

SYNTHESIS

COMPULSORY LICENCES FOR EXPENSIVE MEDICINES: LEGAL AND ECONOMIC CONSIDERATIONS



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■ FORWARD

The problem of expensive medicinal products has occupied us and various government agencies for quite some time now. We see an increase in the number of medicines with a very high cost per patient and wonder how sustainable this situation is in the long term if the trend continues.

Policy makers are constantly looking for measures to control spending on expensive drugs without compromising the quality of care. Although the Belgian Health Care Knowledge Centre (KCE) has evaluated several of these measures in the past, the pharmaceutical sector is constantly evolving, meaning that innovative policy tools have to be developed or new balances found to meet the specific challenges of new types of medicines and industrial strategies.

The Health and Equal Opportunities Committee within the House of Representatives asked the KCE to study the feasibility of a single policy instrument that is anchored in international and national law, specifically regarding compulsory licences. Although compulsory licences have been around for many years and have occasionally been used by low- and middle-income countries to give the local population access to certain medicines, the application of such licences remains limited due to high medicine prices, especially in high-income countries. From that standpoint, giving thought to implementing compulsory licences as a result of the exorbitant prices of medication can certainly be called innovative. Other countries are also currently exploring this approach.

The issue has been looked at from two angles: from a legal as well as an economic perspective. Both are essential for assessing feasibility and identifying possible obstacles to be overcome before the compulsory licensing mechanism can be implemented. The KCE therefore cooperated with two external teams. They each conducted a thorough analysis from their own perspective, legal and economic respectively, which allowed the KCE to formulate balanced recommendations. One of the interesting aspects of this cooperation was that experts from various backgrounds and disciplines worked closely together within the respective teams, with some researchers approaching the subject from the perspective of stimulating and supporting innovation, while others focused on the (health) policy perspective. This resulted in a report rich in content and with a nuanced conclusion that takes both angles into account.

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■ CORE MESSAGES

- There is worldwide concern about the availability and affordability of medicines. These concerns will increase further in the future, given the increasing personalisation of medicines, the complementarity of diagnostics and treatments, and the complexity of new medicines, including biologics.
- In the European Union, setting the price of a medicinal product is, in principle, the responsibility of each Member State individually. The Member States have a broad margin of discretion in this regard. However, this is not always a guarantee of controlling high medicine prices.
- The granting of compulsory licences by governments is presented as a potential legal instrument to bring expensive medicines onto the market at a lower price. However, this study shows that the substantive and procedural conditions for the granting of compulsory licences must be carefully assessed and optimised in order to make this mechanism suitable for achieving the desired result, i.e. ensuring access to and affordability of medicines.
- The pharmaceuticals sector is one of the largest, but also one of the most highly regulated in the world. In practice, developers of pharmaceuticals based on an inventive concept are granted exclusivity for marketing these products through patent law (20 years), possibly extended via supplementary protection certificates (5 years) and, in addition, through data and market exclusivity (8 +2+(1) years).
- However, compulsory licensing currently only has an impact on the protection of medicines against market competition via patent law, but not if the protection is based on data- and market exclusivity. This can only be solved by also putting provisions in place in the regulations related to the putting on the market of medicines for products under compulsory licence.
- Most compulsory medicine licences to date have been granted by authorities of developing countries and emerging economies. There are only a few recent examples of compulsory licences being granted for public health reasons in high-income countries. These examples were not necessarily related to high prices but, rather, to the unavailability of medicines in some countries.
- One of the main conclusions of this report is that compulsory licensing of expensive medicines can only be effective if the broader picture of medicine regulation and the institutional and administrative framework are taken into account.
- In addition, we must bear in mind that stimulating and rewarding innovation is one of the main purposes of patents, data and market exclusivity. Intervention in the protection mechanisms for medicines can have negative consequences for a small country like Belgium, which has an important presence of national and international pharmaceutical and biotechnology companies, in terms of investment in research and development, access for the population to local clinical studies, (high-tech) production capacity,



employment, development of knowledge and competences, competitive position, international trade relations, and so on.

- Finally, when granting a compulsory licence, possible practical problems related to production capacity, access to raw materials, the 'reasonable remuneration' to be paid to the patent holder, and so on, must be taken into account.
- Given the limited availability of comparable empirical data, it is extremely difficult to make reliable predictions about the consequences of compulsory licensing of expensive medicines in Belgium.
- If the government were to consider using compulsory licences, the procedures should be fine-tuned with the aim of creating transparency for all the parties involved. This is necessary in both policy and legal terms (patent law, data and market exclusivity, trade secrets, know-how, transparency, etc.), as well as in terms of practical implementation (methods to determine when a medicine is 'excessively' priced, what constitutes reasonable remuneration for the patent holder, etc.).
- In the first instance, however, a robust, transparent and coherent policy on prices and reimbursement of medicines (preferably coordinated with other EU countries such as in the BeNeLuxA initiative) should be elaborated. In addition, there are valuable alternative measures, including the application of competition law, promoting socially responsible licences for inventions emerging from public research institutions and university centres and elaborating the pharmacy exemption.



■ SYNTHESIS

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1. INTRODUCTION

1.1. Affordable innovation

1.1.1. *A dilemma?*

The rising prices of some medicines are putting pressure on healthcare budgets worldwide. Examples of this include orphan medicines, innovative cancer treatments and so-called ATMPs (Advanced Therapy Medicinal Products), including gene and cell therapy.

In practice, manufacturers of innovative medicines have an exclusive right to market their products for the duration of the patent that has been granted to them and for the period of data and market exclusivity after obtaining their marketing authorisation. This protects their product from market competition and allows them to largely determine the prices themselves. However, high prices are not only charged for innovative medicines for which there is no alternative. Older medicines with only few suppliers on the market (e.g. due to a small sales market) are often supplied at high prices.

One of the rationales for granting a patent and data and market exclusivity is, in general, to compensate innovators for their research and development costs and thus to promote innovation. Following expiry of the patent and the data and market exclusivity, others are allowed to imitate and sell the medicine, which usually reduces the price considerably. At the same time, the patent system ensures that research results are made known (on publication of the patent), which is also important for innovation.

Patent systems also contain various checks and balances (territorial and temporal restrictions, limits in terms of scope and area of application, exclusions, exceptions, exemptions from infringement, etc.). Compulsory licences are also part of these checks and balances.

Compulsory licences allow the government, in certain circumstances, to authorise a third party to manufacture a product or use a method covered by a patent without the consent of the patent holder (e.g. due to a national emergency, anti-competitive behaviour of the patent holder, public non-commercial use, etc.). In effect, a generic company can then imitate a medicine under patent in order to make it available at a lower price. The patent holder will receive compensation for this.

These checks and balances make it possible to strike a balance between the rights and interests of the inventors/applicants/owners on the one hand and, on the other hand, those of the users/licensees of the patented technology, as well as of the general public and key stakeholders. In the case of pharmaceuticals, these are patients, hospitals, healthcare providers and health insurance systems.

Governments are therefore often faced with a dilemma: i.e. it is important to continue to encourage innovation in healthcare while guaranteeing access to and affordability of medicines.

1.1.2. *Little transparency on pricing*

When setting their prices in a particular country, medicine manufacturers take account of several factors, including investment in research and development (including amortisation of the countless candidate medicines that perish in the course of the development process), production costs, selling costs, information and marketing costs, various distribution costs, pricing in other countries, profit margin, and so on.

However, it is increasingly suggested that the government has also made an important contribution to the development of medicines in some cases. It largely finances fundamental and strategic basic research at universities, hospitals and public research centres, who are often involved in the early (and costly) phases of development of new innovative medicines. Universities and research centres with little capacity for the later stages of development then often enter into licensing agreements with companies that can further develop their inventions until they are ready for marketing authorisation.



These circumstances can lead to the government paying twice for an innovative drug: first in early development and then in reimbursement.

Although preclinical and clinical studies and the marketing of medicines require high investment, there is often a suspicion that, in practice, medicine prices are much higher than the costs incurred by manufacturers. Moreover, pharmaceutical companies are not very transparent about their cost structure, profit margins, pricing policy or the risk/profit ratio.^{a b}

1.2. Framework Study on Compulsory Licensing

1.2.1. *A complex legal framework*

The call for a reform of medicine prices is growing louder. However, the government has various options for controlling the prices of medicines (price negotiations, competition rules, etc.), using these with varying degrees of success. In this KCE report, we focus on compulsory licences, an existing instrument that the government can also use for very expensive medicines subject to patents, with the aim of obtaining a lower price and thus to wider accessibility for patients.

Patents are covered by various international treaties (see Box 1). These are the Agreement on Trade-Related Aspects of Intellectual Property Rights (TRIPs Agreement) at World Trade Organisation level, the European Patent Convention and the Paris Convention. However, patents are enforced at the national level. In practice, a patent in Europe (pending the introduction of the European patent with unitary effect) has to be confirmed by each Member State and infringements brought before a national court. The possibility to grant compulsory licences to a third party is enshrined in international law, but they are implemented at national level. However, the granting of a

compulsory licence in the event of excessive pricing is not provided for in literal terms in international regulations, though it is in some national laws.

This study shows that, to date, no high-income country has issued compulsory licences to counter the excessive price of a medicine, with the exception of Canada several decades ago (see 3.3.1). However, the Canadian context at the time is difficult to compare with the current situation in the European Union or Belgium.

Nevertheless, Belgium can today also grant compulsory licences for patented medicines 'in the interest of public health', as stipulated in the Code of Economic Law. This could be the case, for example, in an epidemic when patent holders of essential, patented medical products are unable to manufacture and supply them in sufficient quantities.

This was the case, for example, with the recent COVID-19 pandemic. During that period, the public and political focus on the role of patent law in the pharmaceutical sector breathed new life into the turbulent debate. At national level, a large number of countries have adopted new compulsory licensing rules to meet the dire need for diagnostic kits, medical masks, protective equipment, respirators, vaccines and medicines for the prevention and treatment of patients in emergency situations.

The debate on this has reflected the many divergent views on the impact that restrictions on exclusive patent rights can have on promoting innovation vis-à-vis the availability of essential medical products for public health.

Moreover, this crisis showed how complex the pharmaceutical and biotech markets are and how strong competition is between them. Despite significant government funding, negotiating contract clauses to secure the availability and affordability of vaccines, medicines and diagnostics has been extremely difficult, even at European level. In addition, the COVID-19 crisis has also exposed the shortcomings of current compulsory licensing

^a Kok L, van der Voort J, Berden C, van Buiren K, Gerritsen M. De farmaceutische industrie in het maatschappelijk debat (The Pharmaceutical Industry in the Social Debate). SEO – Economic research. 2014. <https://www.seo.nl/publicaties/de-farmaceutische-industrie-in-het-maatschappelijk-debat/>

^b Vandenbroeck Ph, Raeymakers P, Wickert R, Becher K, Goossens J, Cleemput I, Hulstaert F, de Heij L, Mertens R. Future scenarios about medicine development and drug pricing. Health Services Research (HSR) Brussels: Belgian Health Care Knowledge Centre (KCE). 2016. KCE Reports 271. D/2016/10.273/59.



mechanisms in terms of speed and feasibility of application in medical emergencies.

Furthermore, we must take into account that other, equally complex legal frameworks also apply to medicines, which also have an important impact on the effectiveness of compulsory licences. These include, for example, the regulatory framework for the marketing of medicines, including data and market exclusivity (see Box 2), the regulation of trade secrets and know-how, as well as the regulation of anti-competitive behaviour. Without examining each of these mechanisms in detail, the extensive scientific report describes their association with compulsory licensing.

1.2.2. Economic and health policy implications

There are also downsides to the use of compulsory licences. Compulsory licences can have negative consequences for the innovation and business climate. Companies may decide to reduce their investment in research and development and/or their other business activities. This not only has an economic impact but can also lead to innovative medicines becoming less readily available to patients in Belgium in the long run.

In addition, it should be borne in mind that the reproduction of medicinal products is not an easy task, even when licensed in relation to the relevant patents. This certainly applies to biotechnological medicines and advanced therapies. Production processes (or the optimal versions thereof) are sometimes partly secret (know-how) and it is not always easy for third parties and/or governments to set up such processes, partly in view of the high quality requirements set for pharmaceuticals.

This makes governments more reluctant to impose compulsory licences. To date, they have mainly been used in low-income countries, as leverage in negotiations or as a last resort. In the recent past, hardly any compulsory licences have been imposed in high-income countries because of high medicine prices. Nevertheless, a lot more attention is now being paid to the use of this instrument, not only in Belgium, but also in other high-income countries.

