www.wipo.int/classifications/nice/en/index.html>.
- 225 As at 27 December 2019, protection is possible in 122 countries, see [https://www.wipo.int/madrid/en/news/2019/news\\_0027.html](https://www.wipo.int/madrid/en/news/2019/news_0027.html).
- 226 The term of protection is not less than seven years under Article 18 of the TRIPS Agreement and, under Articles 13(7) of the Trademark Law Treaty and 13(5) of the Singapore Treaty on the Law of Trademarks, ten years with renewal periods of ten years.
- 227 See <https://www.who.int/medicines/services/inn/en/>.
- 228 See [https://www.who.int/medicines/services/inn/inn\\_bio/en/](https://www.who.int/medicines/services/inn/inn_bio/en/).
- 229 In 1993, the World Health Assembly endorsed Resolution WHA46.19, which states that trademarks should not be derived from INNs and INN stems should not be used as trademarks.
- 230 See <https://www.who.int/medicines/publications/druginformation/innlists/en/>. In addition, the INN Extranet, MedNet, grants members free access to the INN searchable database: <https://mednet-communities.net/inn>.
- 231 WIPO document SCT/40/10 Prov., para. 33.
- 232 Article 10bis is also incorporated by reference into the TRIPS Agreement. See Panel Reports, *Australia – Tobacco Plain Packaging*, para. 7.2631.
- 233 Other countries, such as Australia, Canada, Japan, Mexico and South Africa, have established their own reviews of proprietary names under their ministries of health.
- 234 The FDA Division of Medication Error Prevention and Analysis (DMEPA) and the EMA (Invented) Name Review Group (NRG).
- 235 See EMA, "Overview of (invented) names reviewed in September 2018 by the Name Review Group (NRG)", available at: [https://www.ema.europa.eu/en/documents/chmp-annex/overview-invented-names-reviewed-september-2018-name-review-group-nrg\\_en.pdf](https://www.ema.europa.eu/en/documents/chmp-annex/overview-invented-names-reviewed-september-2018-name-review-group-nrg_en.pdf).
- 236 Some types of non-traditional marks, such as sound, colour, shape and aspects of packaging, existed and were recognized internationally as early as the 1950s. The Singapore Treaty on the Law of Trademarks and Rule 3 of its implementing Regulations, in force as of 1 November 2011, provide the technical requirements applied to those marks on the international level. For further information, see <https://www.wipo.int/treaties/en/ip/singapore/>.
- 237 EUIPO Registration No: 001909472.
- 238 *Ross Whitney Corp. v. SKF*, 207 F.2d 190 (9<sup>th</sup> Cir. 1953).
- 239 CTM Registration 002179562 by Glaxo Group Ltd.
- 240 See ss. 18–25 of the Australian Tobacco Plain Packaging Act 2011 No. 148, 2011.
- 241 Article 20 of the TRIPS Agreement reads: "The use of a trademark in the course of trade shall not be unjustifiably encumbered by special requirements, such as use with another trademark, use in a special form or use in a manner detrimental to its capability to distinguish the goods or services of one undertaking from those of other undertakings. This will not preclude a requirement prescribing the use of the trademark identifying the undertaking producing the goods or services along with, but without linking it to, the trademark distinguishing the specific goods or services in question of that undertaking."
- 242 Directive 2001/83/EC of 6 November 2001 on the Community code relating to medicinal products for human use amended by Directive 2004/27/EC Guideline on the Readability of the labelling and package leaflet of medicinal products for human use (January 2009), Guideline on the packaging information of medicinal products for human use authorised by the Community (Revision 13, February 2008), QRD recommendations on pack design and labelling for centrally authorised non-prescription human medicinal products EMA/275297/2010.
- 243 Roughead et al., 2013, p. 6.
- 244 Therapeutic Goods Administration, Australian Department of Health, Draft Therapeutic Goods Order (TGO 79).
