OSLO MEDICINES INITIATIVE
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THE SOCIAL CONTRACT AND HUMAN RIGHTS BASES FOR PROMOTING ACCESS TO EFFECTIVE, NOVEL, HIGH-PRICED MEDICINES

OSLO MEDICINES INITIATIVE TECHNICAL REPORT

Trudo Lemmens, Kanksha Mahadevia Ghimire, Katrina Perehudoff and Navindra Persaud

Oslo Medicines Initiative

Established in 2020, the Oslo Medicines Initiative (OMI) is a collaboration between the WHO Regional Office for Europe, the Norwegian Ministry of Health and Care Services and the Norwegian Medicines Agency. The OMI aims to provide a neutral platform for the public and the private sectors to jointly outline a vision for equitable and sustainable access to and affordability of effective, novel and high-priced medicines.

In line with the Regional Office's European Programme of Work 2020–2025 – "United Action for Better Health", equitable and sustainable access to quality medicines is critical for universal health coverage and for achieving the Sustainable Development Goals. The OMI provides a strong focus on equity and on leaving no one behind, and is underpinned by three pillars: solidarity, transparency and sustainability.

The OMI has commissioned a series of technical reports to summarize relevant evidence and to provide policy considerations as a basis for discussion to inform its work. These reports are also in line with the implementation of World Health Assembly resolutions, in particular, resolution WHA 72.8 on improving the transparency of markets for medicines, vaccines, and other health products.

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Abstract

High prices can significantly restrict access to medicines and may have an impact on health equity. There is no clear understanding of what the social responsibilities and rights are of those involved in the development, production and distribution of medicines. This technical report explores how social contract theories, the global public (health) goods discourse and international human rights can be employed to sketch the broad contours of the responsibilities and rights of key stakeholders – particularly governments and pharmaceutical companies. These three approaches ascertain that stakeholders have specific responsibilities to assist in increasing access to high-priced medicines, yet they remain vague about the precise nature of actions stakeholders should perform to promote access to medicines. This report builds particularly on international human rights, and identifies specific obligations that, if properly implemented, should contribute to better access to medicines.

Keywords

GLOBAL PUBLIC GOODS; RIGHT TO HEALTH; HIGH-PRICED MEDICINES; HUMAN RIGHTS; SOCIAL CONTRACT THEORY; PHARMACEUTICAL GOVERNANCE; ACCESS TO MEDICINES

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Abbreviations

EU	European Union
GPG	global public good
ICCPR	International Covenant on Civil and Political Rights
ICESCR	International Committee on Economic, Social and Cultural Rights
OMI	Oslo Medicines Initiative
PPP	public–private partnership
R&D	research and development
TRIPS	World Trade Organization Agreement on Trade-Related Aspects of Intellectual Property Rights

Executive summary

Background

Pharmaceutical products are an essential component of health care. High prices are increasingly becoming a significant barrier for access to medicines, and are a challenge for annualized health-care budgets even in high-income countries. High-priced medicines can create and augment fundamental inequities at the international level because they usually have limited availability and are unaffordable in lower-income countries while the patents are valid. The COVID-19 pandemic has illustrated again how high prices can undermine global health equity and has invigorated calls to re-evaluate the obligations of those involved in the development, production, funding and distribution of medicines. Pharmaceutical products enter the health system through the interplay of diverse interests and the commitments of many actors, including governments, industry and other members of society.

Objectives and approach

This Oslo Medicines Initiative (OMI) technical report divides societal actors into three categories: government (with its divergent components); the pharmaceutical industry (including service industries that contribute to the research and development (R&D) of medicines); and other actors – including broader civil society, research institutions, funding agencies, not-for-profit organizations, patients, patient advocacy groups, health-care providers, health profession organizations and research participants. It aims to sketch what contributions should be expected from these actors.

This report has two key objectives. The first is to provide a framework – informed by social contract theories, a global public goods approach and international human rights – to identify and organize the obligations of various actors (particularly government and pharmaceutical companies) in promoting access to safe, effective, novel, high-priced medicines. The second is to identify and categorize specific initiatives at various stages of the pharmaceutical production and supply chain that can contribute to the fulfilment of these obligations and thereby improve access to medicines.

Findings and policy considerations

Social contract theory and access to high-priced medicines

Social contract theory posits that an implicit agreement between governments and citizens – including organizations and institutions – supports democratic societies, which imposes mutual obligations on contractual parties. Citizens and private actors agree to

respect the rule of law, in exchange for a government's commitment to protect their rights. Governments violate the civil contract if they fail to organize society in such way that rights are protected. Social contracts enable businesses to operate in ways that benefit society. There is a growing emphasis on the need for businesses to structure their operations in ways that offer the maximum benefit to society.

Applied to the context of medicines, pharmaceutical companies commit to bringing medicines to the market that address health needs in exchange for profits that compensate their investment and support them to achieve their dual obligations: corporate obligations to shareholders, and broader obligations towards society, including future generations. Meeting their obligations requires continued investment in production and distribution of innovative medicines at prices that health systems can bear, thereby connecting to the theme of sustainability that is central to the achievement of the Sustainable Development Goals and that is a core component of the OMI.

Social contract theory requires governments to establish a medicines governance system that promotes equitable and sustainable development, distribution, and coverage of safe and effective medicines. This leads to government-level tensions, however, owing to competing goals of promoting a vibrant commercial pharmaceutical industry to advance economic and industrial objectives, and ensuring access to affordable medicines to advance public health.

Other actors also have specific obligations, such as contributing to reliable research, appropriate prescribing of medicines to patients in need, holding governments and industry accountable, and contributing to the collection and dissemination of relevant health information.

Global public goods and international human rights frameworks

Roles and responsibilities of different actors in social contract theory can be informed by the concept of global public goods, organized around categories of obligations identified in international human rights law – particularly as it relates to the right to health.

Global public goods

Global public goods (GPGs) are defined in economic terms as goods that are public in nature, non-excludable (that is, accessible to all), non-rival (that is, consumption by one does not affect how much of it remains available for others) and global in scope. While the term has been used widely by the global health community, medicines do not fit the economic definition of a GPG easily, since they are consumable and focus on individual patient care. The knowledge associated with the research, production and distribution systems surrounding medicines can be framed as GPGs, particularly where the public sector has contributed to its development. When vaccines and medicines are stockpiled for use in public health emergencies, the stockpile of medicines can be framed as a GPG. A GPG approach necessitates knowledge sharing (about research, patents, regulatory pathways, regulatory data and patient health information) and regional or global collaboration to make medicines that protect global public health available. The knowledge essential to translate complex knowledge into real products could also be considered a

GPG. This GPG framework does not accord with the current pharmaceutical business model, however, where such information is held as commercially confidential.

Human rights obligations in relation to high-priced medicines

A human rights framework provides a useful lens to identify and to organize the obligations of actors involved in the production and distribution of medicines. Although international human rights law primarily binds states and governments, it increasingly recognizes the role of large corporations in the realization of human rights, including health-related rights. International human rights norms are also embedded in national laws and attempts to use international human rights law to help enforce health rights at the national level are increasing.

The framework and concepts developed in authoritative documents and guidelines related to international human rights help to organize various obligations with respect to effective, novel, high-priced medicines. In line with these documents, the authors identify them as follows.

The role of governments under a human rights framework is to:

- establish effective and publicly accountable legal and regulatory tools for ensuring that medicines are safe and effective, in line with established international norms and standards;
- establish effective regulatory tools that help stimulate biotechnological innovation and the development, production and equitable distribution of medicines;
- establish publicly accountable, reliable tools, based on timely, reliable data, to identify priorities for medicine development;
- stimulate R&D through funding initiatives, policy incentives and regulation;
- organize regulatory approval, with attention to medicines prioritization, including the potential need to coordinate approval with funding decisions;
- explore, with ongoing and timely evaluation, conditional approval systems that focus on areas of need;
- coordinate safety and efficacy reviews through the evaluation of comparative clinical effectiveness;
- coordinate international measures to address unmet medical needs (such as rare diseases) – for example, through coordinated regulatory review and research stimuli;
- implement price control mechanisms that reconcile budgetary constraints with the provision of reasonable compensation for pharmaceutical companies and others involved in the development and distribution of medicines; and
- promote access to safety and efficacy data for independent researchers and civil society.

Industry's role under a human rights framework is to:

- participate in the development, production and equitable distribution of medicines in areas of greatest need;
- provide data access to governments, researchers and civil society actors for the purposes of regulatory review and promotion of further research and safety and efficacy evaluations;
- participate in open science initiatives to promote efficiencies in pre-competitive research and medicine development;
- share relevant data about costs of research, production, marketing and distribution of medicines with governments;
- respect and promote the highest ethical standards in the R&D, marketing and sale of medicines;
- participate in initiatives to promote equitable access to medicines, including through public–private partnerships (PPP);
- participate in technology transfer and socially responsible licensing arrangements – particularly in situations of public health emergencies and to promote equitable access to medicines for populations in countries with limited resources; and
- recognize and acknowledge the contributions of patients, civil society, funding agencies, academic institutions and others in the R&D process – for example, in decisions about pricing, special access, data transparency and licensing.

Within an international structure, corporations – especially pharmaceutical companies – also have specific responsibilities to promote an international and political order which ensures that the distribution of goods benefits those who are most disadvantaged. This is also clearly reflected in the growing discourse around corporate social responsibility and sustainability.

Aspects of these obligations can also be extended to other actors. For example, patients and research subjects are key participants in the development of medicines and the ongoing control of safety and effectiveness. Civil society and independent researchers play a key role in providing independent analysis of safety and efficacy data, and thus contribute to promoting public accountability of governments and pharmaceutical companies. Funding agencies and philanthropic organizations should help to promote research in priority areas. All should promote the highest ethical standards in research and drug development. International human rights terminology thus provides a common normative framework to stimulate further public debate around the realization of access to effective, novel, high-priced and other medicines.

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Introduction: social contract, social goods and human rights approaches

Pharmaceutical products play a crucial role in health care. They enter the health system through the interplay of diverse interests and commitments of various stakeholders: research funders (public and private), research institutions, pharmaceutical companies, contract research organizations, research participants and patients, drug regulatory agencies, civil society, public and private health insurers, and numerous health-care delivery actors. The contour of this interplay is determined by a complex web of interrelated practices, customs and formal and informal rules, which are shaped by broader cultural, economic, social, political, financial, technological and legal contexts. Rules and regulations – including those set by intellectual property laws, pharmaceutical governance regimes, research ethics guidelines, competition law and rules of corporate governance – provide a guiding framework through which national and regional governments and the broader international community try to provide access to medicines as a component of health care.

In parliamentary democracies, political and legal processes that are often said to have their moral foundation in an assumed social contract determine the content of these rules to a significant degree. Social contract theory posits an implicit agreement between governments and citizens – arguably including organizations and institutions – whereby each accepts mutual obligations and rights. Respect for these mutual obligations is deemed to ensure good governance and to deliver positive outcomes for society. Citizens and private actors agree to respect the rule of law, and to fulfil various obligations embedded in the social contract, whereas governments promote justice by respecting the rights of citizens, ensuring proper governance and taking part in the provision of access to social goods. Social contract theory can be used to describe various mutual obligations between pharmaceutical companies, current and future patients, governments (including regional entities such as the European Union (EU)), international organizations, civil society, health-care providers and others involved in the production, distribution and provision of medicines.

When applied to the issue of access to medicines, the social contract can be framed as follows. Pharmaceutical companies have a contractual commitment to bring innovative medicines to the market to promote good health care and save or improve people's lives. In exchange, they can legitimately impose a reasonable price that compensates them for their investments in research, drug development and production, and that enables them to continue performing these activities. They have a duty to respect various governance rules and other duties as good corporate citizens. They also have obligations to provide a return on investment for shareholders (who would expect returns comparable to what might be achieved in other sectors), which may place companies' objectives at odds with global health objectives. Governments and patients (often through health insurers) commit to paying reasonable prices in exchange for access to safe and effective medicines that should contribute to protect or improve patients' health, prevent or reduce hospitalization, and reduce other health-care costs. Governments have an overall duty to provide effective

stewardship of medicines and to intervene where commercial markets are failing. This includes adopting laws and establishing governance systems that promote access to safe and effective drugs, protect patients against unsafe drugs and improper prescription practices, enable an efficient functioning of industry, promote innovation, manage risks and determine reasonable prices. Patients have duties to respect health-care rules, including contributing to proper use of health-care resources, and arguably also a duty to contribute to the production of relevant information – for example, through allowing access to health records and the gathering of relevant information.

Governments, which includes intergovernmental units (such as the EU), obviously play a key role in the implicit social contract. They must establish effective governance rules that help delineate the various obligations and promote their realization. They have to ensure, through good governance, that the social contract commitments of the various parties are respected. Rules embedded in patent, corporate, competition, drug regulatory, health, social security and consumer protection law, health professional standards and research governance – to mention some key components of medicine governance – are deemed to guide and promote respect for various obligations resulting from the social contract. Governments further enter into international agreements to fulfil their obligations, which also has a direct impact on national legal rules.

In practice, the interplay of legal, financial, geopolitical, social, cultural and other factors – and the tension between divergent legal regimes – render governance of medicines extremely complex. Rules focusing on the provision of health care and access to medicines are, for example, in tension with the commitment to shareholder value embedded in corporate and financial law. The latter creates pressure towards charging the highest possible price for medicines, even if rules of responsible corporate governance aim at attenuating some of the corporate drivers. The former aim to ensure access to medicines and sustainability of health-care budgets.

High prices of medicines are increasingly becoming a significant barrier to access, even in high-income countries. Governments or private health insurers tend to be reluctant to cover their costs, and many patients are unable to pay for them out of pocket, or would have to make significant personal sacrifices that may compromise their health and well-being in other ways to do so.