1.2.3. Answers in this KCE study

In this context, the Federal Commission for Health and Equality of Opportunities submitted a research proposal to the KCE to investigate the compulsory licensing mechanism for situations where manufacturers charge very high prices for essential medicines.

This report provides greater insight into the possibilities and anticipated impact of compulsory licensing for expensive medicines in general. In addition, the feasibility and desirability of such compulsory licences in Belgium was also examined.

For this purpose,

- the international, European and Belgian legal frameworks surrounding patents and compulsory licences were analysed, as was the relevant case law;
- the barriers to the introduction of compulsory licensing were clarified and it was examined how these barriers can be tackled;
- the possible (economic) consequences of compulsory licences for the pharmaceutical market were examined by way of a literature review;
- an assessment was made of the proportionality of the instrument and how to select medicines that can be subject to compulsory licensing;
- the pros and cons of compulsory licences were weighed up in terms of public health and the economic climate in Belgium.

The results of the literature review were supplemented with insights from a stakeholder workshop with an international group of participants from the pharmaceutical industry, academia, non-governmental organisations and government institutions (see colophon).



1.2.4. What is not covered in this report?

This KCE report is not concerned with compulsory licensing in emergency situations, such as during the COVID-19 pandemic (see 1.2.1) but, rather, with the possibilities of using compulsory licensing for very expensive medicines. The extensive scientific report does include an overview (Annex 2 of the legal part) of countries that have taken specific measures in the area of compulsory licences in the context of the COVID-19 pandemic. However, that overview has not been included in this summary.

Nor is the focus and scope of this study concentrated on the factors and calculation methods used by pharmaceutical companies to arrive at a price proposal for their medicines.

This report also did not define when a price should be considered "excessive", but referred to methods and elements considered in case law and theoretical economic models. The term "excessive" is used in this report in a broad sense and not in the sense of competition law.

2. PROTECTION OF MEDICINES IN PRACTICE

The pharmaceuticals sector is one of the largest, but also one of the most highly regulated in the world. The industry deals with many areas of law, such as intellectual property rights (patents), trade secrets, competition law, internal market law (free movement), human rights, data protection, as well as research and development (R&D) regulations.

To understand the possibilities, but also the limitations, of compulsory licensing for expensive medicines, it is important to understand the economic and legal framework on the basis of which innovative medicines can temporarily enjoy exclusivity. There are three important elements to this: protection via a basic patent (Box 1 and Figure 1), the strategies with which pharmaceutical companies try to optimise the protection of their medicines (), other legal protection mechanisms including data and market exclusivity (Part 2.2 and Figure 1).

2.1. Protection through patents

2.1.1. No pharmaceutical innovation without protection?

Patents are generally regarded as one of the most important, or possibly the most important pillar on which the pharmaceutical and biotech industry is founded (see also Box 1).



Box 1 – Properties and characteristics of patents

Paris Convention, TRIPS Agreement, Doha Declaration and European Patent Convention

There are a number of international treaties in the field of intellectual property: the Paris Convention for the Protection of Industrial Property (1883)^c and the Agreement on Trade-Related Aspects of Intellectual Property Rights (TRIPS)^d (1994) of the World Trade Organisation (WTO). Linked to this is the Doha Declaration^e which frames the TRIPS Agreement in the context of public health (2001). At European level, there is the European Patent Convention^f.

The TRIPS Agreement stipulates that the holder of a patent has the exclusive right for a maximum period of 20 years to prevent a third party from producing, using, offering for sale, selling or importing the patented invention without the consent of the patent holder.

Only after the protection period has expired may other parties apply for marketing authorisation. In the pharmaceutical sector, we then speak of generic medicines and/or biosimilars.^g

Also for pharmaceutical and biotechnological products

Historically, many countries excluded pharmaceutical products from patentability to ensure access to and the affordability of medicines. However, the exclusion of a 'defined technology area' is no longer

possible for member states of the World Trade Organisation under the TRIPS Agreement.

Based on Article 27 of TRIPS, adopted by Article 52 of the European Patent Convention, patents are granted for **all inventions, in all fields of technology, provided they are new, inventive (i.e. involve an inventive step), are capable of industrial application and are permissible**. Patent applications must also give a clear and full description of the invention. An expert must be able to replicate the invention on the basis of the patent application. This means that a detailed description must be given of at least one way of repeating the invention.

No patentability of discoveries and theories as such

No patents are granted for "discoveries" or "scientific theories" as such, as they are not considered to be inventions. In addition, the application must describe an industrial (read 'specific') application. This additional requirement is important to establish a 'minimum' criterion for medical-biotechnological inventions. These are often based in components in the animal or human body, such as DNA, proteins, cells or tissues. Contrary to some other jurisdictions, isolated biological components are patentable under European patent law, provided that the application describes a specific use.

^c Paris Convention for the Protection of Industrial Property (1883) <https://wipolex.wipo.int/en/treaties/textdetails/12633>.

^d TRIPS - Agreement on Trade-Related Aspects of Intellectual Property Rights, Annex 1C World Trade Agreement, 1994, https://www.wto.org/english/docs_e/legal_e/27-trips.pdf.

^e WTO Doha Ministerial Declaration on the TRIPS Agreement and Public Health 2001; J. Reichman (2009), 'Compulsory Licensing of Patented Pharmaceutical Inventions: Evaluating the Options', 37 Journal of Law, Medicine and Ethics, 247-263, https://scholarship.law.duke.edu/faculty_scholarship/2126.

^f Convention on the Grant of European Patents (European Patent Convention), 17th Edition, November 2020, available at <https://www.epo.org/law-practice/legal-texts/epc.html>.

^g A biosimilar medicine or 'biosimilar' is developed in such a way that it is highly equivalent in terms of quality, safety, efficacy and biological activity to an existing biological medicine already authorised in the European Economic Area (EEA). This means that it contains essentially the same active ingredient, although there may be minor differences between the two medicines. These minor differences can be attributed to the complexity and variability of the active ingredients, and to the complexity of the manufacturing processes used.

**No automatic right to production and sale**

Patents confer a negative exclusive right and not a positive right to produce or sell. A patent implies that the patent holder may prohibit someone else from copying or exploiting the patented invention. In order to place a medicine on the market, the manufacturer still needs to obtain a marketing authorisation (see 2.2.). Moreover, it is also possible that the patent holder may not be able to apply the invention on account of other parties enjoying patent rights concerning certain aspects of the invention.

Territorial restrictions

Patent rights are territorial rights: to obtain patent protection, patent applications must be filed in each country/region where patent protection for the invention is sought, in accordance with the law of that country or region.

In Europe, patent protection can be applied for in any Member State, in accordance with national patent laws or at European level through the harmonised granting procedure practised by the European Patent Office. However, once the patent has been granted, it must be confirmed in all Member States in which the patent holder wishes to protect the invention.

This entails significant costs. In addition, patent holders must assert their rights against any infringing party in a national court on the basis of national patent law. In practice, this leads to parallel lawsuits in different EU Member States and possibly different rulings on the validity of a patent and infringement of the same. It is clear that such a variety of decisions can lead to legal uncertainty.

Towards a European unitary patent?

The EU has been trying for decades to establish an EU patent and centralised jurisdiction. An EU patent is a unitary patent title aimed at providing uniform protection in all the participating Member States. In 2012, these efforts resulted in the adoption of the Unitary Patent Package (UPP)^h.

The UPP provides a legal basis for the creation of European "unitary patents" and for the establishment of a Unified Patent Court (UPC), a centralised and specialised judicial system.

Neither the UPP nor the UPC has entered into force as yet on account of the ratification process being repeatedly delayed. The final preparations are being made in the meantime, with the result that it is expected to be operational at the end of 2022 – early 2023.

Supplementary Protection Certificate (SPC)

Before a new medicine can be brought onto the market in accordance with the relevant regulations, it often undergoes a long period of testing and clinical studies. This can lead to the loss of several years of valuable patent protection. To compensate for this, the patent holder can obtain a protection certificate (SPC – Supplementary Protection Certificate) that offers additional protection for a maximum of five years for the specific product that is being brought onto the market.

An additional extension of six months is possible for medicines intended for children.

Supplementary protection certificates are awarded and managed at national level.

^h The Unitary Patent Package comprises the following three instruments: Regulation (EU) No 1257/2012 of the European Parliament and of the Council of 17 December 2012 implementing enhanced cooperation in the area of the creation of unitary patent protection, [2012] OJ L 361, p. 1–8; Council Regulation (EU) No 1260/2012 of 17 December 2012 implementing

enhanced cooperation in the area of the creation of unitary patent protection with regard to the applicable translation arrangements, [2012] OJ L 361, p. 89–92 and the Agreement on a Unified Patent Court, [2013] OJ C 175, p. 1–40.



It is generally accepted that it is essential to stimulate investment in pharmaceutically oriented research, given the high costs involved in preclinical and clinical research.

An additional argument for defending patents is that they promote the dissemination of knowledge: when the patent is published, others can learn about the invention, the underlying technology and the scientific insights on which the invention is based.

According to multiple authors, carefully defined patent rights, supported by a stable and effective patent management system, encourage innovation ecosystems to thrive and facilitate collaboration. The latter is also important because of the increasing complexity of research and development in the biomedical and pharmaceutical sector.

2.1.2. Incremental patents

The pharmaceutical industry has a particular interest in extending the protection (also called 'evergreening') of so-called 'blockbuster' medicines. These are medicines with annual revenues in excess of US\$1 billion. When the patents for such a medicine have expired, revenues fall due to the introduction of generic competitors onto the market (the 'patent cliff').

One of the strategies to extend protection for these medicines is to apply for patents for 'further medical use', sometimes referred to by critics as 'incremental' patents. After all, the European Patent Convention allows not only the composition or the production process of a medicinal product to be protected, but also a specific therapeutic use of the same.

This creates an opening for the patenting of medicines already known for 'another therapeutic use', provided that such use is new and inventive (i.e. that it is based on an inventive step – see Box 1). In specific terms, the producer can also apply for an additional patent for use of the same active ingredient for the same disease, but then with a different therapeutic

method: e.g. adjustment of the dosage, method of administration, route of administration or target group, if this meets the requirements of constituting an inventive step.

It is therefore common practice for a pharmaceutical company to file an initial patent application when a class of compounds with a particular activity has been identified and to submit new applications at a later stage in the research and development process. For example, when the compound with the strongest activity has been identified, the optimal form of administration, the optimal dosage, and so on.

As a result, the final product may be covered by different patents with different expiry dates. In this example, although these different patents will be owned by the same company, it is also possible that different organisations hold relevant patents, leading to considerable fragmentation of patent rights.

2.1.3. Repurposing existing medicines

Patents for further medical use may also be relevant for what is known as the 'repurposing' of existing medicines.

It can be faster and cheaper to develop a medicine for a new application if it is already known that the medicine is well tolerated by the human body. However, the new use must be demonstrated successfully in clinical studies before the European or national authorities grant a marketing authorisation for the medicine for that specific indication.

Empirical research shows a significant upward trendⁱ over the past ten years (since 2010) for patents with repurposing claims.

ⁱ A. Breckenridge & R. Jacob (2019), 'Overcoming the legal and regulatory barriers to drug repurposing', 18(1) *Nat. Rev. Drug Discov.*, 1–2. M. Aboy et al. (2021), 'Mapping the European patent landscape for medical uses of known products', 39 *Nature Biotechnology*, p. 1336.



2.1.4. 'Me-too medicines'

Another common practice is the so-called "follow-on" or "me too" strategy. This is the development of similar medicines with the same biological mechanism but based on a different compound that has not yet been patented. New patents can then be requested for these new compounds if their structure is deemed inventive.

While the inventive contribution of this type of product (and the fairness of a new term of exclusivity) is questioned, it could nevertheless bring more competitive products onto the market.

2.1.5. A fragmented patent landscape

In certain cases, the strategy of applying for multiple patents relating to the same product and/or possibly successive improvements by other parties, can lead to what are referred to as 'patent clusters' or 'patent thickets'. They create a complex set of overlapping patent rights.

Research by the European Commission^j shows that some individual medicines are protected by dozens of product-specific patent families. Taken together across the different EU Member States, this can lead to more than 1,300 patents and/or pending patent applications for a single product.

A company that wants to enter this market as a competitor must take this complex landscape of patents into account. Patent clusters not only create uncertainty but can also be an effective deterrent to potential competitors. The European Commission has expressed concern about these strategies in its sector inquiry.