- 245 Decreto Supremo 3 de 2010, Articulo 82, available at: [http://www.ispch.cl/anamed/\\_normativa/decisos\\_supremos](http://www.ispch.cl/anamed/_normativa/decisos_supremos); see also ¿Qué es el DCI?, available at: [https://www.minsal.cl/DCI\\_INN/](https://www.minsal.cl/DCI_INN/).
- 246 Case No. 594/2000: Delivered 25 March 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.
- 247 Case No. FCA 1307: Delivered 18 November 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.

- 248 United Kingdom, Intellectual Property Office, *Consultation on Copyright* (2011), p. 80, cited in Australian Law Reform Commission (2013), *Copyright and the Digital Economy*, Discussion Paper 79, Sydney; see [www.alrc.gov.au/publication/copyright-and-the-digital-economy-dp-79/8-non-consumptive-use/text-and-data-mining/](http://www.alrc.gov.au/publication/copyright-and-the-digital-economy-dp-79/8-non-consumptive-use/text-and-data-mining/).
- 249 Directive (EU) 2019/790 of the European Parliament and of the Council of 17 April 2019 on copyright and related rights in the Digital Single Market and amending Directives 96/9/EC and 2001/29/EC, OJ L 130 of 17 May 2019, p. 92.
- 250 Copyright, Designs and Patents Act 1988, Section 29A.
- 251 Article 38 of the Law No. 2016-1231 of October 7, 2016, for a Digital Republic added paragraph 10 to Article L122-5 and para. 5 to Article L342-3 of the Intellectual Property Code (*Code de la propriété intellectuelle*).
- 252 Law on Copyright and Related Rights (Urheberrechtsgesetz), Section 60d.
- 253 See <https://www.who.int/hinari/en/>.
- 254 See <https://www.gov.uk/guidance/copyright-orphan-works>.
- 255 Directive 2012/28/EU of the European Parliament and of the Council of 25 October 2012 on certain permitted uses of orphan works.
- 256 EUIPO Orphan Works Database, available at: <https://euipo.europa.eu/ohimportal/en/web/observatory/orphan-works-db>.
- 257 WHA, Resolution WHA 58.28.
- 258 WIPO, *Intellectual Property and Mobile Applications* (2019) provides a comprehensive overview of the legal ecosystem and IP law considerations that are relevant for designers of mobile applications and provides an overview of relevant business issues.
- 259 See, for example, Topol (2019); Kohli and Geis (2018); Kahn and Lauerman (2018).
- 260 A glossary of Selected AI categories and terms is available at: [https://www.wipo.int/export/sites/www/tech\\_trends/en/artificial\\_intelligence/docs/techtrends\\_ai\\_glossary.pdf](https://www.wipo.int/export/sites/www/tech_trends/en/artificial_intelligence/docs/techtrends_ai_glossary.pdf).
- 261 WIPO, 2019b, p. 31.
- 262 Ibid., p. 34.
- 263 Focus Group for “Artificial Intelligence and Health”, see <https://www.itu.int/en/ITU-T/focusgroups/ai4h/Pages/default.aspx>.
- 264 See Terms of Reference, available at: <https://www.itu.int/en/ITU-T/focusgroups/ai4h/Documents/FG-AI4H-ToR.pdf>.
- 265 See, for example, Society for Laboratory Automation and Screening (2018), “Artificial intelligence to improve drug combination design and personalized medicine”, *PhysOrg*, 25 September; National University of Singapore (2018), “Researchers develop AI platform to rapidly identify optimal personalised drug combinations for myeloma patients”, *Medical Xpress*, 13 August; Masturah Bte Mohd Abdul Rashid and Edward Kai-Hua Chow (2018), “Artificial Intelligence-driven designer drug combinations: From drug development to personalized medicine”, *SLAS Technology* 24(1): 124–125; IMB RXN for Chemistry, available at: <https://rxn.res.ibm.com/>.
- 266 US Patent 10,193,695 B1, granted on January 19, 2019.