Medicines may be costly for different reasons, some of which this report illustrates further. When governments cover medicines out of annualized health-care budgets, they can put a significant strain on limited resources, and as such can have a negative impact on other areas of health care. High prices thus impede access to adequate health care in both direct and indirect ways.

High-priced medicines can also create fundamental inequities at the international level, since citizens of industrialized countries will be more likely to have access to them. This was most starkly demonstrated in the context of the COVID-19 pandemic, when most of the first vaccines were largely unaffordable for low-income countries.

High prices of medicines create tensions at different levels. The burden on health systems sets public health-care funders against pharmaceutical companies, with patients caught in the middle. When governments limit public health funding as part

of responsible resource allocation, patients may feel that legitimate health-care expectations are not met. The resulting political tension can be exploited to reverse funding decisions, including through mobilization of patient advocacy groups and public opinion. Tensions can further exist between government departments – for example, when agencies focusing on economic development support initiatives that contribute to high prices, whereas public health and health care-oriented departments seek lower and more sustainable prices of medicines.

In the context of these growing tensions, it is important to ask what the rights, obligations and responsibilities of the various stakeholders are in relation to access to medicines. Are they respecting their social contract obligations to ensure adequate access to good health care and medicines? If not, what should be expected from the various actors in the complex context of high-priced medicines?

This Oslo Medicines Initiative (OMI) technical report has two key objectives. The first is to provide an ethical, legal and policy basis for the general obligations and responsibilities of stakeholders – government and pharmaceutical companies in particular – in promoting increased access to safe and effective, novel high-priced medicines. The second is to identify, categorize and organize some of the potential obligations and responsibilities for each of these stakeholders. The report approaches this by:

- discussing the extent to which social contract theory provides a moral foundation for obligations of stakeholders;
- exploring how a "global public goods" approach helps identify specific obligations; and
- using an international human rights analysis as a lens for mapping and organizing various obligations, responsibilities and policy options, building particularly on the work of the International Committee on Economic, Social and Cultural Rights (ICESCR) and the United Nations Special Rapporteur on the Right to Health.

This report first describes the concrete challenges of high prices for health systems and patients, with some examples. It then discusses whether and how different social contract theories can help untangle the obligations of various stakeholders in the complex medicines context. The extent of obligations under social contract theory depends in part on the nature of the goods that are to be produced and distributed as part of these obligations. This report, therefore, also briefly explores how a global public goods (GPG) approach, which has frequently been put forward in this context, helps to clarify the foundation of obligations offered by contract law.

The focus next shifts to how a human rights framework constructed around the various components of the right to health can help to clarify and organize specific obligations. This also aligns with what social contract theory prescribes. The framework offered by the right to health, which has gained significant traction in recent years, has the distinct advantage of specifying specific obligations of governments, while it increasingly recognizes the role of private entities in promoting human rights standards. This human rights approach fits with some of the more recent articulations of social contract theory, which emphasize the need to look at the social contract in a broader, global context – not just as a theory that explains the relationship between citizens and governments. This report identifies the

kinds of obligations or responsibilities that can be identified as important components of a human rights-respecting model of access to effective, novel, high-priced medicines, in line with the work of the ICESCR and the United Nations Special Rapporteur on the Right to Health.

1.1 Context: how high prices limit access to potentially life-saving medicines

Examples abound of how high prices of medicines may impede equal access to treatment for often very serious conditions; and where health-care funders are put under pressure to fund expensive medicines – in some cases, even when no strong and reliable information of cost–effectiveness is available. Cancer treatment is one context in which the lack of access to high-priced medicines and pressure to fund medicines with – at times – questionable cost–effectiveness are pertinent concerns. Specifically, newer cancer medications are typically expensive, and sometimes prohibitively so *(1,2)*. Prices are particularly high in the United States, where "the costs were a median of 2.31 times higher than those seen in Europe" *(3)*. For example, in the United States "by 2014, the average cost of a new orally administered cancer medicine exceeded US$ 135 000 a year – up to six times the cost of similar drugs approved in the early 2000s, after adjusting for inflation. 2017 brought the most eye-popping price tag in oncology yet: a one-time cost of US$ 475 000 per patient for a personalized cell-based therapy for childhood leukaemia" *(4)*. Even though countries in the WHO European Region have the ability and the need to exercise more control over the prices of medicines – as they are often funded from fixed public budgets – the unaffordability of cancer drugs and the pressure on health-care funding are also serious concerns there. A study comparing cancer drug prices in Latin American and European countries concluded that under a classic definition of affordability (less than 20% of one day of minimum wage income for a defined daily dose), nearly all surveyed medicines were unaffordable in the studied countries *(5)*. In fact, the prices per defined daily dose of almost all cancer drugs compared exceeded one day's income.

This does not necessarily mean that patients are prevented from having access to life-saving and essential new cancer drugs. In fact, health technology assessments reveal that many – if not most – new cancer drugs are not cost-effective, based on the price and clinical evidence available at the time of assessment *(6)*. Yet, for those that are clinically effective, costs may impose a barrier. For those that are deemed not cost-effective, health-care funders may still be pressured to provide funding, thus raising questions about how to ensure that regulatory and funding decisions are evidence-informed.

The high price of these medicines is a serious challenge for health systems in high- and middle-income countries. Medicines are covered by public or private insurance in many high-income countries, but costs are sometimes borne directly by patients *(7)*. In low-income countries, high prices are "a major, and often insurmountable, barrier" *(8)* to access, as publicly funded benefit packages are small or non-existent. An inverse relationship has even been observed between a country's income and its prices for medicines, associated with the different negotiation powers of governments and with supply issues. Low-income countries face paradoxically often higher prices, including for cancer drugs *(5)*.

Rare diseases – that is, diseases that according to the EU definition do not affect more than one person per 2000 *(9)* – form another context in which patients face significant barriers to access high-priced orphan drugs. Often, they may be the only available treatment option for diseases that have a significant impact on the quality and quantity of life *(10)*. As a result, no competition exists that may drive prices down, but access to the drugs is still imperative for patients, creating strong pressures for governments and health insurers. In one such example, in 2021 the United Kingdom's National Health Service approved a medicine that costs £1.79 million per dose to halt or slow the progression of spinal muscular atrophy – a rare and often fatal disorder *(11)*.

Competition for orphan drugs tends to be low or absent because of the small market size and lack of alternative therapies, thereby creating a monopoly. Particularly when no other treatment options are available, such drugs are easily deemed to be of high value *(12)*. Designation of a drug as an orphan drug for a rare disease often pushes up its price *(13–15)* beyond considerations based on the small population size in which to recoup costs.

Pharmaceutical regulations have themselves contributed indirectly to higher drug prices. For example, particularly in relation to cancer drugs, pharmacogenomics has facilitated the practice of dividing diseases into subcategories with targeted treatments, which makes them more clinically effective and cost-effective. This facilitates rare-disease designation for otherwise common diseases, and orphan drug status recognition for medicines to treat these diseases. The designation comes with significant regulatory advantages reserved for orphan drugs, such as faster drug approval, higher prices on account of their novelty and longer patent terms or data protection *(14,16–19)*. This subcategorization of diseases raises concerns about how to manage the unintended consequences of well-intended regulations, and their potential impact on sustainability of medicines coverage *(20)*.

A worrying development is that even prices of traditional, widely-used, life-saving medicines continue to increase if there is no competition or if no new patents are registered on novel delivery systems. Most novel medicines are protected by patents, creating a monopoly for that product and thereby pushing up prices for the duration of the patent period *(1,21)*. The World Trade Organization Agreement on Trade-Related Aspects of Intellectual Property Rights (TRIPS) has arguably contributed to pharmaceutical monopolies that can result in high drug prices and/or low availability, to the detriment of patients and governments *(22)*. A medicine may be framed as obsolete or as less effective in treating the illness when the patent expires, and a new (typically patented) medicine is often pushed on the market as the new standard of care *(21)*.

There is a trend within the industry for large pharmaceutical companies to buy out smaller biotech firms with successful medicines, reducing competition and resulting in higher prices *(23)*. Nevertheless, the presence of multiple developers including biotech firms may also have the unintended consequence of increasing prices on account of higher transaction costs *(24)*. Production or proper distribution of medicines not covered by patents may be purposively stalled to promote the use of patented medicines. This has been done, for example, through "pay for delay" agreements, whereby brand-name companies pay a generic company to delay the launch of a generic version *(25)*. Prices may also be driven up when medicines coming off patent are slightly altered to prolong

patent protection, or are connected to delivery mechanisms under patent – a practice described as "evergreening" *(26–29)*. Small incremental changes to previously widely available and affordable medicines, in combination with a lack of control over prices, may result in making the prices of essential medicines unaffordable for longer periods than would normally be the case under narrow patent protection.

The excessive pricing of insulin in the United States is a case in point. Insulin was discovered in the 1920s by Canadian researchers who explicitly expressed a commitment to making the drug widely available at low cost. However, the prices for newer forms of insulin in the United States have made the product unaffordable for many patients, forcing patients to reduce their use of insulin, resulting in "kidney failure, blindness, or even death" *(30)*. The reasons for the excessive price – particularly in the United States – are complex. While lack of price control is an important factor, patents on incremental innovations of the product are also part of the explanation *(30)*.

Sometimes the delivery tool creates access impediments. For example, the medicine itself may not be under patent, but the delivery device – such as the technology behind the tool to inject the vaccine – may be associated with monopolistic high pricing *(31)*. Dependence on new technologies is not unique in the context of technological innovation (as with, for example, electronic devices and mobile phones), but when it comes to life-saving medicines, it clearly creates additional ethical concerns.

The pharmaceutical industry tends to invoke costs of medicine R&D to justify high prices, as well as costs of research into drugs that are unsuccessful *(32*; see also *33)*. The industry and some authors argue that medicines for rare diseases, or those to be used for subsets of patient populations, would never be developed if recuperation of the enormous costs involved in the development of these drugs was not possible *(34,35)*. Pharmaceutical R&D cost estimates tend to be based in part on data that are not publicly available, however; thus, they cannot be independently verified. The industry's claim may be based on an inflation of the true costs of drug development *(36–39)*. The prices charged to governments, based on claims of high R&D costs, often fail to factor in prior public investments in early research stages, support provided by publicly-funded medical institutions at various stages of the development process, and stewardship of knowledge along the innovation value chain *(40,41)*.

In reality "drug prices seem to be set at whatever the market will bear" *(42,43)*. In cases where the disease is life-threatening, patients who are able to afford it may want to pay these high prices because of the desperate context in which they find themselves *(43)*. Most often, it creates significant pressure on political decision-makers and health-care funders to cover the medicines. No politician likes to be associated with a refusal to cover the cost of an innovative drug when it is touted as needed to save the life of a desperate patient – even less so when it involves children. The public discussion around Belgium's lack of coverage for a new drug for cystic fibrosis *(44)*, and the coverage for drugs in the United Kingdom aiming to treat rare diseases *(11)* are cases in point.

Social media campaigns, combined with lobbying and often involving mobilization by industry-funded advocacy groups *(45–47)*, can add to the pressure. High-profile campaigns that obtain funding through crowdsourcing have received a lot of attention in recent years. For example, in 2019, in the space of two days, more than 900 000 Belgians contributed to a campaign to fund the €1.9 million cost of a novel medicine for spinal

muscular atrophy for a Belgian baby, even before the drug was officially approved by the European Medicines Agency *(44)*.

A final comment is warranted about the global context of high prices, which will be further discussed in another OMI technical report focusing on high-priced medicines in the WHO European Region. Opioids are not often discussed in the context of high-priced medicines, but there are paradoxical crises in high- and low-income countries with respect to these drugs. In some high-income countries – particularly in North America – opioids have been aggressively and even fraudulently promoted, including through questionable publications, conferences, university lectures and various marketing practices, resulting in over-prescription *(48,49)*. Prices do not constitute a significant barrier, since opioids in North America are generally covered by public or private insurance funds. The promotion of opioids has contributed significantly to their overconsumption and the resulting devastating public health crisis, which is associated with more than 500 000 deaths in the United States *(50)* and more than 23 000 in Canada *(51)* since 2016. In contrast, opioids in low-income countries are comparatively expensive and, hence, not readily available – particularly in poorer populations – resulting in inadequate pain relief *(52–54)*. This example highlights the complexity and global diversity of the problem of high prices of medicines, as well as the importance of stewardship to avoid both over- and under-prescription.

1.2 Challenge of accessing high-priced medicines: lessons from COVID-19

The issue of inequitable distribution of effective, novel, high-priced, life-saving drugs has most recently come into focus in the context of the COVID-19 pandemic. The urgent demand for COVID-19 vaccines has vastly outpaced supply, and countries have been competing for access to sufficient doses to enable them to immunize their citizens. Competition between countries, the urgent need for sufficient doses and the limited supply of vaccines has inflated prices *(55)*. Negotiations between individual countries and pharmaceutical companies were conducted – certainly initially – largely without transparency towards the citizenry about prices and several contractual provisions. In an October 2021 report, the United States-based advocacy organization – Public Citizen – scrutinized some of the contracts between governments and vaccine producer Pfizer that it had been able to obtain. According to its findings, the "contracts offer a rare glimpse into the power one pharmaceutical corporation has gained to silence governments, throttle supply, shift risk and maximize profits in the worst public health crisis in a century" *(56)*. The report discusses how several contracts contain confidentiality clauses, in addition to contractual provisions related to protection against liability, which are seen as a key tool to ensure industry participation in an emergency pandemic response *(57)*. Some countries have also been contractually required to put up sovereign assets, such as embassy buildings, as potential indemnity for future legal costs *(58)*.