2.1.6. Exceptions to patent protection

Under the TRIPS Agreement, countries can grant exceptions to the exclusive rights conferred by a patent. These exceptions must not unreasonably conflict with normal exploitation of the patent and must not prejudice the legitimate interests of the patent holder, taking into account the legitimate interests of third parties.

The following specific exceptions to patent law are important in the context of pharmaceuticals:

- **The Bolar exception:** In order to be able to market a generic medicine or biosimilar shortly after the patent has expired, conducting research before the patent expires is permitted. This includes medical tests that are necessary to demonstrate the safety and efficacy of the generic medicine, which is necessary for market authorisation.
- **Research exceptions:** Permission should not be sought for the use of a patented invention when it is for scientific purposes. To date, in Belgium, an invention may therefore be freely used to conduct research on the invention itself, or to use the invention as a research instrument to advance scientific research. With the introduction of the European unitary patent (see Box 1), this exception will be limited to research on the invention itself.
- **Exception for pharmaceutical compounding:** The patent holder cannot oppose the preparation of the patented medicinal product in pharmacies, including hospital pharmacies. The condition is that this preparation is for individual use on the basis of a medical prescription. A complicating factor can be access to ingredients and/or the complexity of the preparation.

Together with compulsory licences, these exemptions form an important element of *checks and balances* within the patent system. A proposal to

^j European Commission, Pharmaceutical Sector Inquiry - Final Report, https://ec.europa.eu/competition/sectors/pharmaceuticals/inquiry/staff_working_paper_part1.pdf.



strengthen the compulsory licensing mechanism must therefore also take account of the scope, interpretation and use of these exemptions in Belgium.

2.2. Additional protection

Due to the long development phase of some innovative medicines, the remaining validity of a patent can be very limited when the product comes on the market.

Moreover, many steps in the innovation process cannot be patented or are declared invalid in patent disputes because they are not considered to fulfil the requirements for patentability (including the “inventive” character).

This is one of the reasons why European and Belgian regulations provide for various forms of additional protection that are either implicitly accepted or explicitly included in the TRIPS and other international treaties and regulations.

This includes among others data and market exclusivity (see Box 2), trade secrets, data protection, copyright protections, and so on. A government considering compulsory licensing for expensive medicines also needs to take these protection mechanisms into account.

An extensive discussion of the additional forms of medicine protection was included in chapter 4 of the scientific report. In this summary, we confine ourselves to a brief overview of data- and market exclusivity and trade secrets, including know-how.

2.2.1. The background of exclusivity rules

An innovation system that does not recognise and reward the risks and significant investment of preclinical and clinical studies would jeopardise the incentives to invent and develop innovative products. Such a risk is particularly high if the underlying technology is not patentable, or if the underlying patents are either too limited and susceptible to invalidity attacks, or if they are granted at the very early stages of the investigation and are due to expire before marketing authorisations are granted.

That is why the European Union grants data and market exclusivity to the manufacturer for medicinal products when awarding a marketing authorisation (see Box 2). Such data and market exclusivity is particularly interesting for pharmaceutical companies when there is no protection provided by patents or SPCs or when this protection is weak. This may concern situations in which the technology is predictable or where the core of the invention is focused on natural phenomena or data. It may also concern cases where patent protection is very narrow or conditional. Examples of this are new formulations, physical form, synthetic process or a new medical use of a known compound (see 2.1.2).

In principle^k, the EU framework does not provide for any exceptions to data and market exclusivity for medicinal products produced under compulsory licence. This has to be taken into serious account by a government that wants to grant compulsory licences for medicines as well as by the holder of the compulsory licence (see 4.2.1).

^k Currently, European countries only accept exemptions from these exclusivity provisions in the case of exports to countries with public health problems.

**Box 2 – Data and market exclusivity: the 8+2+1 rule^{1 m}****Eight-year exclusivity on data**

Collecting preclinical and clinical data necessary to obtain a marketing authorisation for a new medicine takes time and requires major investment. That is why Art. 39 of the TRIPS Agreement stipulates that the data required to obtain a marketing authorisation is protected against unauthorised use by third parties and is contrary to fair trade practices.

One way to ensure this protection is to grant exclusivity to data. In practice, this means that, for a period of eight years, only the manufacturer who generated the data can avail itself of the data or refer to them. Data exclusivity is separate from the patent and starts, in contrast to the patent, automatically from the granting of the marketing authorisation for the medicinal product in question.

Once this protection period has expired, manufacturers of generics or biosimilars can avail themselves of the test data submitted originally in order to demonstrate that their medicine is 'equivalent' to the medicine originally authorised.

It is true that producers of generics or biosimilars are able to submit an application for a marketing authorisation at an earlier stage based on test data that they generate themselves. However, conducting clinical trials entails significant costs and, moreover, repeatedly conducting clinical trials for the same medicinal product also raises ethical questions.

Two-year market exclusivity

When the period of data exclusivity has ended, the patent holder also enjoys two additional years of market exclusivity (the 8+2 rule) before a third party can place a generic medicine on the market. During these two years, the producer of a generic medicine or biosimilar may use the existing test data to prepare and facilitate the marketing authorisation to be granted. In this way, the medicine or biosimilar can be placed on the market shortly after the end of the market exclusivity.

An extra year of protection is sometimes possible, e.g. in the case of a new indication for an existing medicine, provided additional clinical data is submitted (8+2+1).

Data and market exclusivity are, in principle, independent of the duration of any patent. Under current EU regulations, the exclusivity can extend beyond the expiry of the relevant patents.

Specific exclusivities for orphan drugs and medicines for paediatric use^{n o}

Orphan drugs are given ten years of market exclusivity from the date of the marketing authorisation (with a possible extension of 2 years for paediatric use). This exclusivity effectively and completely prevents generic competition. The underlying idea is that orphan medicines need specific and predictable protection. The potentially small market for these products requires legal certainty and attractive incentives. Without these incentives, companies would not be interested in developing innovative medicines for such patients.

¹ Directive 2001/83/EC of the European Parliament and of the Council of 6 November 2001 on the Community code relating to medicinal products for human use, [2004] OJ L 311, 67-128.

^m Regulation (EC) No. 726/2004 of the European Parliament and of the Council of 31 March 2004 laying down Community procedures for the authorisation and supervision of medicinal products for human and veterinary use and establishing a European Medicines Agency, [2004] OJ L 136, 1-33.

ⁿ Regulation (EC) No. 1901/2006 of the European Parliament and of the Council of 12 December 2006 on medicinal products for paediatric use and amending Regulation (EEC) No 1768/92, Directive 2001/20/EC, Directive 2001/83/EC and Regulation (EC) No 726/2004, [2006] OJ L 378, 1-19.

^o Regulation (EC) No. 141/2000 of the European Parliament and of the Council of 16 December 1999 on orphan medicinal products, [2000] OJ L 18, 1-5.



On the other hand, such exclusivity can lead to abuse if the system is not carefully designed and applied. An overly protective system of data and/or market exclusivity can become a major risk factor for unjustified distortions of competition, excessively long extensions of monopoly rights, disproportionate medicine pricing and access to healthcare.

Some authors emphasise the risks and potential additional costs for patients and society^P in terms of the exclusivity allowing innovators to charge consumers 'monopoly prices', as well as rewarding 'low-innovation' output in a way that is inconsistent with its public-health value. As a market-driven incentive, there is a risk of data and market exclusivity encouraging investment in 'me-too' products and discouraging investment in truly innovative products for less lucrative conditions.

2.2.2. *Know-how and trade secrets*

Know-how is confidential business information resulting from research or experience that gives a company a competitive advantage and is kept secret from others. Know-how may include technical information such as manufacturing process information, clinical trial data, formulas and recipes. This information can be recorded in any form or even be kept solely in the memory of an inventor or employee.

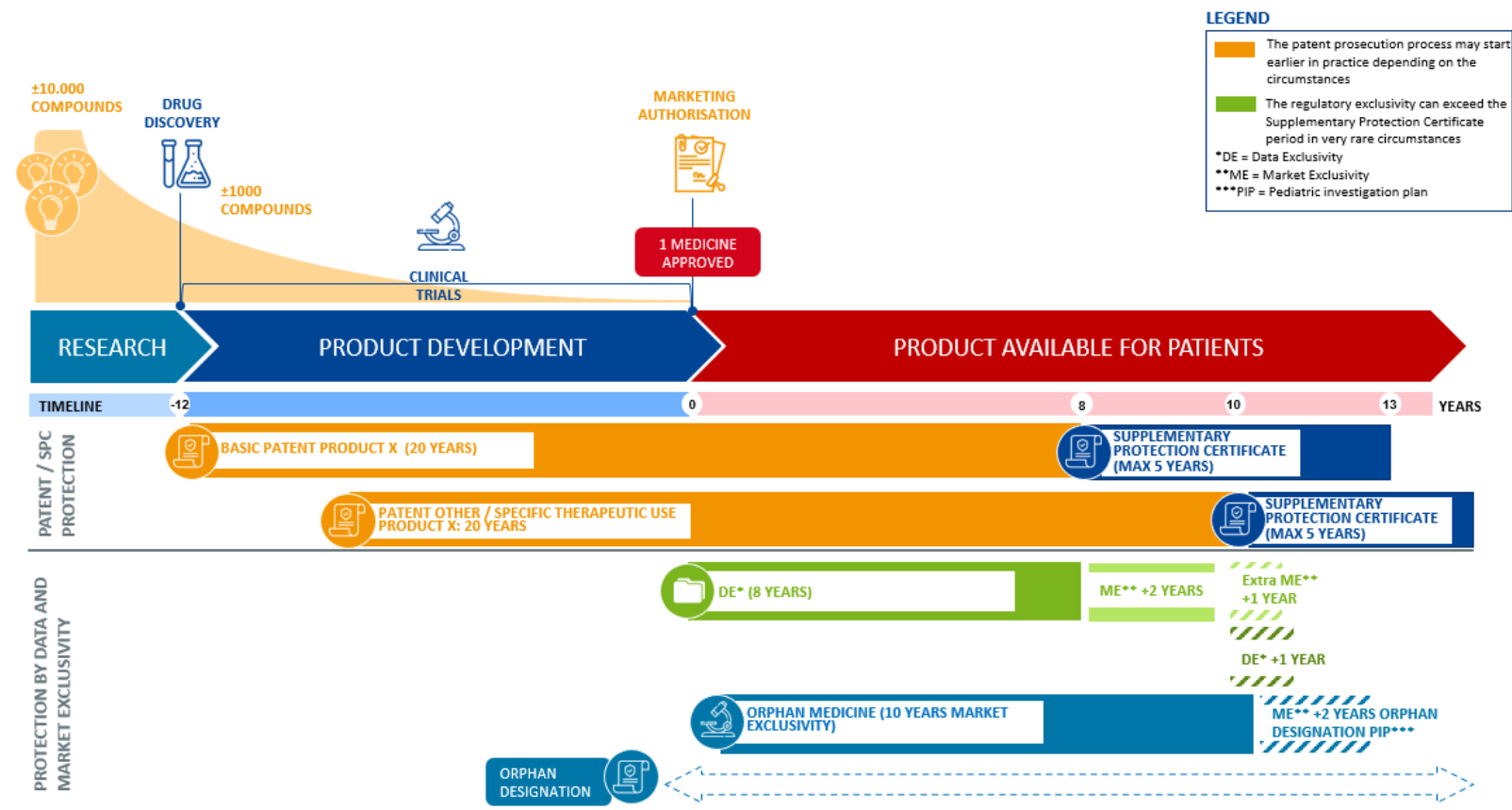
Trade secrets can consist of know-how as well as commercial information, such as distribution methods, lists of suppliers and customers, advertising strategies and financial information. All this information can be protected as a trade secret in the European Union^Q. To be considered a trade secret, the information must, in accordance with:

- be commercially valuable on account of its being secret;
- only be known to a limited group of people;
- be subject to reasonable measures taken by the rightful holder of the information to keep it confidential. Examples of such measures include non-disclosure agreements for business partners and employees.

Know-how and other trade secrets can also hinder the effective use of compulsory licenses as they can complicate the optimal production of replacement generic medicines or biosimilars.