- 267 WIPO, 2019b, p. 126–130.
- 268 Cutting-Edge Health Technologies: Opportunities and Challenges, Joint Technical Symposium by the WHO, WIPO and WTO, Geneva, 31 October 2019; WIPO, 2019b, p. 143; WIPO document SCP/30/5.
- 269 See OECD and EUIPO (2019); European Commission (2019b).
- 270 Article 41.5 of the TRIPS Agreement.
- 271 All documents of the WIPO Advisory Committee on Enforcement are publicly available at: <https://www.wipo.int/enforcement/en/ace/>.
- 272 WIPO document CDIP/5/4 Rev.
- 273 WTO document WT/L/540, see Chapter IV, section C.3(iii) and Annex II.
- 274 See [https://www.wipo.int/treaties/en/text.jsp?file\\_id=305582](https://www.wipo.int/treaties/en/text.jsp?file_id=305582).
- 275 WIPO, Advice on flexibilities under the TRIPS Agreement, [https://www.wipo.int/ip-development/en/policy\\_legislative\\_assistance/advice\\_trips.html](https://www.wipo.int/ip-development/en/policy_legislative_assistance/advice_trips.html).
- 276 WIPO documents CDIP/5/4 Rev., CDIP/6/10, CDIP/7/3, CDIP/7/3 add., CDIP/8/5, CDIP/9/11, CDIP/13/10, CDIP/15/6.
- 277 See WIPO, Exceptions and limitations to patent rights, [https://www.wipo.int/patents/en/topics/exceptions\\_limitations.html](https://www.wipo.int/patents/en/topics/exceptions_limitations.html).
- 278 WIPO documents SCP/26/5 and SCP/27/5.
- 279 The report is available at: <https://apps.who.int/iris/bitstream/handle/10665/66919/a73725.pdf>.
- 280 For records of the special session, see WTO document IP/C/M/31.
- 281 WIPO document CDIP/5/4 rev., para.34.
- 282 See <http://www.wipo.int/ip-development/en/agenda/flexibilities/database.html>.
- 283 See Chapter III, section D.5(a).
- 284 See Chapter IV, section C.3(a)(iii).
- 285 See Chapter II, section B.1(g)(v).
- 286 See Chapter IV, section C.3(a)(i).
- 287 See <https://apps.who.int/iris/bitstream/handle/10665/330145/9789241517034-eng.pdf?ua=1>.
- 288 The panel in *Australia – Tobacco Plain Packaging* considered that para. 5 of the Doha Declaration confirmed its view that Articles 7 and 8 of the TRIPS Agreement provided important context for the interpretation of Article 20 of that Agreement. Panel Reports, *Australia – Tobacco Plain Packaging*, para. 7.2411.
- 289 For an explanation, see Chapter IV, section C.3(f).
- 290 Panel Reports, *Australia – Tobacco Plain Packaging*, paras. 7.2409–7.2411 (WT/DS435/R, WT/DS441/R, WT/DS458/R, WT/DS467/R). In their respective appeals, Honduras (WT/DS435/23) and the Dominican Republic (WT/DS/441/23) claimed that the panel erred in finding that para. 5 of the Doha Declaration on the TRIPS Agreement and Public Health constitutes a subsequent agreement within the meaning of Article 31(3)(a) of the Vienna Convention. At the time of writing this report, the Appellate Body has not yet issued its reports.
- 291 See Chapter IV, section C.3(a)(iii).

- 292 WTO document IP/C/73.
- 293 Ibid. For the earlier Extension Decision that was adopted by the TRIPS Council in 2002, see WTO document IP/C/25.
- 294 WTO document WT/L/971.
- 295 WTO document IP/C/64. For the earlier TRIPS Council Decision to extend the transition period in general, see WTO document IP/C/40.
- 296 Article 18(8), Law No. 31/2009 of 26/10/2009 on the Protection of Intellectual Property.