Fearful of not obtaining sufficient doses, many high-income countries stockpiled large quantities of vaccines *(59,60)*. Options to limit export of vaccines were explored in several countries *(61,62)*. Several high-income countries – including Canada, EU countries, Switzerland, the United Kingdom and the United States – blocked low-income countries'

requests to waive patent rights for COVID-19 vaccines so that generic versions could be produced at cheaper prices *(63,64)*, even though some of these countries (such as the United States) appear to have reversed course since. It is worth noting, however, that the manufacturing capacity in low- and middle-income countries would remain a key challenge, even if patents were waived. Other issues remain with the supply of components and technological expertise, particularly for novel vaccine platforms.

The competition between countries for urgent access to life-saving drugs, hoarding of these drugs by some countries and the limited supply of vaccines has resulted in a power imbalance between pharmaceutical companies and governments in several countries. As a result, some low-income countries ended up paying higher prices than high-income countries for the COVID-19 vaccine, after negotiations with pharmaceutical companies *(65,66)*. What is abundantly clear is that, at this point in time, low-income countries still do not have access to sufficient doses. Market mechanisms have fundamentally failed to provide equitable access to life-saving vaccines, owing to a complex interplay of poor bargaining power of governments in low-income countries, international patent protection, lack of technological capacity to promote domestic production and increased purchasing power of high-income countries.

The actions taken by countries and the pharmaceutical industry in the context of the pandemic have highlighted long-standing issues – specifically the complex interactions, power imbalance and potential conflict of interests embedded in the relations between governments, pharmaceutical companies, multilateral institutions, large philanthropic organizations (some – such as the Bill and Melinda Gates Foundation – with major influence on global health policy *(67)*) and broader civil society.

These power imbalances and the conflict between economic, trade and industrial policy and global public health policy have been starkly reflected in the outcome of the vaccine contract negotiations between industrialized countries and pharmaceutical companies. They have resulted in the national hoarding of vaccines and differential prices – in this case often higher prices for countries with fewer resources; restricted access to vaccines for low-income countries (because of a combination of prices, problems with supply chains and vaccine infrastructure, and political factors); and objections and even strong lobbying against patent waivers by many high- and middle-income countries, industry and some philanthropic organizations. This has created what some describe as "vaccine apartheid" *(68)*. Policy experts and advocacy groups, as well as government officials of some countries, have repeatedly called for action – particularly from high-income countries and industry itself – for more equitable distribution of COVID-19 vaccines, including through patent waivers *(69)*. The public pressure exercised by some large philanthropic organizations on maintaining patent protection, and their relations with industry, have also been criticized in this context *(70,71)*.

1.3 Ensuring medicines are safe and effective: value of transparency

While access to medicines is a key issue, it is central to the social contract that the industry must demonstrate to medicine regulators that novel medicines are safe, of high quality and effective. These regulatory standards and processes mitigate the risks associated

with novel medicines and the perverse incentives that exist to inflate benefits claims and reduce manufacturing costs. For the health systems and the patients who pay for them, medicines must perform as claimed and must add value to what is already available. They must be prescribed appropriately, based on reliable evidence. As the experiences of growing antibiotic resistance and the opioid crisis illustrate, over-prescription of medicines has a very serious impact on public health.

There are also concerns that novel medicines ultimately may not offer the long-term benefits that are claimed at market launch and on which prices are based. Health systems are pushed to provide coverage of expensive medicines, based on the limited information available at launch. In the long term, those benefits might not be achieved, reducing their cost–effectiveness. Hence, it is imperative that the therapeutic value of medicines is rigorously evaluated, and that reliable information is available about their safety and effectiveness. Since the necessary data often accrue over time, and time is critical for patients with life-threatening diseases with no other options, it should be noted that these patients are often willing to accept higher risks than medicines regulators. Data sharing and access to data are increasingly seen as essential components of a reliable drug regulatory system and of promoting reliable pharmaceutical R&D *(72)*.[1] This has also been stressed repeatedly in the rare-disease context, where patient privacy issues may require specific interventions *(74)*. Independent scrutiny of efficacy and safety claims of medicines post-marketing is especially important for orphan drugs, and for medicines developed in emergency epidemic and pandemic contexts; development is often expedited and the medicines are often introduced through conditional routes, with reduced initial evidence requirements *(75)*.

Transparency has been emphasized for some time. It resulted, among other things, in the establishment by WHO of the International Clinical Trials Registry Platform *(76,77)* and in the WHO Transparency Resolution in 2019, which endeavours to improve "the transparency of markets for medicines, vaccines and other health products" by encouraging transparency in pricing, and factors impacting medicine pricing such as clinical trial costs *(78)*. The call for data sharing has intensified again in the context of COVID-19 vaccines. Increased international collaboration between governments – and between governments and pharmaceutical companies – in gathering data, monitoring safety and sharing analyses on a timely basis with each other and other stakeholders can be considered crucial for creating better preparedness for future pandemics *(79)*. Pharmaceutical companies obtained significant health data from early on in the pandemic – for example, Israel agreed to provide Pfizer with access to anonymized health data in exchange for COVID-19 vaccines *(80)*. In this case, since the data provided to Pfizer were gathered for public health purposes and by public agencies, it seems even more obvious that there should be no claim that it was confidential commercial information belonging to and solely for the use of the company *(81)*.[2]

1 For a discussion on the definition and exploration of the concepts of "availability" and "accessibility" to information, see Vogler *(73)*.

2 Transparency is also important for other reasons. For instance, transparency of research data may stimulate scientific research because of efficiencies (avoiding duplication and early identification of potential safety issues) *(82,10)*. Novel initiatives of data sharing and open science at the early stages of drug discovery may contribute to lower development costs and accelerate innovation *(83)*. Finally, transparency of prices can be identified as a key tool for reasonable price determination *(84)*.

1.4 Consequences of limited access to life-saving drugs

Regardless of the context in which concerns about the impact of high prices of medicines are explored, the consequences can be severe for both patients and the sustainability of health systems. When dealing with effective medicines for serious and catastrophic diseases, such as cancer and some orphan diseases, consequences include "limited access to timely diagnosis, to affordable, effective treatment, and to high-quality care" *(85)*. For other medicines (for example, in the case of a lack of access to affordable opioids), patients may be compelled to live in pain that might otherwise be treated. For conditions such as diabetes or severe allergies the costs of medicinal products including insulin and EpiPens may lead to unsafe medicine practices and may result in death.

The frameworks used to determine cost–effectiveness generally take into account the impact of non-treatment, which may result in other health issues and more expenses related to additional health care and other types of intervention. For example, lack of treatment could result in unnecessary hospitalization, which is among the highest expenses in the health system. It also has a broader impact on society as a result of lost work days.

There is broad recognition that these challenges have to be urgently addressed. Indeed, various stakeholders – including governments, consumer groups, international organizations, experts and some pharmaceutical companies – have explored a number of initiatives, and have made numerous recommendations on how to achieve better access to effective, novel, high-priced medicines. Public–private partnerships (PPPs) have been established – particularly for communicable diseases that predominantly affect low-income countries. Other initiatives and recommendations relate to *(41,85,86)*:

- improving the transparency of R&D costs, of price-setting mechanisms for medicines and of clinical trials data;
- improving regulation of drug pricing;
- developing targeted payment and reimbursement mechanisms (such as managed entry agreements);
- improving real-world evidence of effectiveness;
- collaborative and adapted procurement approaches to strengthen demand-side bargaining power and financing arrangements;
- reforming the patent regime;
- establishing universal health coverage for essential medicines; and
- improving the reliability of global supply chains.

2

Actors/stakeholders

A vast range of actors play a key role at the national, supra-national and international levels in relation to access to effective, novel, high-priced medicines. For the purposes of this report –written in the context of an initiative focusing on the identification of obligations and contributions for achieving such access in the WHO European Region – actors are divided into three categories: governments, the pharmaceutical industry and others. The authors recognize that these three categories are broad: within each are a plethora of actors. The third category of "others" is particularly extensive and amorphous, and includes very divergent stakeholders. Delineation of the three categories is connected to the goal of identifying initially – using a social contract, a GPG and human rights lens – some of the key obligations of the two major players in medicines governance in the Region: government and pharmaceutical industry actors. The third category is present to emphasize that several other actors play crucial roles at the research, production and distribution stages of the supply chain that delivers medicines to patients. These also arguably have specific roles and responsibilities under social contract and human rights approaches, some of which overlap with those of governments and industry. They tend to be involved more in the background, at the political level, however, as well as in the further implementation stage when a policy framework has been established. While this report identifies some examples of their respective roles and responsibilities in section 6, they will not be discussed in detail.

The first category – governments – comprises various government ministries and departments. For this report, reference to governments includes supra-national authorities. Clearly, not all government departments are aligned on issues related to access to effective, novel, high-priced medicines. As WHO acknowledges, there is "an inherent conflict of interest between the legitimate business goals of manufacturers and the social, medical and economic needs of providers and the public to select and use drugs in the most rational way" *(87)*. This translates, at the government level, into tensions between departments and agencies focusing on economic and industrial growth and international trade on the one hand, and those implementing public health on the other. Competing government goals of promoting a vibrant commercial pharmaceutical industry and access to affordable medicines result in pulls in different directions.

For example, research funding agencies and medicines agencies in charge of evaluation and supervision of medicines may impose data transparency rules to promote independent scientific analyses and regulatory accountability; whereas government agencies in charge of promoting economic development may focus on patent enforcement, and push for the recognition of pharmaceutical data as confidential commercial information. There can even be a clash, or at least some tension, between agencies mandated to promote a component of public health. For example, medicinal agencies mandated to review medicinal products tend to focus on the approval of medicines with a favourable risk/benefit profile in experimental conditions, without much attention to how the medicine performs in standard care compared to other treatment options that are available *(88)*. Once a medicine is approved, pressure is created on government agencies involved in health-care funding to ensure access to the product. Pressure for funding often results

from an interplay of industry lobbying and patient advocacy, and various trade, industry, economic and political components.

As a result, approval of medicines may create pressure on funding when the price is very high, even when the long-term, clinical effectiveness and the comparative efficacy is unknown. Experience with performance-based risk-sharing agreements in the Region reveals that government funders rarely scale back funding, even when continued funding has been made conditional on the production of evidence within a specific time frame and the conditions have not been met *(20)*. The connection of such risk-sharing agreements on the funding side with adaptive licensing systems, whereby approval is also made conditional on obligations of further evidence gathering, may not solve the problem of pressure, if such decisions cannot be reversed should the anticipated benefits not occur.

Divergent interests, or at least a divergent focus, also exist at the international level, where organizations like WHO have actively promoted data sharing, whereas the World Intellectual Property Organization focuses more on the international recognition of intellectual property rights. Initiatives to coordinate the agendas of governmental and international agencies in this context are in place, but the tension is worth mentioning here. Indeed, a coherent response to the challenge of high prices and access to medicines will generally require coordination at national and international levels to ensure that competing or divergent interests of various agencies and departments do not impede desired actions – for example, with respect to transparency *(89,90)* – and that potential unintended consequences of novel strategies are identified and addressed.

Although divergent interests and priorities within this category are recognized, this technical report focuses on the government holistically, as it explores the issue of broad governmental obligations and responsibilities towards increasing access to effective, novel, high-priced medicines. At the same time, it is imperative that the complexities arising from the divergent views within this category are recognized. Section 6 sets out a list of actions that could be framed as part of the obligations of governments in relation to access to medicines. These need to take into consideration the fact that different government entities are inevitably involved, and that coordination across departments remains a key challenge. The suggested actions are not exhaustively discussed, since this would exceed the scope of this report, but it is important to recognize the complexity of the various interactions and tensions between governmental goals and objectives.

The second category – the pharmaceutical industry – comprises various industry actors involved in the medicine R&D, regulatory compliance, production and marketing stages. The private biomedical sector is not homogeneous and includes small and medium-sized biopharmaceutical enterprises, R&D-based or originator companies, contract research organizations, medical communications agencies, contract manufacturing organizations and in some countries also private commercial research ethics committees.

While each actor has a crucial role to play in increasing access to effective, novel, high-priced medicines, this report focuses on the rights and responsibilities of pharmaceutical companies in increasing such access. In the context of the WHO European Region, it is predominantly the brand-name companies that play a leading role, with generic companies

playing a role in initiatives of medicines that are off-patent, or where, for example, voluntary licensing options are pursued – which is rare in high-income settings. There is, however, no strict separation between brand-name and generic companies. Some brand-name companies have majority stakes in generic companies, and some companies that largely focus on generic products may also be involved in the development and production of patented medicines.

It is also important to note here that large brand-name companies tend to be publicly listed and have duties to shareholders, which often comprise large-scale pension firms and other financial institutions. These duties create pressure towards short-term profit and growth, even though some sovereign investors may also be purchasers of the medicines whose prices they are simultaneously attempting to reduce.

Within the context of high-priced medicines, small, start-up biomedical companies often play a significant role – for example, in the development of novel medicines for rare diseases. Their interests and focus, and the market dynamics that drive them, differ from those of large pharmaceutical companies. This report does not identify specific obligations relevant to the size and corporate structure of pharmaceutical companies, but instead observes that whether and how companies might be able to implement specific recommendations may depend, to some degree, on their nature.

Larger, brand-name companies also exercise significant control over many of the stakeholders in this broad category. As the main steward of the R&D process, they issue contracts with contract research organizations, communications agencies and contract manufacturing organizations, and tend to direct the outcomes of communications and marketing efforts and the scope and approach of clinical trials, as well as further knowledge translation in scientific publications *(91)*. They also often have a significant impact on stakeholders that this report groups in the third category – for example, through the funding of patient advocacy groups and connections with large philanthropic organizations. This category comprises all other actors: civil society, large philanthropic organizations (such as the Wellcome Trust, Howard Hughes Medical Institute, Bill and Melinda Gates Foundation and Institut Pasteur), health professionals and health profession organizations, patients, research participants, patient advocacy organizations and others.