^P S. Sorscher (2009), 'A longer Monopoly for Biologics?: Considering the Implications of Data Exclusivity as a Tool for Innovation Policy', 23 *Harvard J. L. & Tech.*, at 285-87,

^Q Directive (EU) 2016/943 of the European Parliament and of the Council of 8 June 2016 on the protection of undisclosed knowhow and business information (trade secrets) against their unlawful acquisition, use and disclosure, [2016], OJ L 157, 1–18.

Figure 1 – Patents and data and market exclusivity^r

^r This figure is based on an existing figure of the European Federation of Pharmaceutical Industries and Associations: <https://www.efpia.eu/about-medicines/development-of-medicines/intellectual-property/>



3. A CLOSER LOOK AT COMPULSORY LICENCES

3.1. International legal frameworks for compulsory licensing

The basic assumption is that patent holders are in principle free to decide whether they wish to exploit their invention themselves or license it to third parties for further exploitation. In the case of a compulsory licence, the government or a court (depending on the structure of the legal system in a particular country) can also force a patent holder to license the rights.

3.1.1. *International legal bases for compulsory licences – autonomy of the Member States*

Several legal bases are included in the texts of the Paris Agreement and in the TRIPS Agreement (see **Box 3**) on the basis of which the rights to a patented product or to a process can be used by the government or by third parties without the permission of the patent holder. These legal bases are as follows:

- **Medical emergency and/or extreme urgency.** Each member country of the World Trade Organisation has the right to determine for itself what a medical emergency is and does not have to negotiate with the patent holder beforehand. In principle, overpricing by a patent holder could be regarded as a medical emergency or situation of extreme urgency, but this has never been applied in high-income countries. There is therefore no case law on this.
- **Public non-commercial use.** Governments are permitted to authorise a government agency or a contractor to use a patented invention for non-commercial purposes (sometimes referred to as '**government use**'). In many cases, this is the easiest way to meet an urgent public need. The government can decide on this ex officio without having to ask a third party and without having to negotiate with the patent holder first.
- **Dependence on other patents:** When a patented product cannot be commercialised without recourse to another, initially patented invention. It may concern improvements to products whose initial product represented significant technical progress, but which are blocked by this patent holder. This ground is quite important for promoting access to patented inventions that represent important technical progress of considerable economic significance. It shows that compulsory licences can be granted for reasons related to economic considerations, although prior negotiation with the patent holder is required.
- **Public interest/Public health.** In many countries, compulsory licences exist for reasons of public interest or public health. This ground is also explicitly confirmed in the Doha Declaration. The use of this legal basis for compulsory licensing could in principle be justified in the case of excessive prices, given that high prices put pressure on healthcare budgets and, by extension, public finances. Negotiations will have to be conducted with the patent holder prior to the compulsory licence.
- **Abuse** Measures may be necessary to prevent the misuse of intellectual property rights by the patent holders in order to rule out practices that unreasonably restrict trade or adversely affect the international transfer of technology. This legal basis may also be relevant for compulsory licences in the case of high prices. High pricing can be regarded as 'abuse' in terms of both competition law and patent law. Based on this legal ground, no prior negotiation with the patent holder is required.
- **Non-exploitation/insufficient exploitation.** 'Failure to work' and 'faute d'exploitation' are the official terms in the Paris Convention that refer to the situation in which an invention is not (sufficiently) exploited by the patent holder. The *failure to work* legal basis will most likely be of limited use in dealing with cases of high pricing by patent holders. High pricing implies by definition that 'the patented invention is in operation and being exploited'.



Article 31 of the TRIPS Agreement allows Member States to determine the legal bases for the granting of compulsory licences themselves. In principle, this gives Belgium (and other member countries) the freedom, e.g. in the context of public health, to introduce a specific compulsory licence in the case of high prices for medicines under patent, provided that the mechanism meets the conditions and restrictions of the TRIPS Agreement (see Box 3).

Box 3 – International agreements on compulsory licences

Agreements have been reached in various international treaties concerning the use of compulsory licences. Belgium is also required to adhere to these agreements. We present a brief overview here:

The Paris Convention stipulates that every country has the right to initiate legal measures to issue compulsory licences, e.g. on the basis of 'non-exploitation or insufficient exploitation'. In order to give patent holders the opportunity to exploit their patent, a compulsory licence based on this ground may not be granted within four years of filing the patent or three years of the patent being granted.

Article 31 of the TRIPS Agreement refers to 'other uses without the consent of the patent holder'. The article contains a range of legal bases for Member States to grant such use (see also 3.1.1) as well as a detailed set of conditions and limitations. These conditions state, among other things, that the granting of such 'other use without permission' must be assessed on a case-by-case basis. In addition, appropriate remuneration must be paid to the patent holder, with such use without authorisation being of limited duration and an export restriction imposed on the products manufactured.

An overview and detailed discussion of these conditions are included in Section 5.2.1.2. of the comprehensive scientific report but have not been included in this summary.

The **Doha Declaration** recognised that the TRIPS Agreement could create significant obstacles to the effective use of compulsory licensing for the purpose of guaranteeing access to medicines. One of the problems in the TRIPS conditions is that the use of compulsory licences is authorised predominantly for the supply of the domestic market. This

poses a problem for countries with no or limited pharmaceutical production capacity. This difficulty was solved by means of a protocol amending the TRIPS Agreement that does allow the import of medicines under compulsory licence. It is the only amendment to the TRIPS Agreement since the 1990s and aims to facilitate access to medicines in developing countries.

While the compulsory licensing system and the amendment by the Doha Declaration are open to all WTO members, many high-income countries, including the EU and its Member States, have agreed not to use the mechanism (preferring to opt out) and therefore not to import generic medicines produced under compulsory licence for their own supply of medicines or to export compulsory licensed generics to other high-income countries. After all, the amendment was intended to support access to medicines in developing countries.

3.1.2. Reasonable remuneration for the patent holder

One of the most important conditions in Article 31 of the TRIPS Agreement is the allocation of 'adequate' remuneration to the patent holder when a compulsory licence is granted. The interpretation of what is 'adequate' and the procedure for determining the remuneration are left to national law. The term 'adequate' was a proposal by the United States that was preferred to the term 'fair and equitable' endorsed by other countries. This part was one of the most controversial and ambiguous parts of the TRIPS Agreement.

Determining the remuneration for the patent holder is very difficult in practice. On the one hand, there must continue to be a price advantage for the generic medicine and, on the other hand, the remuneration for the patent holder must also be 'reasonable'. The 'economic value' of the patent is likely to depend on the degree of inventiveness (this is higher for a pioneer patent, for example), the scope of the patent, the size of the market, the maturity of the technology, its relevance, the degree of competition from replacement technologies, the revenue that can be generated by the licensee, and so on.

There is currently no common method of determining what constitutes adequate or reasonable compensation. There are guidelines from the World



Health Organisation (WHO)^s specifying different methods. However, these estimation methods are primarily intended for low-income countries and are less specific for high-income countries, such as Belgium.

Inspiration can also be drawn from (scarce) case law where compulsory licences were imposed in high-income countries. In the case *MSD v Shionogi* in Germany (see 3.3.3), the Bundespatentgericht (Federal Patent Court)^t ruled that the specific context of the case must be taken into account when determining the royalty. In this case, the judge made reference to the deterrent effect of the patent, the contribution of the patent to the development of the substance in question and the extent to which further development was necessary. The amount of the licence fee was then determined by means of an estimate. A rate of 4% of the net sale price of the product was established. However, it must be taken into account that the ground for granting a compulsory licence in this case was based on the public interest and not on high pricing. In addition, the patent holder did not exploit the patent, which is different from the situation in which a compulsory licence is considered due to the high price of a developed medicine that the manufacturer actually wants to bring onto the market.

It is clear that there are many practical difficulties involved in determining reasonable compensation for the patent holder. After all, this requires access to data on direct and indirect costs, as well as on reasonable returns and profit percentages for the patent holder. This again demonstrates the importance of transparency.

3.2. Belgian legal bases and conditions for compulsory licences

3.2.1. Code of economic law

Belgium recognises the agreements concluded in the Treaty of Paris. In addition, as a member of the World Trade Organisation, it is bound by what the TRIPS Agreement and the Doha Declaration stipulate with regard to compulsory licensing of patented inventions and technologies (see Box 3).

The Belgian legislator has so far provided for different legal grounds for granting compulsory licences in specific circumstances. For example, the Minister of Economic Affairs can grant a compulsory licence if the patent holder does not exploit or insufficiently exploits the patented invention (Art. XI.37§1(1°) Code of Economic Law), but also if the patent is dependent on other patents.

In 2005, an additional legal basis was created for the granting of a compulsory licence for 'public health reasons'. This legal basis was established following the implementation of the EU Biotechnology Directive. Article XI.38 of the Code of Economic Law stipulates that a compulsory licence may be granted for:

- medicines, medical devices, diagnostic products or derivative or combinable therapeutic products;
- a method or product relevant to the production of one or more of the foregoing products;
- diagnostic methods outside the human or animal body.

The applicant for the compulsory licence must prove that he/she/it has the resources necessary for the substantial and continuous manufacture and/or application of the patented invention in Belgium.

^s WHO/TCM/2005.1, available at https://www.who.int/hiv/amds/WHOTCM2005.1_OMS.pdf.

^t Federal Patent Court, Case No. 3 Li 1/16, Judgement 21 November 2017, ECLI:DE:BPatG:2017:211117U3LI1.16EP.0 (2018) 120 GRUR, 803.



The patent holder remains the owner of the patent and can still grant a licence to other parties. In addition, restrictions may be imposed on the scope and duration of the compulsory licence. Interestingly, the procedure for applying for this compulsory licence differs from the previous procedure in the Code of Economic Law: a compulsory licence for 'reasons of public health' is granted by the 'Crown' and not by the Minister of Economic Affairs. Moreover, the compulsory licence is granted on the advice of the Advisory Committee on Bioethics and not of the Compulsory Licensing Committee. Finally, there is no express condition that negotiations must have failed before a compulsory licence can be granted.

There are no known cases so far in which compulsory licences have been granted in Belgium on the basis of this procedure.

3.2.2. Proposal to amend the law

At the end of August 2019, a bill^u was submitted to amend the Code of Economic Law with regard to the application of compulsory licences to medicines. The petitioners argue that *'in order to protect public health and the financial capacity of the social security and health insurance system, a proposal is made to extend the pre-existing compulsory licensing system. The Minister of Health will henceforth be able to impose compulsory licences for a medicine on his own initiative, including where there are serious indications that the sales prices applied are disproportionate in relation to the production costs.'*

The proposed amendments to the Code of Economic Law can be found in Parliamentary document DOC 55 0407/001. The bill is pending at the time of writing this report and additional amendments have been tabled in the

meantime^v. An extensive discussion of this bill is included in Section 5.3.3. of the scientific report of this KCE study.

3.3. Compulsory medicine licensing in other countries

To date, compulsory medicine licensing has mainly been used by low-income countries (an overview is given in the extensive scientific report). In the past, however, some high-income countries have also made use of compulsory licences or have explicitly included the possibility of imposing them in their legislation or policies. In this summary, we provide a brief overview of a selection of countries.

3.3.1. Canada – a history of compulsory licensing

After great concern about excessive prices, Canada^w decided to grant compulsory licences for imported medicines in the 1960s. As there was no domestic medicine manufacturing industry at the time, this allowed mostly smaller Canadian companies to obtain the right to manufacture generic medicines under compulsory licence or to import the active ingredient and process it into a medicine.

In 1983, Canada's *Eastman Committee*^x determined that compulsory licensing had saved \$211 million that year on a total medicine bill of \$1.6 billion. Compulsory licensing had not, however, led to increased competition. On the other hand, the committee found that Canadian research capacity (particularly for basic medical and pharmaceutical research) suffered at the hands of compulsory licensing. In 1987, the so-called Bill C-22 followed, which amended the law to guarantee patent holders a longer protection period (up to 17 years).

^u Belgian Chamber of Representatives. 20 September 2019, bill amending the Code of Economic Law regarding the application of compulsory licences to medicinal products. DOC 55 0407/001.

<https://www.lachambre.be/FLWB/PDF/55/0407/55K0407001.pdf>

^v <https://www.dekamer.be/kvvcr/showpage.cfm?section=flwb&language=nl&fm=/site/wwwcfm/flwb/flwbn.cfm?legislist=legisnr&dossierID=0407>.

<https://www.dekamer.be/FLWB/PDF/55/0407/55K0407002.pdf> en <https://www.dekamer.be/FLWB/PDF/55/0407/55K0407003.pdf>

^w SHAPIRO, D. M. & SWITZER, L. N. 1993. The Stock Market Response to Changing Drug Patent Legislation: The Case of Compulsory Licensing in Canada. *Managerial & Decision Economics*, 14, 247-259.