- 297 Republic of Rwanda, Ministry of Trade and Industry, Revised Policy on Intellectual Property in Rwanda, adopted in November 2018, available at: [https://www.aripo.org/wp-content/uploads/2020/04/Rwanda\\_Revised\\_Policy\\_on\\_Intellectual\\_Property\\_2018.pdf](https://www.aripo.org/wp-content/uploads/2020/04/Rwanda_Revised_Policy_on_Intellectual_Property_2018.pdf).
- 298 See Chapter II, section B.1(g)(v).
- 299 See <https://wipolex.wipo.int/en/text/458363>.
- 300 The provision in the revised Bangui Agreement reads as follows: "Jusqu'à la date du 1<sup>er</sup> janvier 2033 ou à la date à laquelle ils cessent d'être PMA, les Etats membres ayant le statut de PMA ne sont pas tenus d'appliquer les dispositions de l'annexe I en ce qui concerne les brevets consistant en ou se rapportant à un produit pharmaceutique et les dispositions de l'annexe VIII en ce qui concerne les informations confidentielles".
- 301 WTO document LT/UR/A/2.
- 302 WTO document WT/ACC/UKR/152, paras. 425, 433 and 512.
- 303 WTO document WT/L/508.
- 304 WTO document WT/L/846.
- 305 WTO document WT/L/508/Add.1.
- 306 WTO document WT/ACC/KHM/21, paras. 204–206 and 224.
- 307 WTO document WT/MIN(03)/SR/4.
- 308 See World Bank (2005, 2009). For the OECD publications series, Best Practice Roundtables on Competition Policy, see <http://www.oecd.org/daf/competition/roundtables.htm>. In particular, see: Designing Publicly Funded Healthcare Markets (2018); Excessive Pricing in Pharmaceuticals (2018); Generic Pharmaceuticals and Competition (2014); Competition Issues in the Distribution of Pharmaceuticals (2014); Competition in Hospital Services (2012); 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). See also UNCTAD (2015b).
- 309 See, for example, OECD (2018), Excessive prices in pharmaceutical markets, DAF/COMP(2018)12, in which the OECD Secretariat notes: "The application of competition law against high prices in the pharmaceutical sector requires a deep understanding of market dynamics and sectoral regulation, and of the various regulatory responses that may be deployed to address high prices. As such, it may be appropriate to explore various avenues for intervention, if possible in cooperation with the applicable sector regulator." See also WTO document IP/C/W/651 of 1 February 2019, a submission of South Africa to the TRIPS Council inviting WTO members to share, *inter alia*, experiences relating to excessive pricing in the pharmaceutical and medical technology sector.
- 310 See also Robert D. Anderson and William E. Kovacic, "The application of competition policy vis-à-vis intellectual property rights: the evolution of thought underlying policy change," in Anderson, Pires de Carvalho and Taubman (eds.), 2020.
- 311 See, for example, contributions prepared by Brazil and Peru to the WIPO Advisory Committee on Enforcement, WIPO/ACE/13/5 of 21 August 2018, and discussions on Promoting Public Health through Competition Law and Policy, held at TRIPS Council meetings on 19 November 2018 and 13 February 2019, WTO documents IP/C/M/90 and Add.1, and IP/C/M/91 and Add.1.
- 312 See Robert D. Anderson, Anna Caroline Müller and Antony Taubman, "The WTO TRIPS Agreement as a platform for application of competition policy to the contemporary knowledge economy," in Anderson, Pires de Carvalho and Taubman (eds.), 2020.
- 313 "Exclusive grant-back 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.
- 314 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, Antitrust Guidelines for the Licensing of Intellectual Property (2017); 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 Enforcement Guidelines (2016), <http://www.competitionbureau.gc.ca/eic/site/cb-bc.nsf/eng/04031.html>; an unofficial translation of Japanese Fair Trade Commission, Use of Intellectual Property under the Antimonopoly Act (2007, 2016) is available at: <https://www.jftc.go.jp/en/pressreleases/yearly-2016/January/160121.html>. For a comparative analysis including a wide range of economies, see Robert D. Anderson, Janning Chen, Anna Caroline Müller, Daria Novozhilkina, Philippe Pelletier, Antonella Salgueiro, et al., "Competition agency guidelines and policy initiatives regarding intellectual property: a cross-jurisdictional analysis of developed and emerging economies," in Anderson, Pires de Carvalho and Taubman (eds.), 2020.