These actors are lumped together, not because their interests are aligned, but because of the particular focus of this report on the mutual obligations of governments and the pharmaceutical industry. While this third category contains very divergent actors, with often aligned – but sometimes conflicting – interests, many play a crucial role in the overall promotion of access to medicines. For example, civil society groups were key to holding governments and pharmaceutical companies accountable for historical failures with access to medicines during the HIV/AIDs crisis *(92–97)*. Advocacy work has had a huge impact on national and international initiatives that have facilitated access to medicines in this and other contexts. For example, the Access to Medicines Index, which ranks some of the world's largest pharmaceutical companies on the basis of their contributions to increasing access to medicines in low- and middle-income countries, publicly recognizes the best performers. Through this recognition, it endeavours to foster competition, encouraging companies to take further action to increase access to medicines *(98)*.

Advocacy organizations have also influenced the development and further interpretation of international agreements related to intellectual property (such as the Doha Declaration), and various initiatives to lower prices of life-saving medications.

Many civil society organizations continue to take an active role in the implementation of various access to medicines programmes, such as the Access to Medicine Foundation, which established the Access to Medicine Index *(98)* – often working in close collaboration with governments and international and philanthropic organizations, such as Médecins Sans Frontières. Several civil society organizations have, for example, been very vocal in their criticism of national governments and international stakeholders – including philanthropic organizations – for their opposition to the implementation of patent waivers in the context of the COVID-19 pandemic *(99,100)*. Some civil society groups focus on promoting standards that are directly relevant to the components of this report, such as those pushing for broad transparency obligations in the health-care context *(101–103)*. All this illustrates the crucial role of civil society in exercising, for example, pressure towards the further implementation of obligations of governments and industry, and in imposing democratic accountability. How they can continue to do so is, however, not part of this report.

Professional organizations are obviously also an essential component of promotion of access, since effective, novel, high-priced medicines tend to be available by prescription only. They are key in the development of clinical practice guidelines, professional controls on prescription behaviour, development of conflict of interest standards, educational initiatives and so on.

Finally, the role of patients is, of course, also crucial. Increasing access to effective, novel, high-priced medicines aims to benefit them in the first place. They are also often research participants, thereby making an essential contribution to the implementation of access to medicines measures. Access to relevant patient information, adverse event reports, protection of privacy and patient experiences with medicines need to be on the table when discussing the role of governments and industry. However, access to patient data also raises privacy and confidentiality concerns.

For all these reasons, this report recognizes the existence of a broad third category of actors and will at least acknowledge in the discussion of the potential responsibilities of stakeholders some of the ways in which they can contribute to better access to medicines, even if the focus of this report remains primarily on identifying obligations of governments and pharmaceutical companies.

3

Social contract theory: rights and responsibilities

Social contract theory is a key theory used to explore questions about the relationship between citizens and their country's government; obligations of industrialized countries towards the global south; obligations of current generations towards future generations; and the shape of public interest obligations of private organizations. It helps to identify the broad content of these obligations. Some have explicitly used social contract theory to explain what kind of mutual obligations countries, organizations and citizens have in relation to ensuring good health and health care *(104–107)*. This section discusses briefly how social contract theory can provide a moral foundation for the rights and responsibilities of governments, pharmaceutical companies and others in promoting access to effective, novel and high-priced medicines. It does so primarily at a broader theoretical level, and may not easily translate in identifying concrete obligations.

3.1 Rights and responsibilities of governments towards citizens

Traditional social contract theories invoke a contractual arrangement to explain why governments came about, what citizens and governments explicitly and implicitly agree to in order for civil society to exist, and what each of their rights and responsibilities are under this contract. The theories "work at a 'pre-legal' level [and] try to establish rights and responsibilities that the legal system ought to recognise" *(108)*.

In contrast with pre-enlightenment views of governance, traditional social contract theories started from the premise that citizens are free and equal *(109–111)*. A common thread among contract theories is the view that citizens and governments enter into a hypothetical civil contract, whereby citizens agree to be subject to the rule of law, in exchange for the establishment of a society in which governments have obligations vis-à-vis their citizens – in particular to protect their rights *(112–118)*. Governments violate the civil contract if they fall short of fulfilling their obligations.

Rawls, the most contemporary of traditional social contract theorists, used a social contract approach to set out the principles for global justice *(116)*. The contract in the international context, according to Rawls, is between "peoples" which, through their representatives, agree about the basic rules of peaceful coexistence and a commitment to respect of rights and justice according to principles and norms of international law. This includes respect of treaties and undertakings, respect for human rights, and the recognition of a duty to assist other people living in unfavourable conditions. The introduction of the notion of human rights, as reflective of transnational legal-contractual obligations between governments and between governments and citizens can already be seen here.

Contemporary political theorists argue that modern-day reality demands that other parties – specifically organizations – are considered part of the social contract *(108,119)*. Nussbaum, for example, points out how the power of multinational corporations in the global market has "eroded the power and autonomy of nations" *(114)*. In many countries, corporate entities influence politics through lobbying and connections with political parties; organizations may hold monopolistic or oligopolistic positions and have the ability to influence markets and market prices.

This is particularly relevant in the context of health care, where corporate entities perform critical public functions, such as developing medicines that have the dual impact of improving the health of individuals and the health of a country's population, which have the potential to promote the economy and social cohesion. Additionally, R&D of essential medicines is to a significant extent determined by corporations and by large not-for-profit organizations that are often connected to industry stakeholders (such as the Bill and Melinda Gates Foundation). The complex connected process of medicine innovation is a good illustration of how multiple stakeholders are involved in the development of essential medicines and how collaboration is essential. It is clearly a context where it would seem reductionist to frame obligations under a social contract as exclusively or even primarily focused on the relationship between governments and individuals. Social contract theories must therefore also apply to organizations.

Commentators have also pointed out that social contract theory must go beyond the focus within corporate law on corporate obligations to shareholders, precisely because of the societal impact of corporate actions. Indeed, different sections of society should be seen as being party to the social contract *(119–121)*. Contemporary social contract theory recognizes organizations' broader obligations towards "society as a whole, including future generations" *(119–122)*. Given the contemporary challenges of global poverty, diseases and transmissibility of pathogens beyond borders and increasing economic and social disparities, society as a whole is not limited to people living locally within the proximity of where the organization has its headquarters *(119)* or carries out its business. The recognition of broader obligations connects to the theme of sustainability that is central to the achievement of the Sustainable Development Goals and is a core component of the OMI.

When it comes to the issue of determining what it means to have obligations towards society, current-day contract theories emphasize the global, broad understanding of "society" *(114,123–130)*. They emphasize global justice – that the social contract must be international in nature *(131)* – "parties are bargaining as individuals for a just global structure" *(114)*. Pogge suggests it is "undeniable that … there is a global institutional order that importantly affects the options and incentives societies and their rulers face in their relationships with one another and even affects profoundly the domestic institutions and cultures of especially the smaller and weaker societies" *(128,130)*. The moral foundation of global justice is founded on the idea that, although different societies are endowed with different natural resources, this form of natural resource lottery must not dictate a society's wealth and income *(124,132–135*; but see also *136)*.

The primary objective is to "optimize … the position of the least well off" *(114*; see also *128)*. The principle of global distributive justice asserts that there is a responsibility to reduce global poverty and take explicit steps to "prevent and mitigate the harms … continually

caused for the world's poorest populations" *(123,128 137)*. The OMI, with its emphasis on solidarity and sustainability, can be identified as part of a broader conversation to achieve this goal. This also connects to the broader WHO commitment towards universal health coverage and the partnerships established to achieve it *(138,139)*.

3.2 Limitations of social contract theory

While the theoretical framework of social contract theories is compelling, its implementation is underdeveloped and not well defined. Social contract theories remain vague about how responsibilities can be enforced; for example, how organizations – specifically multinational pharmaceutical companies – can be required to honour their obligations towards society. Nussbaum recognizes that, in the global context, organizations cannot be compelled to fulfil their responsibilities; these responsibilities must remain thin and flexible, and would need to be revisited in the future *(114)*.

While these contemporary social contract theories do not specify in detail how the theory applies to the pharmaceutical sector, it can be extrapolated that, like other organizations, pharmaceutical corporations have obligations under the social contract. They are expected to contribute to global justice by assisting individuals in all societies – particularly those who are weak, poor or marginalized – to achieve good health. It can be argued that one manner in which they might assist in achieving good health would mean assisting in increasing access to effective, novel, high-priced medicines – including for those infected by rare diseases.

Hence, within an international structure, international organizations, governments and corporations should be strongly encouraged to collaborate to promote an international and political order organized in such a way that the distribution of goods benefits those who are most disadvantaged. Because of their increasing power and influence, corporations – especially pharmaceutical companies – also have specific responsibilities in this international order, and should voluntarily become proactive in increasing access internationally. This is clearly also reflected in the growing discourse around corporate social responsibility and sustainability.

3.3 Ensuring good health: an obligation under social contract theories

Promoting good health is identified by some as a key obligation under social contract theories *(104)*. Health care is mentioned by others as an essential part of social contract theories *(105,106)*. This would include the duty for governments to ensure equitable access to health care for their citizens *(105,140)*. Others have suggested that the development of public health policies that aim to promote health, prevent health problems and educate the public should be seen as part of the social contract obligations of governments *(107)*. Obligations under social contract theory have also been identified in other areas of health care, such as in relation to health research, where citizens should arguably be given a more central role, leading to participant-led research *(141)*.

While social contract theories have helped to build recognition of the existence of rights and responsibilities in the health context between governments and their citizens, and between multinational pharmaceutical companies and society globally, the discourse is largely silent[3] on whether – and, if so, what – rights and responsibilities other stakeholders in the health sector, such as research institutions, would have in increasing access to effective, novel, high-priced medicines *(107,140,142)*.

In other words, several social contract theories emphasize broad obligations to promote equitable health care, but they are largely silent about how that can be fulfilled in practice. There is also not much detailed discussion in social contract theories of the specific obligations of the pharmaceutical industry in this context.

3 While some social contract theorists have explored rights and obligations in respect of patients, for example, the focus is very different from determining what the rights and obligations of these stakeholders would be in increasing access to effective, novel, high-priced medicines. In the context of patients, scholars primarily focus on the need to ensure patient participation in research.

4

Health GPGs: rights and responsibilities

4.1 Health, health care and medicines as GPGs

In the context of debates around equitable access to health care, the concept of GPGs has been discussed since the early 2000s and has gained significant traction over the years. Yet there is some confusion about what the term encompasses. The term is often invoked when arguments are made for the need to ensure equitable health care at a global level. “Health” and “health care” are, in this context, sometimes invoked as examples of GPGs *(143)*. In this sense, the term refers to important goods, or goods that seem essential to all *(34)*. This expanded use of the term connects to the identification of health care as a public good in some theories of justice. Walzer, for example, emphasizes how some goods are so essential for human well-being that they ought to be provided to all on the basis of need *(144)*. Governments thus have an obligation to ensure the fair distribution of these goods, and should tightly regulate, restrict or exclude markets to the extent that they hinder broad access.

In many countries, national health systems are structured in such a way that many patients may not be able to access high-quality treatment because of their inability to pay and lack of health insurance *(145)*. Such restrictions to access are typically observed in countries with the lowest gross domestic product per capita, but they are also observed in the United States – one of the wealthiest nations, which has large wealth disparities and a small publicly funded national health service. Even in countries where overall health care is publicly funded, some key components of health care may not be available on an equitable basis. Canada’s health system, for example, does not guarantee access to essential medicines or dental care. These restrictions on access to high-quality treatment seem to run counter to the notion of health as a public good.

Under such a broad meaning of the term GPG, an argument could be made that governments have to ensure access to effective, novel, high-priced medicines. But the concept does not provide a clear basis for identifying related stakeholder obligations. For example, it offers little insight into how to reconcile coverage for such medicines with issues of affordability and finite health-care budgets. Effective, novel, high-priced medicines cannot be considered GPGs without further analysis of their comparative merit and the sustainability of funding. Smith and MacKellar point out that the use of the term ”GPG” for everything important “overstretches and devalues the validity and usefulness of the concept” *(146)*.

Equating health and health care as GPGs has value as a primarily rhetorical tool for advocacy, to emphasize the unique nature of health and the importance of health-care products and practices, including medicines, for people’s well-being. The use of the term thus reflects an ideal, which the international community should strive to realize: equitable access to health care for all.

The use of the term "public good" may also find more traction in the context of specific medicines. For example, one of the driving philosophies behind advocacy groups' push to make AIDS treatment more accessible and affordable was that antiretroviral therapies "should ideally be 'merit goods', goods that are available to everyone regardless of income" *(93)*. The seriousness of the illness, but also its infectious nature – and thus the broader, global risk associated with infectious diseases – may also underlie the framing of medicines for such diseases as GPGs. This connects also to a narrower use of the term, discussed in the next section.

4.2 GPGs in the more restricted economic meaning of the term

A second use of the term, which provides a basis to identify more specific obligations in the context of effective, novel, high-priced medicines, is the economic definition. According to this, GPGs are non-excludable (that is, no one can be excluded from consuming such a good) and non-rival (that is, one person's consumption does not diminish what remains available of the good to others) *(34,147–149)*. Classic examples include air, water, parks and national security *(150*; see also *145,148)*.

In this meaning, the term GPG can be invoked in the mitigation and control of infectious diseases, and in relation to research and evaluation (such as health technology assessment, and safety and efficacy evaluations).