^x EASTMAN, H. C., FRASER, R. D., LASKIN, J. I. & KENNEDY, W. A. 1985. Report of the commission of inquiry on the pharmaceutical industry.



3.3.2. France – Art. L613-16 of the Intellectual Property Code

The amendment of the Intellectual Property Code in France in 2005 inspired the creation of an additional legal basis in Belgium for the granting of compulsory licences for 'public health reasons' (see 3.2.1).

The French Article L613-16 states that, if the interests of public health so require, the Minister may grant ex officio compulsory licences for pharmaceuticals, medical devices, processes to manufacture such products, as well as ex vivo diagnostic methods.

The patents on these products, processes or methods can only be subject to the compulsory licensing system in the interest of public health, i.e. if they are not made available to the public in sufficient quantity or quality. However, French law also explicitly states that compulsory licences can be granted for medicines that are offered at abnormally high prices.

When the purpose of the licence is to put an end to an anti-competitive practice or in cases of urgency, the Minister is not obliged to seek an amicable settlement with the patent holder.

3.3.3. Germany – MSD vs Shionogi

This ruling by the Federal Patent Court (see also 3.2.1) on the medicine Isentress with the active ingredient raltegravir for the treatment of HIV is one of the few cases in which a European court has granted a compulsory licence for a medicine.

The Japanese pharmaceutical company Shionogi had taken out a European patent for the active ingredient raltegravir (also in Germany, among other places). However, the validity of the patent was disputed, also at the time of the ruling in 2017.

In 2008, the American Merck Sharp and Dohme Corporation (MSD) brought the medicine Isentress with the active ingredient raltegravir onto the market.

Shionogi notified MSD in 2014 that their medicine came under the protection of its patent. Negotiations between the two parties for a licence were unsuccessful. In 2017, the judge granted MSD a compulsory licence on the basis of 'the public interest' of the continued availability of this medicine to combat HIV. If MSD had been forced to discontinue sales, patients treated with raltegravir would have had to switch to other medicines at significant risk of side effects, interactions, or therapy failure. Therefore, according to the court, the 'public interest' condition was met.

3.3.4. The Netherlands – multilevel toolbox and evaluation framework

There is also a lively debate in progress in the Netherlands concerning the affordability of medicines. Various opinions have been delivered on mechanisms to ensure fair prices for medicines. These recommendations led to a proposal from the Dutch Minister for Medical Care for a 'multi-level toolbox'^y with various measures, including compulsory licences (see Box 4).

In this proposal, the Dutch minister also points out that compulsory licences can only be used in exceptional situations, if the public interest so requires. In practice, however, a compulsory licence has never yet been granted for a medicinal product in the Netherlands. In addition, when a compulsory licence is granted, the licence holder is still required to obtain a marketing authorisation. Although the Dutch minister points out that regulatory provisions for data and market exclusivity are harmonised at EU level, he wants to explore the possibilities of introducing a waiver of this exclusivity in cases where a compulsory licence is granted.

In a recent publication, an assessment framework^z is also proposed to determine whether granting a compulsory licence is opportune in a given context. This framework is summarised in Box 5.

^y Letter from the Minister for Medical Care, 15 June 2018, Meeting year 2017-2018, TK 29 477, 32 805, no. 489, pp. 3-15.

^z A. de Jong (2020), 'Persoonlijke beschouwing over de inzet van de dwanglicenties bij hoge prijzen van medicijnen' (personal consideration of



Box 4 – Dutch multilevel toolbox for fair medicine prices

The following mechanisms are included in the proposal of the Dutch Minister for Medical Care:

National measures:

1. Amendment of the Medicines Pricing Act
2. Financial arrangements for medicines
3. Modernisation of the reimbursement system for medicines
4. Price transparency (e.g. the Fair Medicine Initiative)
5. Compulsory licences

Decentralised measures:

6. Transfer of expensive medicines from extramural care to intramural care
7. Reinforcement of preference policy for insurers, platform for the purchase of expensive medicines, better sourcing of medical devices
8. Further development of the system of barcoding pharmaceuticals and medical devices
9. Facilitating pharmaceutical preparations in the pharmacy

International measures:

10. Research and monitoring of the impact of supplementary protection certificates, data exclusivity and market exclusivity
11. Coordination of Health Technology Assessments (HTAs) and price negotiations (e.g. BeNeLuxA and International Horizon Scanning

Initiative), sharing technical expertise, exchanging best practices and price and market information; exploring common policy solutions and joint positions.

Box 5 – Dutch proposal for an assessment framework for compulsory licences

Proportionality: Can the use of a compulsory licence be justified from the perspective of the relative size of the patient group, the effect of the patented medicine on the health situation of the patient group and the budgetary implications?

Patent: Does it concern a relevant patent that prevents access to the market and is difficult to 'bypass'?

Production capacity/imports: Can the medicines be manufactured by the holder of the compulsory licence at a reasonable price and within a reasonable period of time? If not, can they be imported?

Other legal barriers: Are there legal provisions that prevent the licence holder from obtaining a marketing authorisation, e.g. trade secrets, data and market exclusivity?

Reasonable remuneration: What costs are associated with granting the compulsory licence?

Other risks: Are there any other risks associated with the granting of a compulsory licence, e.g. the risk that medicines will not reach the Dutch market in time?

the use of compulsory licences in the case of high medicine prices), ABDTOPConsult, June 2020, available at https://www.eerstekamer.nl/overig/20200702/persoonlijke_beschouwing_ov_er_de/meta



4. CONSIDERATIONS FOR THE EFFECTIVE USE OF COMPULSORY LICENCES

As stated earlier in this summary, there are a large number of barriers that can make the effective use of compulsory licences more difficult. These obstacles are partly at the legal level, partly at the practical level, as well as at the health policy level and the economic level. In this section, we provide a summary overview of these barriers and, where possible, propose some solutions.

4.1. Considerations within the current legal framework for compulsory licensing

4.1.1. *The legal basis for compulsory licences*

As indicated in 3.1.1, the TRIPS Agreement provides for several legal bases for the government to grant compulsory patent licences. One of the legal bases that can be considered for expensive medicines is that of 'public interest/public health'. This latter legal basis has also been provided for by the Belgian legislator since 2005.

However, the law does not include a definition or give examples of what can be regarded as 'public health reasons'. This is remarkable because the introduction of compulsory licences for public health reasons is inspired by French legislation, which does refer to specific situations in which the licence can be issued.

However, the parliamentary documents do refer to some examples, such as in the case of insufficient stocks, if the quality of the medicinal product is unsatisfactory or in the case of abnormally high prices. Such specifications could be introduced through a legislative amendment of Article XI.38 of the Code of Economic Law.

In addition, other legal grounds may also be considered. We note that public, non-commercial use is repeatedly used as a legal basis for 'government use'

in other WTO member countries. The government then permits a government agency or commercial contractor to use a patented invention for the benefit of the general public. The government can decide on this ex officio without having to ask a third party and without having to negotiate with the patent holder first.

In some other countries, including the United States, compulsory licences are also granted as a remedy against anticompetitive practices.

4.1.2. *Setting the standard for excessively expensive medicines*

One of the main challenges is to determine the 'standard' for granting a compulsory licence due to high pricing. From what point in time is a medicine considered 'excessively' expensive?

In light of the decision-making practice of the national and European competition authorities regarding excessive pricing practices, there are a number of factors that are taken into account by these authorities, including (1) the way the relevant market functions and the existence of actual and potential competition (e.g. price elasticity, barriers to entry, agreements to prevent entry); (2) the mismatch between the price applied and the reference price; (3) the disparity between price and economic value (e.g. product age, therapeutic value); (4) whether investments have been made for research and development and whether commercial risks have been borne; (5) the extent to which companies are aware of the adverse effects of pricing practices on the health system and patients; (6) whether similar pricing practices have been introduced in other countries.

The decision-making practices of competition authorities also provide extensive insights into how costs can be calculated, although these cases do not follow a single uniform method. In addition, almost all the decisions taken by competition authorities in this context still relate to medicinal products whose patent protection period has expired. However, these decisions also make it clear how important it is to have access to data on the costs of developing and marketing the medicine. The competition authorities in most countries have extensive investigative powers to collect confidential commercial information concerning costs and prices. However,



they frequently point to the difficulties involved in identifying, collecting and analysing such data for the purpose of assessing pricing practices.

Without proper powers and guidelines, it will be impossible in principle to make an assessment as to whether the pricing is fair or excessive. Alternatively, the burden of proof (to show that the price is not excessive) can be shifted to the pharmaceutical company, in which case, however, guidelines will still be needed to ensure correct and transparent cost calculation. As previously stated in 1.2.4, an in-depth investigation into the elements and calculation methods via which companies arrive at a price proposal for medicines was not within the scope of this study.

4.1.3. Determining reasonable/adequate remuneration

As indicated in 3.1.2, it is desirable to have guidelines on how the reasonable/adequate^{aa} remuneration for the patent holder is calculated, on what method and data this calculation should be based, and who should make this calculation.

The key question, of course, is what is 'reasonable' or 'adequate'. A choice could be made in this regard on the basis of the Guidelines^{bb} of the World Health Organisation (WHO). In this document, the WHO specifies several methods. Even then, access to data on direct and indirect costs remains necessary in order to determine what is reasonable.

In view of the importance of this information in various areas, the government may consider introducing measures to make the information accessible to the competent authorities.

^{aa} Article 31(h) of the TRIPS Agreement refers to the term 'adequate', while Article XI.38 of the Belgian Code of Economic Law refers to the term 'reasonable'.

4.1.4. Extending the expertise of the Advisory Committee on Bioethics

The Advisory Committee on Bioethics provides (non-binding) advice on compulsory licensing for public health reasons. It is unclear what the scope of this advice is, especially since this committee consists of bioethical experts. The question could be asked whether this committee is the most appropriate actor to advise on whether the granting of a compulsory licence is justified, what the reasonable remuneration should be and the scope, duration and conditions of use of the licence.

It seems appropriate for the Advisory Committee to call on additional expertise with an economic background for the formulation of adequate advice and/or, as indicated earlier, involve the Belgian Competition Authority.

4.1.5. Solutions for dealing with patent clusters – patent pools and clearing houses

Medicines are increasingly protected by a patent cluster, i.e. a multitude of granted patents and patent applications, instead of by a single patent (see also 2.1.5). It is therefore essential to clarify in the Code of Economic Law that compulsory licences can be granted not only in respect of a single patent/patent application but can also relate to clusters of patents/patent applications where that is the case.

Patent clusters can make it more difficult to impose compulsory licences and also have an impact on the normal functioning of the market. In cases of fragmentation of patent rights, it is often very difficult for a company to obtain licences from all the relevant patent holders, preferably at a reasonable price (the so-called 'royalty stacking' problem). A possible solution, when it comes to different patent holders, can be found in encouraging the formation of patent pools. A patent pool is an agreement between two or more patent

^{bb} UNDP and World Health Organization. Remuneration Guidelines for non-voluntary use of a patent on medical technologies. WHO/TCM/2005.1. https://www.who.int/hiv/amds/WHOTCM2005.1_OMS.pdf



holders related to the same invention/technology. Via the agreement, they grant (cross) licences to use one or more of each other's patents, or to license them as a package to third parties. These licences are then granted on fair and non-discriminatory licence terms, including a reasonable price. This is essential to prevent royalty stacking.

Although patent pools are rather unusual in the pharmaceutical sector, they can certainly be used as a tool to counteract the blocking of market competition by patent clusters. An example of a successful case in this regard is the [Medicines Patent Pool](#), a United Nations-sponsored organisation that aims to promote access to life-saving medicines for low and middle-income countries. The organisation works together with governments, organisations, industry, patient groups, society and other stakeholders to pool and license intellectual property with the aim of facilitating the production of generic medicines and the development of new formulations. The organisation has entered into agreements with patent holders of HIV, hepatitis C and COVID-19 medicines, as well as for the use of technology platforms and serological diagnostic tests, including for the detection of COVID-19.

In addition to patent pools, other mechanisms have also been described in the literature, such as 'clearing houses'. These are platforms or intermediaries that bring together owners and users of goods, services and information. The clearing house acts as a neutral intermediary or platform for a wide variety of technologies to be licensed (a kind of "supermarket" for technologies and licences). The clearing house brings patent holders and licensees together by providing standard or one-stop licences, just like the patent pool, at a reasonable price. The difference between the patent pool and the clearing house relates to the governance, the legal organisation and the structure of the model. The objectives are similar.