- 315 Judgment of the State Council of 12 February 2014, No. 693, available from the webpage of the Administrative Justice ([https://www.giustizia-amministrativa.it/portale/pages/istituzionale/visualizza/?nodeRef=&schema=cds&nrg=201209181&nomeFile=201400693\\_11.html&subDir=Provvedimenti](https://www.giustizia-amministrativa.it/portale/pages/istituzionale/visualizza/?nodeRef=&schema=cds&nrg=201209181&nomeFile=201400693_11.html&subDir=Provvedimenti)); Hadrian Simonetti, Appeal, Non-application, Judicial Review on the Acts of the Public Administration for Antitrust Purposes (Notes to the Consiglio di Stato – Italian Supreme Administrative Court – Judgment, sec. vi, no. 693/2014, 2014, available at: <http://iar.agcm.it/article/view/11060>; Giovanni Galimberti and Evelina Marchesoni, "Italy: the abuse of a dominant position by Pfizer in Xalatan case", *Bird&Bird*, May 2014, <https://www.twobirds.com/en/news/articles/2014/global-life-sciences-may/italy-the-abuse-of-a-dominant-position-by-pfizer-in-xalatan-case>.

- 316 Recent mergers between pharmaceutical companies have been reported as resulting in reduced R&D activity in the sector. For a recent overview of EU case law, see Catherine Derenne and Bertold Bar-Bouyssière (2019), “Pharma and mergers: an overview of EU and national case law”, *e-Competitions Bulletin Pharma & Mergers*, 14 February: 89174; and, for example, LaMattina, 2011. Derenne and Bouyssière report on “close to 100 pharmaceutical mergers from all over the world since [...] 2004”.
- 317 European Commission, 2019a.
- 318 Article 10bis is also incorporated by reference into the TRIPS Agreement, see Panel Reports, *Australia – Tobacco Plain Packaging*, para. 7.2631.
- 319 See Anderson, Müller and Taubman, “The WTO TRIPS Agreement as a platform for application of competition policy to the contemporary knowledge economy,” in Anderson, Pires de Carvalho and Taubman (eds.), 2020.
- 320 Panel Reports, *Australia – Tobacco Plain Packaging*, para. 7.2680. The panel found that Australia’s tobacco plain packaging (TPP) measures themselves did not constitute an act of unfair competition. It further found that the complainants had not demonstrated that the TPP measures compel market actors to engage in acts of unfair competition of such a nature as to create confusion, or amounting to misleading indications or allegations, or otherwise to engage in such acts of unfair competition against which Australia was bound to assure effective protection, see section 7.3.6 of the reports.
- 321 For more details on tariff data, see Chapter IV, section D.1.
- 322 See [www.haiweb.org/medicineprices](http://www.haiweb.org/medicineprices).
- 323 See the report of the July 2018 SPS Committee meeting in WTO document G/SPS/R/92/Rev.1.
- 324 See the report of the November 2018 SPS Committee meeting in WTO document G/SPS/R/93, paras. 3.38–3.44.
- 325 Ibid., paras. 3.45–3.47.
- 326 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, and sectors (iv) and (v) under “Professional Services”.
- 327 If one takes into account horizontal limitations listed in some schedules (i.e. limitations applying across all scheduled sectors), partial commitments dominate.
- 328 Robert D. Anderson, Anna Caroline Müller and Philippe Pelletier (2016), “Regional Trade Agreements and Procurement Rules: Facilitators or Hindrances?” A version was published as Robert Schuman Centre for Advanced Studies (RSCAS) Research Paper No. RSCAS 2015/81, December 2015.