With respect to the first category, the COVID-19 pandemic has revealed again how health-care measures to avoid or control communicable diseases and pandemics, such as the stockpiling of vaccines or antivirals, should be considered GPGs: all should be allowed to benefit from ensuring easy and equitable access to essential medicines, and from other measures to prevent communicable diseases in a global context. Earlier examples substantiating this argument include the HIV/AIDS, Ebola and SARS epidemics *(145)*. Other specific actions in relation to communicable diseases and public health crises can also be considered non-excludable and non-rivalrous. For example, the provision/sharing of relevant data and related tools, and collective action at the international level – including to control and reduce antibiotic resistance – can be framed as required under a GPG approach *(151)*. Measures to control over-prescription and to support targeted and controlled new antimicrobial drug development can be considered GPGs. Some argue that new antimicrobials themselves and the effectiveness of antimicrobials might be better framed as common goods rather than public goods, since they are rivalrous *(152)*.

Recognizing the significant benefits that can be derived through global action on improving public health and fostering health equity *(153–155)*, multiple initiatives have been undertaken – involving governments, international organizations, advocacy organizations, the private sector and research institutions – that can be framed as reflecting a commitment to GPGs as components of public health-care initiatives. Examples include the Global Fund to Fight AIDS, Tuberculosis and Malaria, and the Coalition on Epidemic Preparedness Innovations, as well as actions taken by WHO and the World Bank *(34,156–157)*. Initiatives to reduce antimicrobial resistance, optimize antimicrobial use and develop sustainable antimicrobial development – such as the WHO Global Action Plan on Antimicrobial Resistance – are also good examples reflecting a GPG approach *(158)*.

A second concrete application of GPG in the context of medicines is in relation to knowledge components and regulatory aspects of medicine development and production. As Moon et al. *(34)* point out, medicines have two components: "the scientific knowledge[4] and a physical product". The physical end-product – such as a pill – is not a GPG in the economic sense, as it is "excludable and rival in consumption". Once it is consumed, it cannot be used by someone else. Yet, many components of what can broadly be prescribed as knowledge production in relation to medicines can be treated as public goods. In particular, this includes:

- basic scientific research, which often takes place in public institutions;
- pharmaceutical R&D, often involving the public and a variety of industry actors, as well as patients and research participants;
- regulatory standards aimed at identifying safety and efficacy, at both pre-market and post-market levels, as well as the knowledge produced as part of regulatory processes; and
- further assessments, such as health technology assessments.

Knowledge production can be subject to limitations, however. For example, merely because knowledge is available, it does not automatically mean that it is usable: knowledge may be difficult to comprehend and use. Similarly, even if data related to pharmaceutical products are publicly available, they can only be used effectively by those that have the requisite experience and resources. It can be argued that the training, skills, equipment and other resources needed to translate knowledge into useful, safe, effective products are immense, and that these may in themselves be considered GPGs to some extent.

4.3 Implications of the GPG approach

In the domestic context, governments are heavily involved in providing GPGs. In addition to direct investments, they may provide incentives to industry, such as taxation or advanced purchase commitments, to stimulate their production by the private sector. At the global level, there is no global government[5] to encourage and implement provision of GPGs *(34)*. To address this challenge, multiple recommendations have been made, chief among which is the need to increase collaboration among stakeholders *(157,159)*. To achieve this objective, however, collaboration is needed at all levels – global and regional – to address common challenges. In the context of the WHO European Region, collaboration at the regional level should be considered a key tool to promote access to GPG components of medicines for maximum public benefit *(34)*.

Additionally, experts have made recommendations aiming to mitigate the spread and impact of contagious diseases. Suggestions include improving medical technology, strengthening R&D, implementing robust surveillance and preparedness systems, establishing mechanisms for collective financing, providing appropriate insurance arrangements,

4 Technology often plays a key role.

5 WHO is a Member State-guided United Nations body that endeavours to encourage and implement the provision of GPGs through the setting of norms and standards, advocacy, development and the hosting of platforms and training, among others. But the reference to "global government" here means that there is no government body governing the world as there are governments in countries.

strengthening global institutional structures and improving global information sharing and resources for disease research *(159)*. It seems clear that coordination must happen at various levels, through national, regional and international cooperation.

These strategic goals with the purpose of addressing global health security risks remain vague with respect to who should be responsible for undertaking specific tasks to promote the creation and distribution of GPGs. The responsibility, if identified, typically focuses on international organizations and on governments. Responsibilities placed on the government typically require actions to correct market failures or functions to improve health systems within their national boundaries. Improving national health systems can have spill-over effects that can contribute to improving global health *(160)*. For example, a robust national surveillance system can contribute, in collaboration with other countries' surveillance systems, to a global surveillance system; and a robust regulatory system in one country can support evaluation and introduction of novel medicines for wider regional blocs or other countries. Precise actions that governments should perform are not easy to specify more generally, however, as specific requirements may vary from country to country, depending upon their domestic particularities and unique challenges. Pharmaceutical companies are encouraged to participate voluntarily *(161)*, but there are few recommendations for specific actions that pharmaceutical companies must perform to assist in achieving the objective of health equity globally, and often the recommendations made are non-specific and non-binding.

4.4 Conclusion: GPGs and high-priced medicines

The use of GPG terminology has its limitations in relation to identifying the obligations of stakeholders to ensure fair access to effective, novel, high-priced medicines. The concept of GPGs can be invoked as an ideal that governments ought to strive for – namely, the need to treat effective medicines as a good that should be equally accessible to all, across international borders.

Overall, the concept of GPGs is more concretely useful in the context of arguing for reliable supply (including via stockpiling) of vaccines or antivirals for infectious diseases such as COVID-19. To the extent that specific medicines are considered candidates for public health interventions, a GPG argument can be invoked for specific obligations. Coordinated action to combat public health threats associated with overuse or misuse of medicines – such as the risk of antibiotic resistance – can also be framed as a GPG-based obligation. For other aspects related to the distribution of effective, novel, high-priced medicines, the GPG argument is harder to make.

As noted earlier, however, the language of GPGs can also be invoked to argue for system strengthening interventions that facilitate R&D and increase access, such as knowledge sharing, basic research, information about regulatory pathways, clinical data and pharmacovigilance *(34)*. As the next section shows, this aligns with obligations related to knowledge sharing as a component of a human rights-based analysis.

5

Human rights law: duties and responsibilities

5.1 International human rights law and access to medicines

Social contract theories emphasize the role of law in the implementation of the obligations of governments, citizens and organizations.[6] Citizens and organizations arguably precisely accept to abide by the rule of law as an obligation under the implicit social contract that governs their relations with their government. Rawls's social contract theory explicitly emphasizes the obligation to respect human rights. With the growing recognition of the need to explore social contract theory in a broader, global context, this report proposes that international human rights can be employed as a basis to untangle the specific rights and responsibilities of actors in relation to access to effective, novel, high-priced medicines, as a component of a social contract approach.

The power of international human rights law comes not only from its normative value as reflecting "high-priority norms" *(162)*, but also from its legally-binding effect on those countries that commit to it (through a process called ratification). When it comes to health-related rights, and specifically also the right to access medicines, the ICESCR is the most important source of international human rights. To date, 171 countries have ratified the ICESCR, and 173 countries have ratified the International Covenant on Civil and Political Rights (ICCPR), which means most governments around the world are legally bound to some rights related to access to medicines (see Table 1 for a list). Other sources of human rights law applicable to countries in the WHO European Region include the European Convention on Human Rights, which binds member states of the Council of Europe, and the EU's Charter of Fundamental Rights.

Through human rights treaties such as the ICESCR, countries make legal commitments to their residents and promises to other countries, such as to assist one another. Under international human rights law, it is primarily governments (rather than companies or other private entities) that are responsible for realizing these rights; this is also one of the limitations of international human rights treaties. That responsibility is shared with the international community, however, and – as is increasingly emphasized – the private sector. Moreover, governments have obligations to create the conditions to regulate the private sector for the achievement of human rights. Section 5.2 presents four criteria to assess whether countries have taken "reasonable" action on their human rights obligations towards access to medicines.

It is increasingly recognized that private entities, and specifically pharmaceutical companies, also have human rights responsibilities vis-à-vis access to medicines, as described in section 5.3.

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6 As Moon et al. *(34)* explore certain types of financial contributions to R&D – which include public direct funding, private direct investment, public and private spending on innovative and patented medicines – and contributions to R&D made by pharmaceutical research entities and academic institutions in the EU, this report will not elaborate on what is discussed in detail there.

Table 1. Human rights obligations of governments for the provision of medicines

Human rights related to access to medicines	Obligations
Right to life	Countries should provide [access to] emergency and essential health care (including essential medicines), as part of the obligations towards citizens' fundamental right to life, enshrined in article 6 of the ICCPR.
Right to health and right to equality	Countries should provide essential medicines on a non-discriminatory basis as a "core" obligation of governments under the right to health, enshrined in article 12 of the ICESCR (see also article 2.1 of the ICCPR).
Right to enjoy the benefits of science	Countries should ensure adequate financial support for R&D of public importance, and prevent unreasonably high costs for access to essential medicines, as enshrined in article 15.1(b) of the ICESCR.
Right to freedom of expression	Countries should respect, protect and promote the right to seek, receive and impart information about medicines, as enshrined in article 19(2) of the ICCPR.
Right to protection of private and family life	Countries should ensure the right to access information that is relevant to make health-related decisions: related case law – particularly under the European Convention on Human Rights (article 8) – has been framed as a component of the right to private and family life.

ICCPR: International Covenant on Civil and Political Rights; ICESCR: International Committee on Economic, Social and Cultural Rights; R&D: research and development.

International human rights law contributes a deeper, more granular and practical understanding of governments' specific obligations towards their citizenry in this report (compared to the more abstract theories of the social contract and GPGs). The human rights in the main treaties applicable to all people – the ICESCR and the ICCPR – offer a range of high-priority norms that reflect minimal standards all countries ought to respect and promote.

These human rights also come with a notion of entitlement, or standards that can be enforced, that citizens can claim from their governments and public institutions. Although the ICESCR and the ICCPR are legally-binding instruments for ratifying governments, these standards are difficult to enforce in practice without strong domestic human rights norms. This does not mean that countries without strong domestic norms are inevitably failing in this respect. But if they do, there is no legal mechanism to hold them to account. Encouragingly, international human rights law has been an important basis for domestic access to medicines litigation by patients and groups of patients around the world *(163,164)*. Other types of domestic and regional law, such as competition law, can also be an important vehicle through which human rights related to medicines are realized *(165)*.

Enforcing human rights and holding governments accountable for violations before an international tribunal (instead of a domestic court) or in a transnational context remains challenging. The Optional Protocols to the ICCPR and the ICESCR do offer individuals

(who have exhausted domestic remedies) to file a complaint against a country for an alleged violation of their right(s) contained in these treaties, however. One such case was filed by Nell Toussaint against the Government of Canada (Toussaint v. Canada [2018]), in which the complainant – an irregular immigrant – sought access to essential health care (including medicines) *(166)*.

Many of the applicable international human rights are also embedded in supra-national (such as the European Convention on Human Rights and the European Charter) and national legal instruments (such as national constitutions) that are (more) directly enforceable. The interpretation of related rights at the national level will often be guided by international human rights norms.

The rights enumerated in Table 1 mostly belong to the category of economic, social and cultural rights which have aspirational components and are therefore harder to enforce. A key reason is that they require active implementation through government intervention (rather than abstaining from interference with a right), with the degree and speed of implementation inevitably depending on available resources. With respect to most components of the right to health, for example, governments have an obligation to "progressively realize" the right. Its definition as the right to "the *highest attainable* standard of physical and mental health" also reveals that progressive realization depends on available resources and technical capabilities.

International human rights law recognizes, however, that specific core obligations exist with respect to the right to health – such as providing essential primary health care, care related to childbirth and children's health care, and measures to control infectious disease *(89,167)*. The progressive realization component of the right to health comes also with obligations that can be scrutinized *(89,167–168)*. Authoritative interpretation by the International Committee of the ICESCR has provided details about core obligations of governments under the right to health *(169–171)*. Providing access to medicines as determined essential by WHO *(172)* is among the core obligations.

More recently, a reasonableness standard has been put forward as an important component of the realization of social rights under international human rights law. This reasonableness standard, embedded in the 2008 Optional Protocol to the ICESCR (United Nations ESCR 2008), has been refined in the context of access to medicines as containing three specific components *(168)*:

- taking deliberate, concrete, and targeted measures to mobilize sufficient domestic resources;
- seeking low-cost options; and
- pursuing international assistance in the realization of access to medicines.

The reasonableness standard is a flexible standard that takes account of the local context; as such, it is particularly relevant in the context of high-priced medicines. It aligns with the concept of sustainability that is a key component of the OMI and of the Sustainable Development Goals.

The concept of progressive realization, the flexibility of the reasonableness standards and the frequent emphasis in human rights law on access to essential medicines make it clear that human rights cannot be bluntly invoked to justify any claim for medicine coverage. Delineating the obligations of countries with respect to access to medicines becomes particularly complex when it comes to high-priced medicines, when concerns about the sustainability of the health system are at stake. Human rights claims in relation to access to medicines have gained traction in the context of the HIV/AIDS epidemic, and have been particularly successful in the context of public health crises when low-income countries have been faced with challenges in funding life-saving medicines. References are frequently made to the need to ensure access to essential medicines – a concept that deserves some clarification. WHO introduced the concept in 1977 *(173)* and now defines them as follows:

> Essential medicines are those that satisfy the priority health care needs of a population. They are selected with due regard to disease prevalence and public health relevance, evidence of efficacy and safety and comparative cost–effectiveness. They are intended to be available in functioning health systems at all times, in appropriate dosage forms, of assured quality and at prices individuals and health systems can afford *(174)*.