To address a particular public health problem, an initiative could be taken at international level to negotiate joint public health-oriented licences with the patent holders.

While they can certainly be important in promoting the development of different solutions to a health problem and are obviously much more constructive in nature than compulsory licensing, it remains unlikely that patent pools can completely replace the use of compulsory licensing for expensive medicines.

4.2. Post-marketing authorisation exclusivity considerations

4.2.1. Dealing with data and market exclusivity

If the government wants to set up an effective system of compulsory licensing for expensive medicines, care must be taken at the interfaces between patent law and patent strategies as well as with regard to data and market exclusivity (see 2.2)

Unlike the compulsory licensing regime for patents, there is currently no form of 'exemption' or 'waiver' from the EU exclusivity rules for medicines. Even in cases of national public health emergencies or urgent public needs, there are no explicit exemptions or restrictions in EU law that would allow a generic medicine or a biosimilar to be brought onto the market without having to deal with the aforementioned data and market exclusivity.

This is a complex situation. The granting of compulsory licences for patents is a matter for national law. The legal requirements for marketing authorisation for medicinal products (including the granting of data and market exclusivity) are mainly an EU matter. In other words, these interacting legal frameworks are inconsistent with each other.



4.2.1.1. Inclusion of exemptions in national or international law

In the literature^{cc dd} and in a number of countries, such as the Netherlands, there is a plea for the inclusion of legal provisions in national and international legislation that allow an exemption from data and market exclusivity for generic medicines in certain circumstances.

Such provisions could be applied for reasons of public interest (including public health), in the case of compulsory patent licensing (also for non-commercial use by government), and/or in situations of national emergency or extreme urgency.

These authors propose that the holder of the marketing authorisation for the reference medicinal product should be paid an appropriate fee as compensation for the use of the data protected by data exclusivity. In other words, the authors encourage countries to consider replacing data exclusivity regimes with a form of data protection that recognises and rewards the investment in generating the data but does not allow the investor to exclude others from using the data.

4.3. Practical considerations in the production of generic medicines or biosimilars under compulsory licence

4.3.1. Access to know-how

As explained in 2.2.2., protection via know-how and trade secrets is an important addition to patent protection and data and market exclusivity. Developers and manufacturers of medicines carefully determine what information and data they include in their patent applications and marketing authorisation application files (in accordance with the requirements of the legal framework) and which data they do not have to disclose. As a result, a licence holder may not be able to manufacture the medicine under compulsory licence solely on the basis of information disclosed in the patents, information available in the public domain, or clinical trial data.

For this reason, robust arrangements need to be put in place to ensure access to clinical trial data and missing know-how so that the licensee can apply for marketing authorisation and produce a high-quality medicine. It is indicated that there is an increasing demand for transparency on the basis of the European regulation on clinical studies^{ee}, the rules^{ff} established by the EMA and the recent case law (see the scientific report).

On the other hand, it is argued that data needed to demonstrate the safety and efficacy of new medicines still does not require the disclosure of know-how on how to effectively manufacture complex medicines. It can be argued

^{cc} E.F.M. 't Hoen et al. (2017), 'Data exclusivity exceptions and compulsory licensing to promote generic medicines in the European Union: A proposal for greater coherence in European pharmaceutical legislation', 10 *Journal of pharmaceutical policy and practice*, 19.

^{dd} E.F.M. 't Hoen (2022), 'Protection of Clinical Test Data and Public Health: A Proposal to End the Stronghold of Data Exclusivity', in: C.M. Correa & R.M. Hilty (eds.), *Access to Medicines and Vaccines*, Springer, Cham.

^{ee} Regulation (EU) 536/2014 of the European Parliament and of the Council of 16 April 2014 on clinical trials on medicinal products for human use, and repealing Directive 2001/20/EC, [2014] OJ L 158, 1-76.

^{ff} EMA (2014), EMA policy on publication of clinical data for medicinal products for human use, POLICY/0070, EMA/240910/2013, 2 October 2014, available at: http://www.ema.europa.eu/docs/en_GB/document_library/Other/2014/10/WC500174796.pdf, cf. EMA (2018) EMA's Clinical data publication (Policy 0070) report Oct 2016- Oct 2017, 16 July 2018, EMA/630246/2017, available at: http://www.ema.europa.eu/docs/en_GB/document_library/Report/2018/07/WC500252071.pdf.



that more information needs to be made public to allow such products to be manufactured as safely as possible, even if they are produced under compulsory licence. However, according to the Clinical Trials Regulation, confidentiality must be respected where it is essential to protect “commercially confidential information”, unless there is ‘an overriding public interest’. It remains to be seen what exactly “overriding public interest” entails and whether this can be effectively enforced.

4.3.2. Access to raw materials and production capacity

The production of generic medicines also depends on the availability of raw materials. Such availability could be hindered if pharmaceutical companies or suppliers were to impose restrictions or unreasonable conditions - including high prices - on those raw materials.

Moreover, granting a compulsory licence is only useful if the licence holder has sufficient and appropriate production capacity. This can be a problem, especially for complex biotechnological medicines. Certainly in less industrialised countries, the necessary knowledge and competences may be lacking to set up such production capacity. Furthermore, this can be too expensive in some cases.

In high-income countries with a well-developed pharmaceutical and biotech sector, such as Belgium, this should not be a problem at first sight. On the other hand, we have to take into account that Belgium is only a small sales market. In addition, Belgium, along with other EU Member States, does not avail itself of the possibility of importing medicines produced under compulsory licence. There is no consensus in the literature about lifting this ban. Nor was the European Commission prepared to lift this ban when there was a great need for COVID-19 vaccines, despite the large available production capacity within Europe.⁹⁹

So even for a small country like Belgium, the ability to produce a medicine under compulsory licence will depend on the medicine in question, access to raw materials and the availability of necessary funding and capacity to set

up the production of the medicine in question. In view of the previous legal uncertainty and lack of clarity regarding the extra costs (reasonable remuneration for the patent holder, compensation for the use of data, etc.), the production of a generic medicine or a biosimilar in our country will not always be straightforward.

4.4. Considerations regarding the exemption for pharmacy preparations

Pharmacy preparations are sometimes presented as another effective means of ensuring the accessibility of certain medicinal treatments, most notably when required for very rare diseases that are treated with almost “tailor-made” medicines.

These preparations are subject to European pharmaceutical legislation (which considers these preparations to be non-industrial and therefore outside its scope) and to national legislation (which regulates their quality and conditions), as well as to patent law in some States.

In Belgium, patent law stipulates that patent protection does not apply to preparations prepared “on prescription”, “in the pharmacy” for “individual cases” (pharmacy exemption).

Following the development of highly complex preparations requiring special precautionary measures, the quality standards for preparations were tightened in Belgian legislation. This allowed pharmacists to outsource certain preparations under their responsibility to a production unit (holder of a preparation license under Belgian law). Strictly speaking, only preparations that are prepared “in the pharmacy” come under the Belgian pharmacy exemption. Given that this Belgian patent exemption was introduced in 1980, it would be useful to clarify its application in relation to these new “outsourcing practices” (by amending the legal text or via circulars).

⁹⁹ https://www.europarl.europa.eu/doceo/document/E-9-2021-000463-ASW_EN.pdf



In addition to patent law, Directive 2001/83/EC on medicinal products sets out certain specific conditions to ensure that the pharmaceutical preparation is not subject to the same rules that apply to industrial medicinal products (marketing authorisation, etc.).

However, the Member States are free to set the rules for these preparations (threshold value for what can be considered industrial, quality requirements, subcontracting conditions). In Belgium, for example, the quality requirements for the preparation of ATMPs in pharmacies are stricter than in other countries ("Good Manufacturing Practice" requirements for the preparation). This may explain why only one ATPM has been prepared and used in Belgium thus far under the exemption for hospitals.

Moreover, Belgium demands that no licensed alternative may be made available for this type of preparation. It is still not clear, however, whether this alternative is considered available, even if its price would make it inaccessible to patients in practice.

4.5. Social and economic considerations in the granting of compulsory licences

4.5.1. Possible positive consequences

4.5.1.1. Improving access to medicines

The immediate benefit of granting a compulsory licence is better access to the medicine for patients who need it. Lack of access is particularly distressing when patent holders choose not to supply certain countries, e.g. because there is insufficient demand or insufficient capacity to pay.

Although the latter was primarily a problem for low-income countries historically, this may also arise in the future in high-income countries, e.g. in the case of extremely expensive medicines, or for countries with a small

market or with a limited patient population, such as in the case of orphan medicines.

The extent to which compulsory licences can increase access for patients naturally depends on the production capacity available in that country to produce local versions of the patented medicine according to the same quality standards and in the desired quantities (see also 4.3.2).

4.5.1.2. Lowering of prices

While we can expect lower prices with compulsory licences, this largely depends on the specific context. Based on more than fifty case studies^{hh}, albeit in low-income countries with a context different to that in Europe or Belgium in terms of public health and access to medicines, researchers found that compulsory licensing of medicines can reduce prices by an average of 60% to 70%.

However, compulsory licences do not always lead to lower prices. Domestic production can also be expensive, in the case of complex production processes for example, because a small market size does not result in sufficient compensation for the fixed costs associated with setting up a production infrastructure or because high remuneration amounts have to be paid to patent holders. In addition, the generic product may still have to go through a lengthy and expensive evaluation process before it receives marketing authorisation due to the existing data exclusivity on the original medicine.

hh URIAS, E. & RAMANI, S. V. 2020. Access to medicines after TRIPS: is compulsory licensing an effective mechanism to lower drug prices? A review of the existing evidence. *Journal of International Business Policy*, 3, 367-384.



4.5.1.3. Freeing up resources to invest elsewhere

When compulsory licences effectively lead to lower prices, this releases resources that can be invested elsewhere. When these freed-up resources are invested in health programmes that are safe, effective and cost-effective, it has a positive impact on public health.

4.5.1.4. Local industrial development

In the short term, compulsory licensing can have a stimulating effect on the development of local industry. If production was initially carried out abroad, a transfer of production to domestic companies can provide a boost to the development of new economic activity within national borders. Local companies gain market share, which allows them to grow, establish capital stock, build expertise, develop human capital, and so on.

This can be an attractive strategy with significant long-term economic benefits, especially in countries that are in full economic development. Notable examples of this include India, Brazil and Thailand. These countries have used compulsory licensing in recent decades to successfully develop a domestic pharmaceutical industry. In practice, this has mainly been aimed at the production of generic medicines.

Whether this strategy is attractive for high-income countries with a well-developed innovative pharmaceutical and biotech industry (such as Belgium) is difficult to determine. In the long term, the negative economic consequences of the regulated granting of compulsory licences could be greater than the positive consequences.

4.5.1.5. Acceleration of innovation

Some authors argue that patents rather inhibit investment in innovation. They argue that, in practice, the value of a patent consists of granting an exclusive right to market access coupled with claiming higher prices.

In addition, it excludes others from producing their invention and developing product-specific know-how. As a result, patents slow down the speed of innovation, as well as limit the dissemination of knowledge and the sharing of innovative production processes. In that regard, however, compulsory

licensing can have a positive effect on stimulating research and development activity.

Other authors use the counterargument that patents do indeed speed up research and development on account of knowledge and information becoming available as soon as the patent is published. Third parties can use this information in their own research, given the "exception for research" (see 2.1.6.) included under patent law.

4.5.2. Possible negative consequences

4.5.2.1. Less local investment in research and development by the pharmaceutical and biotechnology industry

Several authors hypothesise that if a pharmaceutical company is confronted with compulsory licensing, it will respond by reducing research and development expenditure in the country concerned. Indeed, in general, innovation theories predict that companies will reduce their investment - be it financial investment in new research and development, as well as in technology transfer - in a country where they cannot fully exploit their intellectual property rights. After all, the granting of compulsory licences reduces the expected profit that they can derive from innovation.

Companies would therefore be inclined to move their research and development to other locations with comparable or lower labour costs, equal access to resources and a highly skilled workforce. Multinational companies in particular will have the opportunity to select the most promising regions for further investment.

This has an impact on local employment and the build-up of knowledge and expertise. Furthermore, Belgium is a very attractive country in which to conduct clinical studies, given the expertise available and the high concentration of (academic) hospitals. Pharmaceutical companies confronted with compulsory licensing in Belgium may be inclined to conduct their clinical studies elsewhere.