- 329 For the full content of GPA parties’ schedules (Appendix 1), including the relevant thresholds, see [https://www.wto.org/english/tratop\\_e/gproc\\_e/gp\\_gpa\\_e.htm](https://www.wto.org/english/tratop_e/gproc_e/gp_gpa_e.htm).
- 330 Before leaving the EU, the UK participated in the GPA as an EU member. On 27 February 2019, parties to the GPA adopted a decision inviting the United Kingdom to become a party to the GPA, in its own right, after leaving the EU.
- 331 Including through their agent HealthAlliance Limited, see Note 1 to Annex 2 of New Zealand.
- 332 Additional statistical information is available at: [https://www.wto.org/english/tratop\\_e/gproc\\_e/gp\\_gpa\\_e.htm](https://www.wto.org/english/tratop_e/gproc_e/gp_gpa_e.htm).
- 333 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).
- 334 WTO document GPA/108/Add.9. It is recalled that the GPA applies to the entities, goods and services that are specified in each individual party’s schedules.
- 335 WTO document GPA/123/Add.7.
- 336 WTO document GPA/108/Add.4. The reported value was expressed as 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.
- 337 The following WTO disputes have addressed, among others, health-related measures: *EC – Hormones* (DS26 and DS48); *Canada – Pharmaceutical Patents* (DS114); *EC – Asbestos* (DS135); *EC – Approval and Marketing of Biotech Products* (DS291, DS292 and DS293); *Brazil – Retreaded Tyres* (DS332); *US – Continued Suspension* (DS320); *Canada – Continued Suspension* (DS321); *US – Clove Cigarettes* (DS406); and *Australia – Tobacco Plain Packaging* (DS435, DS441, DS458 and DS467).
- 338 See Appellate Body Report, *EC – Asbestos*, para. 172.
- 339 See Appellate Body Report, *Brazil – Retreaded Tyres*, para. 144. See also Panel Report, *US – Clove Cigarettes*, para. 7.347.
- 340 Panel Report, *Canada – Pharmaceutical Patents*, WTO document WT/DS114/R, para. 7.50.
- 341 Ibid., para. 7.38.
- 342 Panel Reports, *Australia – Tobacco Plain Packaging* (DS435, 441, 458 and 467). At its meeting on 27 August 2018, the DSB adopted the Panel Reports in WT/DS458/R and WT/DS467/R, complaints by Cuba and Indonesia, respectively. Honduras appealed certain findings by the same Panel in its report WT/DS435/R on 19 July 2018, and the Dominican Republic appealed certain findings in report WT/DS441/R on 23 August 2018 (see documents WT/DS435/23 and WT/DS441/23, respectively). At the time of writing this report, the Appellate Body has not yet issued its reports.
- 343 The TPP measures consist of two sets of requirements, namely, format requirements that standardize the presentation of tobacco products and their retail packaging, and trademark requirements that, *inter alia*, permit the use of word marks in standard lettering on retail packaging, but prohibit the use of stylized word marks, composite marks and figurative marks. The TPP measures operate in conjunction with other legislative requirements that were not challenged in these disputes, including graphic health warnings.
- 344 Panel Reports, *Australia – Tobacco Plain Packaging*, paras. 7.2604–7.2605. The WHO Framework Convention on Tobacco Control (FCTC) is available at: <https://apps.who.int/iris/bitstream/handle/10665/42811/9241591013.pdf;jsessionid=D04BBF65D9B0131FE2E7D2B7465326BD?sequence=1>; the Guidelines for implementation of Article 11 of the FCTC are available at: [https://www.who.int/fctc/guidelines/article\\_11.pdf?ua=1](https://www.who.int/fctc/guidelines/article_11.pdf?ua=1); and the Guidelines for implementation of Article 13 of the FCTC are available at: [https://www.who.int/fctc/guidelines/article\\_13.pdf?ua=1](https://www.who.int/fctc/guidelines/article_13.pdf?ua=1).