WHO publishes a list of essential medicines that functions as a guide for countries to determine, based on national factors, which medicines are essential. Some have questioned the usefulness of the concept in high-income countries *(175)*. Because of the reference to prevalence and public health relevance, and the emphasis in human rights of the need to take into consideration the sustainability of health systems, the question of whether this does not de facto exclude most high-priced medicines, such as those for rare diseases, also arises *(176,177)*. However, the concept of essential medicines is still relevant and useful in this context, even if the characteristics of traditional essential medicines may not fully align with those of rare diseases *(177)*.

It is important to recognize that the concept of essential medicines does allow for national and regional flexibility, and that it puts a lot of emphasis on the evidence required to decide whether public coverage provides value for money *(173)*. While high-priced medicines that offer only limited benefit over existing ones would not be reconcilable with the notion of essential medicines (which governments should make available as part of their human rights obligations), a life-saving drug for a rare disease could. Key here is that the decision to recognize a human rights obligation to provide access to medicine needs to be part of a coherent and publicly accountable evidence-informed medicines policy that uses the various tools governments have at their disposal to identify health care needs, determine coverage, control prices and ensure rational use. Furthermore, from a human rights perspective, it is important to emphasize the equity-promoting value of ensuring that people have access to important life-saving drugs, and that the rarity of a disease should not be a reason to prevent health needs from being addressed.

Some have suggested that because of the additional evidentiary challenges with respect to establishing drug safety and effectiveness in rare diseases, and the additional challenges with price determination, a separate “rare essentials” list ought to be established *(176,178)*.

Other rights are also particularly relevant in relation to effective, novel, high-priced medicines and can be considered to create concrete obligations. The right to enjoy the benefits of science creates obligations to ensure that R&D leads to the development of products that are available to all. The right to freedom of expression and, in the European context, the right to the protection of private and family life create obligations related to transparency of data *(91,179)*. The right to freedom of expression has been used concretely in the domestic context – for example, in Canada (Doshi v. Attorney General Canada [2018]) – to recognize that drug regulatory agencies have an obligation to provide access to safety and efficacy data submitted in the context of medicines approval *(180,181)*. Finally, the right to non-discrimination obliges governments to ensure access to relevant medicines for all, and particularly to promote access to health care for marginalized and disadvantaged populations. In relation to medicines in the context of the WHO European Region, this would come with obligations towards those who may currently often be excluded from proper access to health care, such as irregular migrants. As noted above, the right to non-discrimination could also play a role in the recognition of important medicines for those suffering from rare diseases.

5.2 Government obligations for ensuring access to medicines

The core obligations of governments for ensuring access to medicines can be translated into concrete policy actions. Table 2 presents four criteria for governments and courts to assess whether countries have taken reasonable action on essential medicines. These criteria have been proposed previously, based on the authoritative interpretation of the ICESCR by the United Nations Committee on Economic, Social and Cultural Rights. The justification for selecting these criteria and a detailed description of them is available elsewhere *(168)*. Not all of these obligations are easy to apply in the context of high-priced medicines, however.

Table 2. Human rights duties of governments for ensuring affordable access to medicines

Specific duty	Actions countries should take
Sufficient public spending	Countries should ensure sufficient public spending on a basic package of essential medicines for all. This was estimated to cost US$ 12.90 to US$ 25 per person per year in 2016 *(168,182)*.
International cooperation	Countries should seek international assistance and technical collaboration for sustainable domestic essential medicines programmes. Financial assistance may be a temporary measure to supplement legitimate shortfalls in public funding for pharmaceuticals. This could include exchanging, pooling or sharing knowledge, resources and technology, and/or exerting downward pressure on medicines' purchase prices *(183)*.
Efficient spending	Countries should improve efficient public spending on pharmaceuticals through the promotion of low-cost generics and biosimilars, and appropriate price controls, among other measures; and through the use of TRIPS Flexibilities when all other measures fail to yield affordable medicines.

Table 2. Contd.

Specific duty	Actions countries should take
Non-discrimination	Countries should ensure the domestic medicines policy is non-discriminatory by providing financial protection to people and groups in vulnerable positions, among other approaches. A substantive equality approach requires that those who are already disadvantaged receive additional support to reduce health-related inequalities. This could be used within the context of the WHO European Region as an argument to address inequities faced by racialized minorities, people with disabilities and other disadvantaged groups. Arguably, this could also be invoked to argue for access to medicines for rare diseases.

TRIPS: World Trade Organization Agreement on Trade-Related Aspects of Intellectual Property Rights.
Source: Perehudoff & Forman *(168)*.

5.3 Responsibilities of pharmaceutical companies and PPPs

It has been recognized for some time that the private business sector (such as pharmaceutical companies) has human rights responsibilities in relation to access to medicines *(184)*. This applies to all companies involved in the development, production and distribution of medicines. When it comes to large pharmaceutical companies, the increased role they play and their power in relation to access to important social goods, such as pharmaceuticals, makes the case for recognizing their human rights responsibilities even stronger *(185)*.

In 2008, Paul Hunt, the former United Nations Special Rapporteur on the Right to Health, proposed a set of guidelines identifying the human rights obligations of companies in relation to access to health (called the Guidelines) *(186)*. The Guidelines centre around the understanding that the private pharmaceutical sector has a "central societal mission" to develop medicines that are accessible to all who need them *(187)*. The Guidelines also identify a number of responsibilities of pharmaceutical companies, and clarify that these responsibilities are incumbent on any PPP and on companies' conduct within such partnerships *(186*, paragraph 44*)*.

In line with the Special Rapporteur's discussion on human rights obligations of both pharmaceutical companies and the PPPs in which they play a key role, this section discusses the human rights responsibilities of both actors in this category, even though it should be recognized that they are influenced by different market mechanisms, submitted to different pressures and have different goals. Indeed, PPPs often have different characteristics, and some are more closely aligned with the interests of industry than others. Addressing the differences between PPPs exceeds the scope of this technical report, so this discussion builds directly on the earlier categorization.

The publication of the Guidelines was followed by more general guiding principles for business and human rights in 2011, also known as the Ruggie Principles *(188)*. These require companies to take responsibility for the respect and protection of human rights, and to redress any human rights violations that may occur in relation to the entity's

business activities. Several pharmaceutical companies have stated that they recognize the Ruggie Principles *(188)*.

It should be noted that government support and strong regional and/or international cooperation are required to ensure further specifications of and compliance by industry for the obligations inspired by these guidelines. While some companies have supported them, this is insufficient for achieving their full realization. Accountability and enforcement mechanisms need to be explored at the national, regional and international levels. One challenge is that governments often have disincentives to insist on the realization of human rights standards in relation to access to medicines because of the economic role of corporations, trade protectionism, the overall influence of industry on government decision-making and industry capture.

Human rights responsibilities of pharmaceutical companies and PPPs (arising from the Guidelines) that are relevant for medicines are identified in Table 3. This includes all those that illustrate specific responsibilities industry has in relation to medicines, although some may be less relevant for the context of access to high-priced medicines in the WHO European Region.

Table 3. Human rights responsibilities of companies and PPPs for ensuring access to medicines

Category	Actions companies and PPPs should take
R&D	
Guideline 21	Companies and PPPs should observe the highest ethical and human rights standards, including non-discrimination, equality and the requirements of informed consent. This is especially vital in those countries with weak regulatory frameworks.
Guideline 22	Companies and PPPs should conform to the Declaration of Helsinki on ethical principles for medical research involving human subjects, as well as to the WHO Guidelines for Good Clinical Practice *(189,190)*.
Guideline 23	Companies and PPPs should publicly commit to contributing to R&D for neglected diseases (through in-house R&D or contributions to external initiatives, or both). Companies and PPPs should publicly disclose how much they contribute to and invest in R&D for neglected diseases.
Intellectual property	
Guidelines 26–27	Companies and PPPs should respect the letter and spirit of the Doha Declaration on the TRIPS Agreement and Public Health (2001) and the right of countries to use, to the full, the provisions in TRIPS (1994), including flexibilities, such as compulsory licensing and parallel imports.
Guideline 26	Companies and PPPs should make and respect a public commitment not to lobby for more demanding protection of intellectual property interests than those required by TRIPS.

Table 3. Contd.

Category	Actions companies and PPPs should take
Guideline 30	Companies and PPPs should issue non-exclusive voluntary licences with a view to increasing access, in low-income and middle-income countries, to all medicines. The licences should include appropriate safeguards and include any necessary transfer of technology. The terms of the licences should be disclosed.
Guideline 31	Companies and PPPs should, at a minimum, waive test data exclusivity and consent to national drug regulatory authorities using test data in least developed countries and also when a compulsory licence is issued in a middle-income country.
Guideline 32	Companies and PPPs should not apply for patents for insignificant or trivial modifications of existing medicines in low- and middle-income countries.
Pricing, discounting and donations	
Guideline 33, 35	Companies and PPPs should consider all the arrangements at their disposal with a view to ensuring that their medicines are affordable to as many people as possible, with attention to access for disadvantaged individuals, communities and populations, including those living in poverty and the very poorest in all markets. The arrangements should include, for example, differential pricing between countries, differential pricing within countries, commercial voluntary licences, not-for-profit voluntary licences, donation programmes and PPPs. The arrangements should extend to all medicines manufactured by the company, including those for noncommunicable conditions.
Guideline 38	Companies and PPPs should disclose as much information as possible about their pricing and discounting arrangements. Companies and PPPs should disclose as much information as possible about the absolute quantity and value of their drug donations; where possible, the number of beneficiary patients treated each year; and the amount of any tax benefit arising from their donations.
Transparency	
Guideline 6	Companies and PPPs should be as transparent as possible. There is a presumption in favour of the disclosure of information, held by the company, which relates to access to medicines. This presumption may be rebutted on limited grounds, such as respect for the confidentiality of personal health data collected during clinical trials.
Guideline 39	Companies and PPPs should take effective measures to ensure that all information bearing on the safety, efficacy and possible side-effects of a medicine is easily accessible to individuals so that they can take informed decisions about its possible use.
Guideline 41	Companies and PPPs should publicly disclose their promotional and marketing policies and activities, including costs.

PPP: public–private partnership; R&D: research and development; TRIPS: World Trade Organization Agreement on Trade-Related Aspects of Intellectual Property Rights.
Source: Hunt *(186)*.

5.4 Contributions of others

The concrete human rights responsibilities of other stakeholders have not been extensively discussed, and for understandable reasons. International human rights law binds countries in the first place. The recognition of international human rights obligations of corporations is connected to their growing power and the blurring of the role of governments and corporations in relation to some areas of public policy. This is certainly also the case with respect to health care and medicines, where multinational corporations play a key role – particularly in the area of medicines.

It is important to recognize, however, that many stakeholders other than governments and those within the broad category of the pharmaceutical industry play a key role in the development, production and distribution of medicines. Few have the same power as governments and corporations, but many contribute significantly to the realization of the core obligations associated with essential medicines, and to the objectives identified hereafter as "areas of responsibility". Some, such as the largest philanthropic organizations, do wield enormous power with respect to global public health policy-making, and can help to shape research priorities within countries or at a global level. They can contribute to broker relationships across stakeholders and may create bridges between industry and other stakeholders. They can also support mechanisms for delivery and access through systems strengthening. Research institutions have an impact on R&D. Professional organizations set policies that contribute to research standards and prescription practices. Civil society organizations have had a huge impact on access to medicines policies and continue to play a leading role in medicines related advocacy. Within civil society, patient organizations play an increasingly important role. They can provide insight into health-care product needs and acceptability of new medicines. They can enable or prevent uptake of novel medicinal products.

Without attempting to be exhaustive, the following sections provide some examples of how these stakeholders can contribute to the realization of international human rights standards in relation to medicines. These contributions often overlap, with many stakeholders potentially playing an important role in the promotion of specific norms. The discussion and tables illustrate some of the potential joint contributions of various stakeholders other than governments and corporations.

6

Classifying various obligations and responsibilities

This OMI technical report has identified a strong social contract basis for the argument that various stakeholders have obligations to contribute to the promotion of access to medicines. Social contract theory is also increasingly emphasizing the broader context in which obligations of various parties to the social contract have to be situated. This includes the broader global context of access to medicines, as well obligations to future generations. Concerns about equity and sustainability of the development and distribution of effective, novel, high-priced medicines should be at the forefront of discussions on how to promote access to medicines.

The concept of GPGs provides further support for specific obligations in relation to some aspects of promoting access to effective, novel, high-priced medicines. The most direct obligations that can be identified relate to areas where medicines need to be stockpiled for the purpose of global public health, and where coordinated effort is required to prevent or counter public health threats associated with medicines (such as antibiotic resistance). The concept seems particularly useful in the current context to support arguments for the promotion of open access to basic research, general knowledge and data sharing, and transparent post-marketing surveillance initiatives.

International human rights law, as elaborated on in various guiding documents, aids understanding and the distillation of various obligations and responsibilities of both governments and industry in relation to access to medicines. This report further suggests that human rights law – particularly as it relates to the right to health – helps to identify and categorize these obligations more concretely as they relate to promoting access to medicines. The categorization of these obligations could also be used to identify what role other stakeholders can play in the complex context of medicine development and marketing. This concluding section puts forward some specific obligations that have been identified, and classifies them according to a human rights framework – particularly as they relate to governments and pharmaceutical corporations.

6.1 Stakeholders

This report classifies stakeholders who affect access to medicines as follows: governments, the pharmaceutical industry and others (see section 2).