However, it is not just the immediate profit motive that can jeopardise private investment in research and development. Simple retaliation by the patent



holder is also possible, partly as a signal to other countries that are thinking of doing the same thing, and partly to influence future domestic policy decisions.

The ability to retaliate depends on the size and scale of the patent holder. A large company with a large product portfolio will have more opportunities to retaliate than a small company focused on one product.

However, retaliatory measures (when perceived as such in the media and public opinion) may meet with public opposition, especially if compulsory licensing was granted for humanitarian reasons.

A case study: compulsory licensing in Canada

Canada is the only well-developed case study^{ii jj} on the impact of the use of compulsory licensing for expensive medicines in a high-income country and its consequences for the domestic research landscape (see also 3.3.3).

An almost twenty-year (1969-1987) policy of granting compulsory licences for expensive imported medicines created a thriving generic industry, operating both domestically and globally, especially through exports to developing countries.

However, the granting of compulsory licences also led to retaliatory actions, with the pharmaceutical multinationals from the United States being reluctant to invest in basic biomedical and pharmaceutical research in Canada. As a result, Canadian research narrowed to the development of me-too medicines.

We would point out, however, that the Canadian model for compulsory licences should be seen in the context of that time, mainly the 1970s and

1980s. The circumstances are very different now and it remains difficult to make the comparison, even vis-a-vis what is presented in the literature as a 'textbook example' of compulsory licensing for expensive medicines in a high-income country.

4.5.2.2. Loss of income due to international effects

For a company, there is not only the risk of loss of income in the country that has issued a compulsory licence but, perhaps more importantly, there is also the risk of consequences at international level.

Although compulsory licences are intended, in principle, for the production of generic medicines or biosimilars for the domestic market, it cannot be completely ruled out that a medicine produced under compulsory licence may nevertheless find its way to foreign markets. There is even an exception provided for this under Art. 31bis of the TRIPS Agreement, although it is surrounded by many guarantees.

In addition, this can also have an indirect international effect for a company through the system of external reference prices. In price negotiations, the current price for medicines in other (reference) countries is used as a guideline. If a perceptibly cheaper price applies in a reference country, this could have an impact on prices in other countries. For new and expensive medicines, however, more and more use is made of so-called Managed Entry Agreements (MEAs)^{kk} and/or other negotiations within the framework of Art. 81 of the convention, with the actual price paid for a medicine remaining secret. As a result, the usability of the system of price comparison between countries has declined sharply.

ⁱⁱ LEXCHIN, J. 1993. Pharmaceuticals, patents, and politics: Canada and Bill C-22. *International Journal of Health Services*, 23, 147-160.

^{jj} LALITHA, N. 2004. A review of the pharmaceutical industry of Canada. Working Paper Series. Gota, Ahmedabad, Gujarat Institute of Development Research.

^{kk} Gerkens S, Neyt M, San Miguel L, Vinck I, Thiry N, Cleemput I. How to improve the Belgian process for Managed Entry Agreements? An analysis of the Belgian and international experience. Health Services Research (HSR) Brussels: Belgian Health Care Knowledge Centre (KCE). 2017. KCE Reports 288. D/2017/10.273/41.



4.5.2.3. *A possible imbalance in tiered pricing*

Several authors indicate that pharmaceutical companies can offer medicines at lower prices in low-income countries by virtue of being able to recoup the costs of research and development by charging higher prices in other countries. We were unable to check the validity of this argument in this and other KCE studies – including the previously cited research on the impact of Managed Entry Agreements.

The introduction of compulsory medicine licensing in high-income countries could undermine the system of tiered pricing between low and high-income countries. The company then has to recoup the investments made in a more limited, smaller market. This could therefore prevent access to medicines in low-income countries by virtue of prices becoming unaffordable in these countries.

4.5.2.4. *Investment by other IP-intensive industries*

In a country that creates an uncertain environment for intellectual property, companies outside the pharmaceutical sector may also be inclined to invest less locally in research and development. In this way, according to some authors, compulsory licensing in one technology sector can discourage foreign direct investment in all industries that rely heavily on intellectual property. Likewise, domestic companies that invest intensively in research and development can relocate to other countries and even relocate their headquarters to countries with a better protection climate for innovation.

However, the empirical literature does not answer the question of the possible net effect of compulsory licences on foreign investment. A number of studies do find a correlation, but do not yet show any causal relationship.

It has been argued that this is less of a problem in low-income countries. If the motivation behind compulsory licensing is one of life-saving treatments for patients or other ethical reasons, the effects may be limited to pharmaceutical investment alone. It is therefore critical that governments planning to grant a compulsory licence have a clear communication strategy about their motives and the context of their decision. In other words, there is a need for transparency not only on the part of the industry, but also on the

part of the government if it wants to avoid side effects, such as a negative impact on investment.

4.5.2.5. *Patients are deprived of essential medicines locally*

In principle, the patent holder can decide not to make certain medicines available in the country that has granted a compulsory licence. This decision will depend on the size of the sales market. Countries with a relatively small sales market, such as Belgium, could be particularly affected by this.

4.5.2.6. *Potentially lower supply of innovative medicines in the long term*

A central theoretical argument in the literature is that the use of compulsory licensing to make medicines more affordable is a short-term strategy with possible negative consequences for the availability of innovative medicines over the long term.

By influencing the return on risky investments, investors would be less inclined to financially support companies that develop medicines. This results in a shrinking of the medicine pipeline, causing the supply of innovative medicines to decrease over time.

Researchers indicate that this argument is extremely difficult to verify due to a large number of assumptions. For example, it is assumed that patent protection is the best possible way to promote the development of innovative medicines.

This assumption does not hold, especially for low-income countries. Low-income countries often suffer from neglected diseases that attract little investment, despite patent protection. The Western innovation model has led to only limited medical breakthroughs for such conditions. This has required additional support in the form of philanthropy, development cooperation and public-private initiatives.



Finally, while the argument that compulsory licensing generally inhibits the development of innovative medicines is theoretically coherent, the empirical evidence for this remains scarce. Some studies^{ll mm} even document positive effects of compulsory licensing on innovation.

5. CONCLUSIONS AND POSSIBLE LINES OF THOUGHT

There is serious concern worldwide about the availability and affordability of medicines. These concerns will increase further in the future, given the increasing personalisation of treatments, the complementarity of diagnostics and treatments, and the complexity of new medicines, including biologics.

Compulsory licensing is presented as a potential legal instrument to reduce the price of certain medicines. If the government wants to use this instrument, a number of procedural and legal barriers must be removed.

Most compulsory licences to date have been granted by authorities in developing countries and emerging economies. There are only a few examples of compulsory licences granted for public health reasons in high-income countries. However, these examples were not necessarily related to high prices but, rather, to the availability of the medicines. Some compulsory licences were also granted by the competition authorities and not through the patent law route of compulsory licences.

The question remains to what extent compulsory licences are effective and sufficient?

One of the main conclusions of this report is that the use of compulsory licensing for expensive medicines must take account of the broader picture of medicine regulation and the institutional and administrative framework for medicines.

After all, the legal basis for compulsory licences is founded in patent law. However, patents are not the only mechanism for protecting medicines. Data and market exclusivity, as well as regulations regarding trade secrets and know-how and other instruments also apply here. Providing access to only one element of this regulatory framework is likely to prevent a competitive product from entering the market in the short term due to other barriers.

^{ll} MOSER, P. & VOENA, A. 2012. Compulsory Licensing: Evidence from the Trading with the Enemy Act. *American Economic Review*, 102, 396-427.

^{mm} MOSER, P. 2013. Patents and Innovation: Evidence from Economic History. *Journal of Economic Perspectives*, 27, 23-44.



Furthermore, it is undeniable that a compulsory licence also initiates consequences for the functioning of other parts of the framework, as well as for the complex ecosystem of pharmaceutical development as a whole.

Another observation is that one of the main objectives for granting patents, i.e. data and market exclusivity, is to stimulate and reward innovation. Intervention in the protection mechanisms for medicines can have negative local consequences for a small country like Belgium, which has an important presence of national and international pharmaceutical and biotechnology companies, in terms of investment in research and development, clinical studies, (high-tech) production capacity, employment, development of knowledge and competences, competitive position, international trade relations, and so on.

The granting of a compulsory licence can lead to practical problems and questions: does the licensee have sufficient know-how to produce the patented medicine, does the licensee have access to the necessary raw materials, can the licensee obtain marketing authorisation in the short term or must additional (expensive) clinical studies be set up, what reasonable remuneration should be paid to the patent holder, is there a risk of lengthy lawsuits, and so on? But also whether there is sufficient production capacity to manufacture the medicine under licence for a small market such as Belgium. After all, we have to take into account that the EU and its Member States do not want to take the option of importing medicines under compulsory licence (EU opt-out with regard to the export exception for implementation of the Doha Declaration and the TRIPS Agreement).

Given the limited availability of comparable empirical data, it is extremely difficult to make reliable predictions about the consequences of compulsory licensing of expensive medicines by the Belgian authorities in the case of high price levels. The fact that Belgium is a small country can have two effects. On the one hand, it could mean that it will not have much impact for a company because it only concerns a limited market while, on the other hand, it may have international implications if Belgian prices are used by other countries as an international reference for pricing. As mentioned previously, prices actually paid for new medicines are rarely disclosed publicly as they are increasingly subject to negotiation. As a result, the system of price comparison between countries has become less useful.

Moreover, the granting of compulsory licences by a small country like Belgium can have a wider impact if other countries follow suit.

Moreover, Belgium is a high-income country that can contribute to the profit margins of developers and manufacturers of (innovative) medicines, meaning that they are able to charge lower prices in low-income countries (internationally tiered pricing). On the other hand, it is unclear to what extent low-income countries really do obtain high discounts on innovative medicines.

Finally, we note that the recent Belgian parliamentary bill for the introduction of compulsory licensing for expensive medicines takes little account of the full regulatory framework for the protection of medicines or of the potential negative effects outlined above. It would be desirable to opt for a 'toolbox' approach, as previously proposed in the Netherlands, in which the compulsory licence is explicitly presented as one instrument within a wider range of possible tools.

In short, the substantive and procedural conditions for the granting of compulsory licences must be carefully assessed and optimised to ensure that this mechanism is suitable to achieve the desired outcome, i.e. ensuring access to and affordability of medicines for patients in need of them.

Set out below are a number of specific elements that can help the compulsory licensing mechanism, in combination with other mechanisms, to better meet the above objective:

1. Although practice shows that compulsory licences are mainly used as a negotiation tool, the procedure for granting compulsory licences still needs to be clarified and strengthened in certain respects. This could include, among other things, establishing a methodology to determine what constitutes an 'excessive price', what a reasonable remuneration amount would be for the patent holder, how expert panels should be put together to advise on this, how to apply for, grant and/or impose a compulsory licence in practical terms, and so on.

Several legal bases are potentially eligible to justify compulsory licensing for expensive medicines. Public, non-commercial use is used by other member countries of the World Trade Organisation as a reason



for so-called 'government use', where the government grants a government agency or commercial contractor permission to use a patented invention for the benefit of the general public.

In many cases, this seems to be the easiest way to meet an urgent public need, as the government can decide to do this on an ex officio basis, without the need for a request from any third party and without first having to negotiate with the patent holder. On the other hand, prior negotiation with the licence holder can ensure that the compulsory licence is seen as a more proportional measure that is only imposed 'as a last resort'.

2. An amendment to European and national legislation may be considered to allow exemptions from exclusivity rules in the event of a compulsory licence being granted. This should be accompanied by careful consideration and investigation of alternative arrangements to counter the competitive advantage in relation to medical data. Such schemes should provide an incentive for making relevant data public and usable through compensation mechanisms or other concessions. However, they must also include an obligation to make this data public and usable in exceptional circumstances (e.g. in the case of a compulsory licence granted by the government). However, this also includes reasonable compensation for the investment made in generating the data.

In addition, the national medicine authorities and the EMA need to tighten up their requirements in terms of data transparency when submitting a dossier for obtaining marketing authorisation. For example, it could be argued that more information should be provided to demonstrate that products are manufactured in the safest possible way.

3. It would be desirable to strengthen the cooperation and exchange of expertise regarding the methodology for determining what constitutes an 'excessive price' or a 'reasonable remuneration' between different Belgian government agencies. This includes, in particular, the FPS Public Health, the FPS Economy and Employment, RIZIV/INAMI (National Institute for Health and Disability Insurance) and the Belgian Competition Authority.