- 345 Panel Reports, *Australia – Tobacco Plain Packaging*, para. 7.1732.
- 346 Ibid., para. 7.397.
- 347 Article 6*quinquies* of the Paris Convention (1967), Articles 15.4, 16.1 and 16.3 of the TRIPS Agreement, Article 10*bis*(1), 10*bis*(3)(1) and 10*bis*(3)(3) of the Paris Convention (1967), Articles 22.2(b) and 24.3 of the TRIPS Agreement. Cuba also invoked Article IX:4 of the GATT 1994.
- 348 Panel Reports, *Australia – Tobacco Plain Packaging*, para. 7.1773, referring to Panel Report, *US – Section 110(5) Copyright Act*, para. 6.66.
- 349 See Figures 4 and 5 in United States Government Accountability Office (2017).
- 350 National Science Board, “Science and Engineering Indicators 2018”, Chapter 4, Table 4-10: Sales and R&D intensity for companies that performed or funded R&D, by selected industry: 2015, available at: <https://www.nsf.gov/statistics/2018/nsb20181/report/sections/research-and-development-u-s-trends-and-international-comparisons/u-s-business-r-d>.
- 351 Ibid., Table 4-9: Funds spent for business R&D performed in the United States, by source of funds and selected industry: 2015.
- 352 The “mailbox” obligation is a transitional one that applies to WTO members which do not yet provide product patent protection for pharmaceuticals and for agricultural chemicals. Since 1 January 1995, when the WTO agreements entered into force, these countries have to establish a means by which applications of patents for these products can be filed. (An additional requirement is that they must also put in place a system for granting “exclusive marketing rights” for the products whose patent applications have been filed.) See “Mailbox” at [https://www.wto.org/english/thewto\\_e/glossary\\_e/glossary\\_e.htm](https://www.wto.org/english/thewto_e/glossary_e/glossary_e.htm).
- 353 For examples of these kinds of measures, see Chapter IV, section A.4(b).
- 354 See [https://www.wto.org/english/res\\_e/reser\\_e/ersd201905\\_e.htm](https://www.wto.org/english/res_e/reser_e/ersd201905_e.htm).
- 355 Innovative pharmaceuticals are defined in this staff working paper as those that are first-in-class because each presents a new pathway for treating a disease and those that are advance-in-class, i.e. that are not first-in-class but receive a priority review designation from USFDA, which is reserved for medicines that potentially offer major advances in treatment.
- 356 For other examples on the national implementation of test data, see Chapter II, section B.1(c)(i).
- 357 See Chapter III, section C.6.
- 358 WHO, “Traditional, complementary and integrative medicine: About us”, <https://www.who.int/traditional-complementary-integrative-medicine/about/en/>.
- 359 Ibid.
- 360 For a definition of herbal medicines, see WHO (1996), *WHO Expert Committee on Specifications for Pharmaceutical Preparations: Thirty-fourth Report*, WHO Technical Report Series, No. 863, Annex 11: Guidelines for the Assessment of Herbal Medicines, available at: <http://digicollection.org/hss/en/d/Js5516e/21.html>.
- 361 Data from the Chinese Chamber of Commerce for Import & Export of Medicines & Health Products, available at: <http://en.cccmhpie.org.cn/>.
- 362 WHO (2013), *WHO Traditional Medicine Strategy 2014–2023*, Geneva: WHO, p. 11.
- 363 WHA, Resolution WHA61.21: Global strategy and plan of action on public health, innovation and intellectual property.
- 364 See also WIPO Glossary, Key terms related to intellectual property and genetic resources, traditional knowledge and traditional cultural expressions, Traditional Knowledge, available at: <https://www.wipo.int/tk/en/resources/glossary.html#49>.
- 365 UN document A/RES/61/295.
- 366 WHO Traditional, complementary and integrative medicine: Activities, <https://www.who.int/traditional-complementary-integrative-medicine/activities/en/>.