This classification serves to identify the obligations and responsibilities of different entities, or the contributions they can make, as a result of their unique role in the issue of access to medicines. It does not mean, however, that all stakeholders within a particular category have the same or even similar interests, priorities or concerns. Rather, as discussed in section 2, even within the category loosely identified as governments, different ministries and administrative departments may – and often do – have diverse priorities and interests.

Ministries of health would typically prioritize health and safety-related issues, while ministries dealing with industrial development, economy, finance and/or innovation would typically have a more economy-driven agenda. Despite these differences, and without minimizing the implications of such differences, for the purposes of this report the group is loosely discussed under the umbrella term of government, and potentially competing interests will be mentioned under that category. A key challenge for governments is how to address these competing priorities and tensions and how to develop a sustainable agenda and make long-term commitments for action.

The category, the pharmaceutical industry, comprises private companies that have a profit motive and develop, test or manufacture medicines, but this group is itself not homogeneous. Rather, it includes entities that may service different market segments, such as "brand-name pharmaceuticals, generic pharmaceuticals, biopharmaceutical small and medium-sized enterprises (biopharmaceutical SMEs), R&D companies, contract research organizations, and contract manufacturing organizations" *(191)*. Regardless of this diversity, this report discusses the pharmaceutical industry group broadly as comprising private profit-oriented companies that are directly involved in the development and manufacturing of medicines, and therefore have a responsibility for the social aspects of medicines. This category also includes PPPs, in line with the Special Rapporteur on the Right to Health's framework *(186)*, even though the broad variety in the role and functioning of PPPs should be recognized. This report sets out a list of obligations that pharmaceutical companies and PPPs can be considered to have to increase access to effective, novel, high-priced medicines from this perspective.

The third category, others, is much less homogeneous, and is set apart here primarily to indicate that there are other significant stakeholders who play crucial roles in promoting access to medicine. More broadly, this category includes civil society (including advocacy organizations), philanthropic organizations, research institutions, patients, health profession organizations and health-care providers. This report provides non-exhaustive illustrations of the types of responsibilities they may have, or the contributions they can make, to promote access to effective, novel, high-priced medicines.

Despite potential conflicts of interest, priorities and concerns within each category, these three categories are created along the lines of the obligations and responsibilities they should endeavour to fulfil to help achieve the overall objective.

6.2 The objective: increasing access to effective, novel, high-priced medicines

It is vital to have clarity on the end goal: to understand what precisely is meant by increasing access to effective, novel, high-priced medicines. Taking a leaf from human rights law related to the right to health *(169)*, the ultimate goal should be dictated by the interrelated duties to **respect**, **protect** and **fulfil** human rights in relation to medicine, including in the following ways.

- **Respect:** governments and the pharmaceutical industry should refrain from curtailing equitable access to effective, novel, high-priced medicines. This includes obligations to refrain from misrepresenting health-related information (such as overselling the

clinical benefits of medicines, lack of proper sharing of risk information) and arguably then also obligations to provide a strong, reliable and transparent evidentiary basis for the regulatory approval and public funding of medicines (this crosses into obligations to protect and fulfil), which includes obligations of proper access to data.

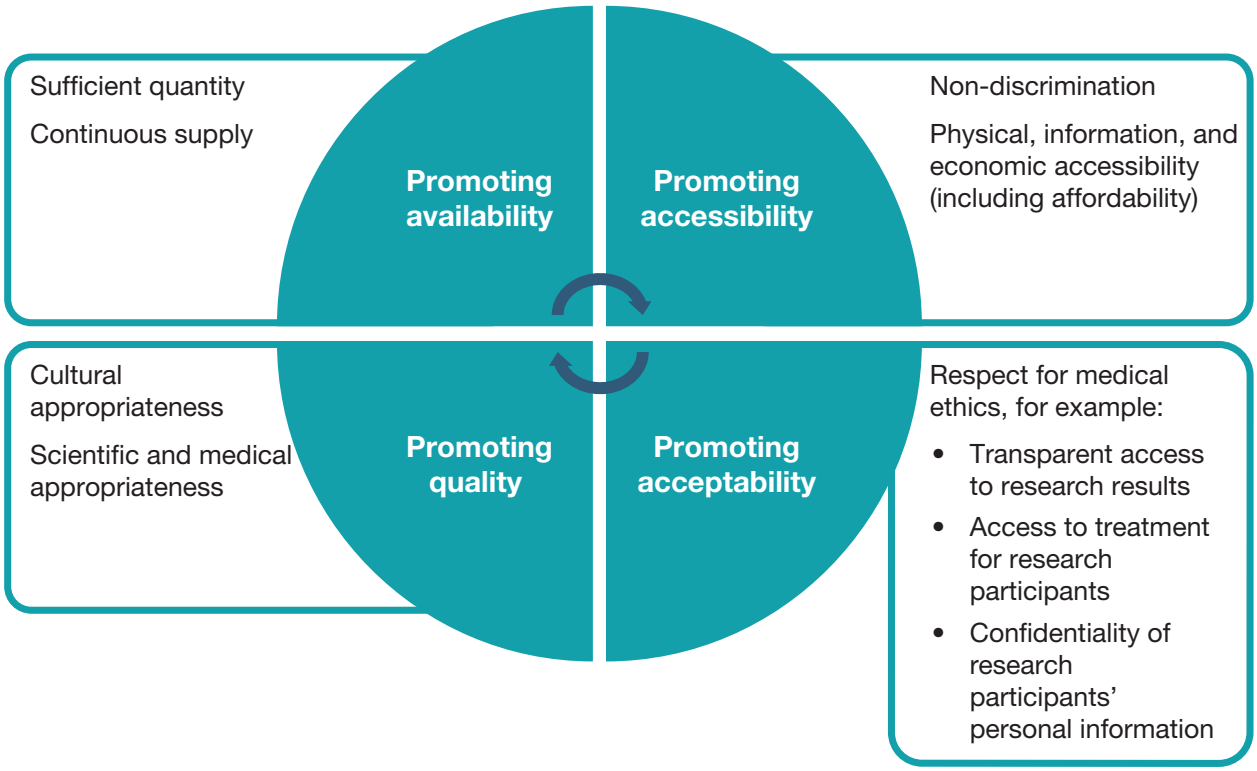
- **Protect:** governments and the pharmaceutical industry should adopt a two-pronged approach to protection: they must avoid making medicines unaffordable – that is, they should proactively take measures to prevent excessively high pricing – and to protect individuals and groups against obstacles to access medicines. This can be seen as part of the broader obligation of governments to enact proper legislation or regulations to ensure equal access to important health-care goods. They should ensure good governance of the safety and effectiveness of medicines. At a minimum, the pharmaceutical industry should collaborate in good faith with the implementation of proper regulations that protect patients (or, in the research context, research participants). Arguably, governments and pharmaceutical companies have to proactively combat misinformation, including misinformation in scientific publications that leads to inappropriate prescription practices.

- **Fulfil:** governments and the pharmaceutical industry should take positive action to facilitate access to medicines. This includes government obligations to support (fund and otherwise promote) R&D. It arguably also includes exploring new models of knowledge production and information sharing (such as open science models, PPPs on product development and socially responsible licensing more generally). It also includes a duty to formulate, implement and review national policies aimed at ensuring access to medicines while addressing tensions that may arise when economic and industrial policy goals contradict and are prioritized over social welfare related goals. This includes establishing policies fostering affordable and sustainable pricing, and exploring alternatives when existing models or treatment options do not work or do not provide sufficient value to justify high prices. The development of PPPs can be situated here as an option to fulfil the right to health obligations.

To achieve these objectives, international human rights law also emphasizes – in connection to these obligations – four distinct components of promoting the right to health: availability, accessibility, acceptability and quality. These four criteria are depicted in Fig. 1.

Each of the stakeholders should be expected to help achieve these four components of promoting right to health. Actions that should be performed by the stakeholders to help achieve these components are described in the following sections under areas of responsibility. Note that the combination of some of these factors requires careful planning and consideration with respect to approval processes and the funding of medicines. For example, availability reflects the notion of scarcity of resources, while accessibility implies that medicines must be available on a non-discriminatory basis and must be economically accessible, which includes the concept of affordability. Governments need to coordinate and balance the need for stringent regulatory approval processes of effective, novel, high-priced medicines with the provision of public funding so that these medicines are accessible to those who need them, thereby ensuring equitable access to potentially life-saving treatments.

Fig. 1. Components of promoting the right to health



6.3 Potential obligations and responsibilities of various stakeholders

If the objective of increasing access to effective, novel, high-priced medicines is to be achieved, specific actions must be identified that each stakeholder should strive to carry out. For this reason, this section lists various possible obligations and responsibilities of these stakeholders. All three categories – governments, the pharmaceutical industry and others – can play a significant role, so although the focus of this report is on the first two categories, some responsibilities are also listed for stakeholders in the third category. Tables 4–6 below set out possible actions that each of the stakeholders (governments, the pharmaceutical industry and other actors) should undertake in order to fulfil their obligations and responsibilities.

Other reports in this series delve into specific issues pertaining to effective, novel, high-priced medicines and suggest ways in which stakeholders could contribute to increasing access. Their key suggestions are also included in the following tables and grouped under the four essential components of promoting the right to health: availability, accessibility, acceptability and quality.

Table 4. Possible obligations and responsibilities for governments

Component	Possible actions for governments
Promoting availability	• Establishing appropriate legal and regulatory infrastructure to promote affordable and sustainable pricing,[a] including by drawing from a comprehensive suite of pricing control measures proposed by the Lancet Commission on Essential Medicines *(182)*. • Coordinating drug regulatory reviews for affordability assessments: exploring ways to better coordinate drug regulatory reviews with assessments of affordability. • Prioritizing or expediting reviews (e.g., of medicines for life-threatening conditions; antibiotics) taking into account equity considerations and the reality of market pressures once medicines are approved. • Considering tiered pricing[b] or differential pricing as a model. • Aiming to adjust ex-factory pharmaceutical prices to local purchasing power at the country level among lower-income countries in the WHO Europe Region *(194)*. • Adopting risk-sharing agreements[c] with arrangements for the transparency of sales prices, discounts and/or rebates *(195)*. • Promoting competition: improving efficient public spending on pharmaceuticals through the promotion of low-cost generics and biosimilars, and other policies to harness competition, including in the area of therapeutic competition.[d] • Investing directly in various initiatives for the R&D of medicines and health products for priority public health conditions. • Creating subsidies and incentives for private industry to invest in the R&D of medicines and health products for priority public health conditions *(195)*.
Promoting accessibility	• Promoting R&D costs transparency: providing appropriate funding conditions to ensure public disclosure of funding amounts and priorities and access to the end products, subject to socially responsible licensing terms that promote access *(195)*. • Ensuring that sufficient public spending is allocated to providing a basic package of essential medicines for all, with particular attention to people and groups in vulnerable positions *(168)*. • Engaging in partnerships and knowledge sharing: coordinating and cooperating with the pharmaceutical industry, international organizations, research institutes and other countries to promote accessibility, including knowledge sharing. • Supporting clinical data transparency: mandating the transparency of data, including at the R&D stages *(34,82,91,179)*. • Enabling price data transparency: mandating the transparency of price components *(195)*. • Seeking international assistance and technical collaboration for sustainable domestic essential medicines programmes *(168)*, which may take the form of demand pooling.[e]

Table 4. Contd.

Component	Possible actions for governments
Promoting accessibility	• Where needed, adopting or revising national laws to support the sharing of intellectual property, data and knowledge related to the manufacturing of medicines and health products required in cases of public health emergencies *(195)*. • Refraining from promoting standards or norms in international law that would limit the sharing of such knowledge (see above), particularly in cases of public health emergencies. • Ensuring that intellectual property and legal frameworks support the promotion and use of, where possible, non-exclusive voluntary licenses on patent expiration and the prevention of data exclusivity extensions.
Promoting acceptability	• Implementing standards for public disclosure of research data and integrity of research and publications, and enforcement of these standards. • Balancing the protection of privacy of research participants with access to data *(10)*. • Enforcing research ethics standards as per the Declaration of Helsinki and other research ethics guidelines.
Promoting quality	• Establishing good pharmaceutical governance with respect to safety and efficacy, including post-marketing surveillance *(196)*. • Initiatives to promote better governance of knowledge, including knowledge dissemination in scientific publications. • Making "small strategic investments to better organize, analyse and gather new data" – e.g., by investing in the strengthening of the WHO European Region's contributions to the WHO Global Observatory on Health R&D *(34)*.

R&D: research and development.

Notes:

[a] For a discussion on factors that should be considered while designing policies appropriate for addressing high prices of medicines and addressing domestic particularities, see Mestre-Ferrandiz et al. *(192)*.

[b] Docteur *(193)* describes tiered pricing as that "under which a product's price is adjusted by a measure of income or ability to pay in the market where the product is sold, so that prices are higher in higher-income countries and lower in lower-income countries".

[c] Docteur *(193)* explains that "risk-sharing agreements may provide means for wealthier countries to limit financial risk for products with uncertain benefit and to allocate spending more efficiently".

[d] Docteur *(193)* notes that "policies to harness competition allow all countries to allocate spending more efficiently while incentivizing innovation and supporting industry productivity".

[e] Docteur *(193)* explains that "demand pooling can help to increase the market power of payers/buyers, relative to sellers, and can help boost incentives and capacity for development of priority therapeutics".