4. It is recommended that a robust, transparent and coherent policy be implemented in relation to the prices and reimbursement of medicines. Initiatives can be taken at European level in this regard, e.g. by exchanging more information on price negotiations and agreements, as well as through better coordination and harmonisation of health policy between Member States.

An inspiring example of this is the BeNeLuxA initiative, under which Belgium, the Netherlands, Luxembourg, Austria and Ireland conduct joint horizon scans of important pharmaceutical innovations, conduct joint assessments of health technology (HTA) and are able to negotiate jointly on prices. One limiting factor of the BeNeLuxA initiative is that joint negotiations can only take place if the company is prepared to do so.

Despite this limitation, such cooperation arrangements help to streamline procedures between Member States of the European Union and strengthen the position of health authorities.

A robust medicine pricing policy is a priority in every respect. After all, imposing a compulsory licence is not an option for excessively expensive medicines that are not (any longer) protected by a patent. This shows in itself that compulsory licensing cannot offer a complete solution to the high pricing of medicines.

5. The patent exemption for pharmacists can be optimised. In the Netherlands, various (hospital) pharmacies invoke this patent exemption for the preparation of orphan medicines. This guarantees their availability and affordability. It seems that this exemption is not widely used in Belgium.

However, producing medicines in the pharmacy at lower prices is only possible for certain medicines (e.g. those that are not too complicated to prepare) in specific circumstances and depending on the availability of raw materials.



6. Inventions and results of research by universities and public research institutions are often licensed to pharmaceutical companies to further develop medicines. Universities and research institutions have developed certain patent and licensing strategies in this regard that enable them to negotiate effectively, grant licences, establish research and development cooperation arrangements with industry and generate revenue.

Principles and instruments have been developed in various countries to encourage these public institutions, as well as public and private research sponsors (such as NGOs), to impose 'socially responsible licence conditions'. This may mean, among other things, that the pricing of the end products does not jeopardise the accessibility of the medicines for patients.

7. Both governments and the pharmaceutical industry have come to the realisation that collaborative models such as patent pools and clearing houses can serve as an interesting alternative to the exclusive exploitation of patents and to single bilateral or cross-licences.

These models can be particularly useful in situations where a large number of related inventions are patented by many different organisations and where access to these inventions is essential for the development and marketing of a (new) product. To gain access to all those patent rights, a multitude of licensing negotiations would have to be entered into, often lead to royalty stacking.

To address a particular public health problem, initiatives could be taken at international level, e.g. through public-private partnerships, to negotiate such one-stop-shop licensing mechanisms with patent holders. This can be a more sustainable alternative to compulsory licensing, as has been the case in the past via the Medicines Patent Pool.



■ RECOMMENDATIONSⁿⁿ

Preamble:

To tackle the problem of excessively priced medicines, the KCE has already recommended in previously published reports that a transparent, robust and coherent policy on prices and reimbursement of medicines should be developed and coordinated with other EU countries^{oo}.

The current report focuses on an additional mechanism that can only be used in exceptional circumstances and for which there is a legal basis in international and national patent law: compulsory licences. Compulsory licences are part of a delicate system of "*checks and balances*" within patent law. If granting a compulsory licence is considered, this must always be accompanied by carefully balancing the interests of public health against the potential negative consequences for, among other things, research and development, clinical studies, (high-tech) production capacity, employment, knowledge and competence building, competitive position, and international trade relations.

For this mechanism to be effective as an instrument to have an impact on exorbitant pricing and for it to be seen as a persuasive negotiating tool, several barriers (legal and practical) need to be removed at European and national level. (A)

Compulsory licences should furthermore only be used in specific situations, also taking other additional mechanisms into account that address instances of excessive pricing. We therefore propose to consider compulsory licensing as part of a broader toolkit that can help safeguard the affordability of medicines in Belgium. (B) The recommendations under section B relate only to the tools and mechanisms reviewed in the context of this report.

ⁿⁿ The KCE bears sole responsibility for the recommendations.

^{oo} Including the following reports: Hulstaert Frank, Pouppez Céline, Primus-de Jong Célia, Harkin Kathleen, Neyt Mattias. Evidence gaps for drugs and medical devices at market entry in Europe and potential solutions. Health Services Research (HSR). Brussels: Belgian Health Care Knowledge Centre (KCE). 2021. KCE Reports 347; Vandenbroeck Ph, Raeymakers P, Wickert R, Becher K, Goossens J, Cleemput I, Hulstaert F, de Heij L, Mertens R. Future scenarios about drug development and drug pricing. Health Services Research (HSR) Brussels: Belgian Health Care Knowledge Centre (KCE). 2016. KCE Reports 271. D/2016/10.273/59; Gerkens S, Neyt M, San Miguel L, Vinck I, Thiry N, Cleemput I. How to improve the Belgian process for Managed Entry Agreements? An analysis of the Belgian and international experience. Health Services Research (HSR). Brussels: Belgian Health Care Knowledge Centre (KCE). 2017. KCE Reports 288. D/2017/10.273/41.



A. RECOMMENDATIONS ON THE EFFECTIVENESS OF COMPULSORY LICENCES IN THE CASE OF EXCESSIVE PRICING

In order to remove the obstacles that exist at Belgian and European level in order to attain a credible and effective compulsory licensing mechanism in Belgium, we recommend the following measures:

To the federal government, in particular to the federal Ministers of Economic Affairs and Public Health

1. Revise the **legal basis and procedure** for granting compulsory licences (Articles XI.37 to XI.40 of the Code of Economic Law) as follows:
 - If excessive pricing is considered to be a possible reason for granting a compulsory licence based on the existing legal ground “**in the interest of public health**”, this must be made explicit in the relevant article.

In doing so, the criteria for assessing the excessive nature of the price and assessing reasonable compensation, as well as the procedure, the expertise required by the competent advisory body and the scope of the advice should be clarified. The use of this legal ground “in the interest of public health” implies a requirement for a prospective licensee to enter into “prior negotiations” with the patent holder.
 - Consider introducing “**government use**” as a new legal basis for granting compulsory licences in the event of excessive pricing. This legal ground does not require prior negotiations with the patent holder and allows public authorities to initiate proceedings ex officio without the request of a potential licensee. This would also require a clear description of the procedure and the conditions under which it can be applied.
2. Consider explicitly stating in the law that the **Belgian competition authority** has the **power** to grant a **compulsory licence** in the case of **competition law violations**.
3. Set up a **working group** of **health economists, experts in patent and competition law, patient representatives and experts from relevant government services (RIZIV/INAMI, FPS Economy, FPS Public Health, FPS Social Security, Belgian Competition Authority)** with the task of drawing up **guidelines on how to determine that a price may be deemed “excessive”**. To that end, one can draw on examples from case law in other high-income countries, as well as the expertise and experience of competition authorities with excessive prices and economic modelling. Factors that are taken into account by the competition authorities and can serve as the basis for these guidelines include (1) the way the relevant market functions and the existence of actual and potential competition (e.g. price elasticity,



barriers to entry, etc.); (2) the mismatch between the price applied and the reference price; (3) the disparity between price and “economic value” (e.g. product age, therapeutic value); (4) whether R&D investments have been made and risks accepted; (5) the extent to which companies are aware of the adverse effects of pricing practices on the health system and patients; (6) whether similar pricing practices have been introduced in other countries.

4. This working group should also determine what a **"reasonable" fee** is for the patent holder if a compulsory licence is granted.
5. Promote **cooperation and exchange of expertise** between the Belgian Competition Authority, the FPS Social Security, the FPS Public Health, the INAMI and the FPS Economy by organising expert meetings and facilitating formal and informal advice or temporary secondments.
6. Work with different EU Member States to coordinate **initiatives for the granting of compulsory licences**. This will become all the more important when the Unitary Patent comes into effect (expected for late 2022, early 2023). Although unitary patent titles will be valid in all participating Member States, compulsory licences will still be granted at national level. In this context, it is also appropriate to collaborate internationally on the methodology for determining whether a price is "excessive" and what compensation is reasonable when a compulsory licence is granted.

To the European Commission

7. Consider **amending the EU Regulations and Directives on data and market exclusivity** to allow for **exemptions from these legal exclusivity provisions** to the extent necessary for effective use of the compulsory licensing mechanisms.
8. Such exemptions may also be accompanied by an **appropriate fee** to compensate for the use of clinical trial data necessary to obtain marketing authorisation. For this reason, a study should be commissioned to examine the possibility to replace exclusivity rules by compensatory schemes.

**B. RECOMMENDATIONS ON OTHER POSSIBLE TOOLS IN THE TOOLKIT*****To the FAMHP and the FPS Economy***

9. Clarify (via regulations or circulars) whether the **preparation of an ATMP** is permitted **under the hospital exemption** if a licensed alternative exists but is not financially accessible (medicine legislation) and whether the **outsourcing of complex preparations** is permitted under the **pharmacy exemption** (patent law).

To the Belgian Competition Authority

10. **Particular attention** should be paid to **excessive pricing in the pharmaceutical sector and other related behaviour** such as unjustified barriers to production in the pharmacy (e.g. through excessive price increases in raw materials, blocking access to raw materials, reserving raw materials, etc.).
11. Promote the **development of expertise** in determining what constitutes an **"excessive" price** for medicines and, to this end, encourage the participation of the Belgian Competition Authority in cooperation initiatives between competition authorities (e.g. Bilateral Cooperation, OECD Competition Committee, European Competition Network).

To the government agencies and non-profit organisations that fund non-commercial clinical trials and the non-commercial research institutions that conduct such trials

12. Provide **guarantees** in the financing conditions and in the licensing conditions regarding **access to and fair pricing of** the medicinal product placed on the market.



COLOPHON

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Reported interests:

All experts and stakeholders consulted within this report were selected because of their involvement in the topic of Compulsory Licences. Therefore, by definition, each of them might have a certain degree of conflict of interest to the main topic of this report.

Membership of a stakeholder group on which the results of this report could have an impact: Christine Årdal (Oslo Medicines Initiative, led by the government of Norway and World Health Organization, <https://www.omi-euro.org/>, Herman Van Eeckhout (Employed at pharma.be, the association of the pharmaceutical research industry in Belgium), Marcela Cristina Fogaca Vieira (Member of the Brazilian Working Group on Intellectual Property (GTPI), a coalition of civil society organizations working on access to medicines in Brazil), Charlotte Weyne (Pharma.be, interest group for the innovative pharmaceutical industry in Belgium)

Owner of subscribed capital, options, shares or other financial instruments: Mark Trusheim (Owner of Co-Bio Consulting which provides services to biomedical firms, universities and non-profit organizations regarding drug development and payment models), Herman Van Eeckhout (Funds invested in funds managed by a private banker, part of which in shares of companies active in the health sector. however, no insight into which companies are involved)

Fees or other compensation for writing a publication or participating in its development: Marcela Cristina Fogaca Vieira (Received compensation for writing on a publication about patentability in Brazil from the GTPI (mentioned above), Received compensation for writing a publication analyzing patent laws in Guatemala, Honduras and El Salvador from ITPC – International Treatment Preparedness Coalition, a non-profit public interest civil society organization)

Participation in scientific or experimental research as an initiator, principal investigator or researcher: Christine Årdal (The above mentioned Oslo Medicines Initiative, seeking to improve the accessibility of innovative, high-priced medicines), Ken Shadlen (Conducting social science research in this area), Herman Van Eeckhout (Pharma.be has commissioned studies aimed at demonstrating and supporting the importance of intellectual property for pharmaceutical research), Marcela Cristina Fogaca Vieira (Researcher at the Global Health Centre, Graduate Institute of Geneva, conducting policy research on pharmaceutical innovation and access to medicines)

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Consultancy or employment for a company, an association or an organisation that may gain or lose financially due to the results of this report: Herman Van Eeckhout (Employed at pharma.be, the professional association of the pharmaceutical research industry in Belgium, for which the protection of intellectual property is one of the most important objectives), Charlotte Weyne (Employed at pharma.be, the professional association of the pharmaceutical research industry in Belgium, for which the protection of intellectual property is one of the most important objectives)



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- **The external experts were consulted about a (preliminary) version of the scientific report. Their comments were discussed during meetings. They did not co-author the scientific report and did not necessarily agree with its content.**
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- **The validation of the report results from a consensus or a voting process between the validators. The validators did not co-author the scientific report and did not necessarily all three agree with its content.**
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