- 367 Notifications containing the words “traditional medicine”, “herbal medicine”, “traditional herbal medicinal products” and “traditional medicinal products” are included, see TBT Information Management System: <http://tbtims.wto.org/en/Notifications/Search>.
- 368 From 1 January 2009 until 31 December 2013, WTO members notified 12 measures; from 1 January 2014 until 31 December 2018, WTO members notified 29 measures.
- 369 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.
- 370 G/TBT/M/51, at paras. 3–9. This STC was subsequently raised in the TBT Committee in 2010 in G/TBT/M/52, 2 at paras. 285–302, in 2011 in G/TBT/M/53, paras. 251–265, G/TBT/M/54, paras. 211–217, G/TBT/M/55, paras. 104–105, in 2012 in G/TBT/M/56, paras. 89–92, G/TBT/M/57, paras. 115–118, G/TBT/M/58, paras. 2.79–2.80 and in 2019 in G/TBT/M/59, paras. 2.109–2.110.
- 371 G/TBT/M/51, at para. 8.
- 372 See Tripathi et al. (2015).
- 373 Convention on Biological Diversity. History of the Convention, <https://www.cbd.int/history/>; Convention on Biological Diversity. The Nagoya Protocol on Access and Benefit-sharing, <https://www.cbd.int/abs/>.
- 374 For the political debate on ABS aspects regarding the sharing of viruses, see Chapter III, section E.
- 375 See <http://www.tkdl.res.in/tkdl/langdefault/common/Home.asp?GL=Eng>.
- 376 For more information on prior art, see Chapter II, section B.1(b)(iv) and WIPO document SCP/12/3 Rev.2, para. 210.
- 377 See WTO document IP/C/W/370/Rev.1 for the latest discussion in the TRIPS Council; see also WTO document WTO/IP/C/M/90/Add.1.
- 378 Information about databases and registries of traditional knowledge and genetic resources that are maintained and managed by WIPO member states and other organizations, as well as about other repositories of traditional knowledge and genetic resources, is available at: [https://www.wipo.int/tk/en/resources/db\\_registry.html](https://www.wipo.int/tk/en/resources/db_registry.html).

- 379 WHO (n.d.), “Implementation of the Nagoya Protocol and Pathogen Sharing: Public Health Implications: Study by the Secretariat”, available at: [https://www.who.int/influenza/Nagoya\\_Full\\_Study\\_English.pdf](https://www.who.int/influenza/Nagoya_Full_Study_English.pdf).
- 380 See documents CBD/COP/DEC/XIII/16 of 16 December 2016, available at: <https://www.cbd.int/doc/decisions/cop-13-cop-13-dec-16-en.pdf>, and CBD/NP/MOP/DEC/2/14 of 16 December 2016, available at: <https://www.cbd.int/doc/decisions/np-mop-02/np-mop-02-dec-14-en.pdf>.
- 381 See footnote 71 in WHO, 2018a; see also WHO, 2018c.
- 382 See “Comments by the World Health Organization on the draft Fact-Finding and Scoping Study ‘The Emergence and Growth of Digital Sequence Information in Research and Development: Implications for the Conservation and Sustainable Use of Biodiversity, and Fair and Equitable Benefit Sharing , dated 9 November 2017”, Geneva:
- WHO, available at: <https://www.who.int/influenza/whocommentscbddsi.pdf>.
- 383 See WTO documents IP/C/W/474 and addenda, TN/C/W/52 and addenda, IP/C/M/92/Add.1, and IP/C/M/88/Add.1.
- 384 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 reports, see WTO document IP/C/M/92/Add.1.
- 385 See <https://www.wipo.int/tk/en/igc/>.
- 386 Ibid.
- 387 WTO documents TN/C/W/59, IP/C/M/92/Add.1, IP/C/M/88/Add.1.
- 388 The latest version of the negotiating text is available at: <https://www.wipo.int/tk/en/igc/index.html>.