Table 5. Possible obligations and responsibilities for the pharmaceutical industry

Component	Possible actions for the pharmaceutical industry
Promoting availability	• Investing in R&D for medicines and health products for unmet public health needs, and publicly disclosing those research priorities and the amounts of R&D investment using a common framework for reporting that is able to untangle some of the cost categories. • Encouraging affordable and sustainable pricing: including sharing with governments relevant data about the costs of production, research and marketing and distribution of medicines; full transparency for accountable pricing; engaging in bargaining/negotiating with a more access-oriented stance, accepting that there is information asymmetry and, for some countries, a lack of negotiating capacity or pricing capacity; supporting countries to pool demand so that a larger and more efficient market is created, to the benefit of society and companies (moving to higher volume, but moderately lower prices). • Sharing real-world evidence to inform managed entry agreements and pay-for-performance models, to ensure that comparative effectiveness and cost–effectiveness can be realistically assessed over time. • Disclosing financing sources for R&D, including public sector grants, prizes and public investments in R&D. • Engaging productively and proactively with policy-makers to test alternative business models for R&D that would deliver GPGs *(34.)* • Respecting the sovereign rights of countries to use to the fullest the flexibilities in the TRIPS Agreement and reaffirmed in the Doha Declaration to protect public health. • Refraining from lobbying for intellectual property standards that go beyond those required by the TRIPS Agreement. • Voluntarily licensing the necessary knowledge and intellectual property to scale up production of essential medicines experiencing potential or actual intellectual property-related supply shortages; where appropriate, include any necessary technology transfer in the licences; and publicly disclosing the terms of the licences. • Cooperating with knowledge-pooling mechanisms such as the Medicines Patent Pool and the WHO COVID-19 Technology Access Pool.
Promoting accessibility	• Coordinating and cooperating with governments, international organizations and research institutes to promote accessibility. • Facilitating transparency of data, including at the R&D stages, and of prices *(34)*.
Promoting acceptability	• Properly recognizing the involvement of patients and research subjects in drug development (e.g., through access to medicines post clinical trials). • Respecting research ethics standards as per the Declaration of Helsinki and other research ethics standards.
Promoting quality	• Ensuring the respect of good production standards. • Collaborating with governments, institutions and other industry players to promote the highest standards of medicines. • Publicly disclosing all information regarding the safety, efficacy and possible side-effects of a medicine, such that regulators, health providers and patients can make informed decisions about the use of such medicines.

GPG: global public good; R&D: research and development; TRIPS: World Trade Organization Agreement on Trade-Related Aspects of Intellectual Property Rights.

Table 6. Possible obligations and responsibilities for other stakeholders

Component	Possible actions for other stakeholders
Promoting availability	• Setting research priorities to encourage research in high-priority areas in collaboration with governments, civil society and others (research institutes and research funders; philanthropic organizations). • Participating in research in high-priority areas (patients/research participants).
Promoting accessibility	• Adopting and promoting research transparency policies (research institutes and research funders). • Requiring those using/relying upon their data to continue to apply their transparency policies (research institutes and research funders). • Promoting the transparency of data, supporting and participating in open science projects to stimulate R&D, and engaging in socially responsible and humanitarian licensing practices to ensure that these contain pricing and availability provisions (research institutes and research funders; philanthropic organizations). • Requesting, at a minimum, open access to research results as a condition for research approval and funding (research institutes and research funders). • Abstaining from lobbying in support of industry pricing and patent approaches that may impede access to medicines (philanthropic organizations; patient advocacy organizations). • Ensuring approaches that balance short-term access requirements with longer-term sustainability of industry (philanthropic organizations). • Encouraging research participants to contribute to the sharing of clinical trial data (civil society/consumer groups/advocacy organizations). • Educating research participants about their rights on confidentiality, and balancing confidentiality with transparency (civil society/consumer groups/advocacy organizations). • Campaigning for affordability and access and holding stakeholders accountable; voicing demand for particular areas of R&D/public health (civil society/consumer groups/advocacy organizations; patients/research participants). • Providing consent to data sharing (patients/research participants). • Participating in research on condition of data transparency (patients/research participants).
Promoting acceptability	• Promoting and enforcing the highest research ethics standards, including in relation to data sharing (research institutes and research funders). • Requiring those using/relying upon their data to continue to respect research ethics standards (research institutes and research funders). • Developing appropriate conflict of interest policies (research institutes and research funders; philanthropic organizations; civil society/consumer groups/advocacy organizations). • Educating research participants about the role of medical ethics, and their related rights (civil society/consumer groups/advocacy organizations). • Facilitating and advocating for the transparency of funding sources (civil society/consumer groups/advocacy organizations).
Promoting quality	• Promoting and supporting independent research on drug safety and effectiveness (research institutes and research funders; philanthropic organizations; civil society/consumer groups/advocacy organizations).

R&D: research and development.

Coordination between various government ministries and agencies within countries, and cross-country collaboration are key to achieving the objective of increasing access to effective, novel, high-priced medicines.[7] To achieve cross-border coordination, the EU is placed in an advantageous position because of its economic and social structure. The values embedded in the European Social Charter, which fosters common European social rights, should inspire such collaboration and support efforts to increase access to effective, novel, high-priced medicines. Some steps towards cross-border cooperation that Member States in the WHO European Region could consider undertaking *(34)* include:

- sharing costs and risks, to reap the rewards or benefits of pharmaceutical innovations;
- negotiating "binding international rules committing each government to invest in R&D and ensure that the resulting data, knowledge and intellectual property are openly shared. Investments could be made domestically, regionally or globally; what is critical is to ensure that all knowledge generated is rapidly put into the public domain as a GPG";
- creating "a pooled regional fund for pharmaceutical R&D that both responds to jointly agreed priorities and ties conditions to its investments to ensure availability and affordability of the end-products" to which "countries at all levels of income across the Region could contribute according to ability to pay"; and
- creating "a pooled regional procurement initiative that would increase the negotiating leverage of governments and pool various risks, including the risk of R&D failure" and supporting the development and sharing of key information on technology landscape/horizon scanning, clinical effectiveness, cost–effectiveness and pricing.

Considering the objective of this report (sketching the conceptual ethical and legal basis of obligations), and the contextual complexity of access to specific forms of medicines, a discussion on the advantages and disadvantages of various specific interventions exceeds its scope. However, to highlight how these obligations might concretely translate into the context of specific medicines, the examples given at the start of the report may help to clarify how some of the normative justifications play out in reality.

Take, for example, insulin for the treatment of diabetes, and epinephrine for the treatment of anaphylactic shock. Both are clear examples of important medicines (in this case clearly to be classified as essential medicines). In the jurisdictions where these medicines have become excessively expensive, the cause of the high prices appears to come from the interaction of regulatory regimes (drug regulation and device regulation; complex rules related to patents on the variations of existing drugs; interaction with or absence of strict price controls) with monopolistic behaviour by manufacturers. Under the obligations identified above, governments should intervene in order to better coordinate regulatory regimes, to enact appropriate price controls, to streamline drug and device regulations and to ensure coverage for these life-saving medicines. Pharmaceutical

7 Docteur *(193)* explains that "recognizing common interests across Member States and working together towards common ends will be much more effective than independent action when it comes to meeting policy goals like obtaining price concessions and directing industry to meet priority health concerns, such as vaccines for a global pandemic". Vogler *(73)* notes that "as an overarching approach, collaboration between authorities across the pharmaceutical value chain (vertical collaboration) in a country and cross-country collaboration is supportive to ensure affordable access to novel medicines. This can help to align different policy objectives."

companies are under obligations to justify their prices, to be transparent about the basis for the high prices, and to work with governments and civil society to keep the prices of these products affordable. They should also have good faith obligations not to game the system by exploiting gaps in the regulatory system and using these gaps to create market opportunities. The obligations of both governments and industry in this example can be framed under the headings of the duty to protect and the duty to fulfil since interests and priorities dictated by political will and political economy play key roles.

When it comes to medicines for rare diseases, how the obligations play out is harder to determine. As noted above, there are concerns about orphan drug regimes potentially contributing to a somewhat artificial subdivision of diseases into smaller disease clusters, not only on a scientific basis, but also because of the financial incentives in doing so *(15,18,20)*. However, a 2020 review by the European Medicines Agency found that incentives remain relevant to encourage the development of medicines for rare diseases. While the review acknowledged some problems with the system, it concluded that "the Orphan Regulation has contributed to important strides in the field of rare diseases and development of orphan medicines" *(197).* The results of the review will inform changes to the legislative framework as well as the EU's pharmaceutical strategy.

Governments should carefully assess how orphan drug designations and related market exclusivities affect drug pricing and adjust, if need be, their approach to the granting of orphan disease status in accordance with existing regulations. Efforts are also needed to coordinate this with decisions about medicines coverage for orphan diseases. The approach of value-based pricing often promoted by industry creates affordability challenges – particularly in the context of diseases for which treatments may be limited or absent. Although value-based pricing may stimulate drug development in such areas, a performance-based approach may need to be adopted that encourages regular periodic review of medicines to ensure that they are safe and effective and achieve the claims made. The performance-based approach is pertinent in the rare-disease context as, for valid reasons, orphan drugs are often introduced to the population with conditional approval and without completion of the randomized controlled trials required for other diseases. Therefore, the need for the stakeholders to collect real-world evidence that supports decision-making and to make it publicly available becomes critical. Governments need to explore and implement incentives to encourage the pharmaceutical industry to collaborate on data collection exercises and make the data publicly available.

There will, however, always be rare diseases where R&D and production costs spread over a small patient population will result in high prices. Obligations to protect would mean here that governments, in collaboration with industry, still ensure equitable access to these drugs for patients on the basis of need. This is embedded in obligations to protect against discrimination and to promote the fulfilment of the right to health for all. The duty to respect in this context would include obligations to ensure adequate information and a solid scientific basis for funding decisions, which should provide for pooled procurement/ joint purchasing to increase volumes and increase possibilities to lower the price per unit.

Under the obligation to protect, governments should ensure that medicines that have been conditionally approved in the context of high-priority medicines development (such as for catastrophic illnesses and rare diseases) do not remain on the market when the conditions for approval appear not to have been subsequently fulfilled by pharmaceutical companies.

The companies, for their part, should be required to respect conditions of approval and live up to regulatory requirements with respect to evidence gathering and transparency of data. They should also share detailed information about R&D and production costs when they are used to justify high prices.

PPPs and various research and funding models can be explored to promote the fulfilment of the duty to provide access to these drugs. Cross-border initiatives with respect to research and funding including pooling resources, such as those undertaken in Europe with the involvement of rare-disease patient organizations, can be seen as part of the obligation to fulfil.

The opioid example reveals inequity of pricing of medicines in a global context and is a good example for emphasizing the important obligations of governments and international organizations with respect to collaboration to promote equitable access to medicines across borders. Civil society organizations may also play an important role here. Cross-border initiatives reflect a recognition of the global context of social contract and human rights-based obligations. Here again, this can be framed as part of the obligations to protect and fulfil.

The COVID-19 pandemic clearly highlights the unavoidable global context of some diseases, and the profoundly unequitable way in which medicines are currently globally distributed. It raises questions about how the most basic standards of access to medicines are being ignored. Furthermore, the pandemic context may be a good example to demonstrate how global inequity in access to medicines may ultimately do harm to everyone, including people in jurisdictions that have been able to negotiate preferential access to vaccines, thereby illustrating the importance of the obligations to respect, protect and fulfil.

The controversy surrounding the recent approval of a medication for Alzheimer's disease in the United States *(198)* evokes overlapping dimensions of obligations to respect, protect and fulfil. Governments have a key role in preventing misinformation in relation to the effectiveness of new medicines – particularly when they involve catastrophic illnesses for which no treatments are yet available. They are also in charge of good governance of safety and efficacy (including arguably through the development of a reliable expert advisory committee structure); and of transparently integrating price and coverage considerations in regulatory reviews and priority-setting. In the case of Alzheimer's disease, the combination of remaining questions around risk/benefit profiles and high pricing – and this in relation to a disease for which many are desperately hoping for a miracle cure – could be seen as very relevant for decisions about regulatory and funding approvals. The duty to protect seems particularly strong here as a foundation for various obligations. At the same time, the recent controversy can also be invoked to emphasize the responsibility of governments to fulfil the obligation to better coordinate drug approval and funding decisions and to avoid inordinate pressure on the coverage of a medicine when its merits have not been clearly established.

This report suggests that international human rights law creates a useful basis for the identification of specific obligations, responsibilities and potential contributions of governments, industry and other stakeholders in promoting access to high-priced, safe and effective medicines. However, it is important to recognize the limitations of human rights law. In addition to the challenges of enforcement, it is clear that international human rights

law, as developed through authoritative interpretations, finds more obvious applications in the global context of access to medicines, and when strong barriers prevent access to essential medicines, they often augment already existing inequities in access to health care. It is in this international context that specific initiatives have been undertaken that reflect efforts to promote human rights in relation to access to medicines – for example, through the development of the Access to Medicine Index.

Using a human rights framework in the context of high- and middle-income countries to explore obligations that ensure access to high-priced medicines is more complex, due in part to inherent issues of resource allocation and the broad sustainability of health systems. Essential medicines can be unavailable due to high prices; a human rights lens can provide a useful perspective for discussions in the European context. As noted above, the concept of essential medicines reflects the importance of a coherent and publicly accountable, evidence-informed drug policy. This report has provided examples of other issues that can be put forward as explicit key components of a human rights-based approach to the development, production and distribution of high-priced medicines, such as issues relating to transparency, access to data and discrimination. Framing access to medicine as a human rights issue does not provide an immediate solution to the challenges that all countries face in determining how to promote the development, production and distribution of health-care products, how to determine cost–effectiveness and fair pricing, how to determine who should have access to new products, and how to identify health-care priorities. But it does provide a framework for identifying immediate obligations, as well as key considerations and values that should guide decision-making with respect to access to medicines. It is worth emphasizing again that international human rights sources explicitly recognize – with reference to reasonableness and progressive realization – that these issues can only be addressed by taking into consideration the very specific societal context in which they arise.

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