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Reform of the pharmaceutical legislation and measures addressing antimicrobial resistance

1. Introduction

For over 50 years, the EU pharmaceutical legislation has set the highest standards of quality, safety and efficacy for the authorisation of medicines while promoting the functioning of the internal market and a competitive pharmaceutical industry. However, ongoing transformations together with the lessons learned from the COVID-19 pandemic and Russia's brutal invasion of Ukraine, call for resolute action to modernise the EU's pharmaceutical framework to make it more resilient, fair and competitive.

Today medicines authorised in the EU are not reaching patients quickly enough and are not equally accessible for patients in all Member States. There are significant gaps in addressing unmet medical needs, rare diseases and the development of new antimicrobials to tackle the growing problem of antimicrobial resistance (AMR). Furthermore, high prices for innovative treatments are a challenge to ensuring timely and affordable access to medicines. Shortages of medicines are also a growing concern, which can have serious consequences for patients.

To remain an attractive place for investment and a world leader in the development of medicines, the EU needs to adapt the regulatory system to developments such as the digital transformation and new technologies to administer medicines to patients. To support EU competitiveness, it is necessary to reduce administrative burden and streamline procedures. Addressing the environmental impact of medicines is important to align this initiative with the objectives of the Green Deal and green economy.

In November 2020, the Commission put forward a Pharmaceutical Strategy for Europe[1] which aims to create a future-proof and patient-centred pharmaceutical environment in which the EU industry can innovate, flourish, and continue to be a global leader. An EU pharmaceutical ecosystem that is crisis-resilient and fit for today's landscape and tomorrow's challenges is one of the central pillars of a strong European Health Union[2] that delivers for citizens. It will complement other key initiatives, including the reinforcement of the EU health security framework with the new legislation on cross-border threats to health and stronger mandates for EU health agencies, the establishment of the Health Emergency Preparedness and Response Authority (HERA) as well as Europe's Beating Cancer Plan and the European Health Data Space.

As a key part of the EU's comprehensive response to these challenges, the Commission is proposing an ambitious revision of the EU pharmaceutical legislation to achieve five main objectives:

1. Make sure all patients across the EU have timely and equitable access to safe, effective, and affordable medicines.
2. Enhance security of supply and ensure medicines are always available to patients, regardless of where they live in the EU.
3. Offer an attractive, innovation- and competitiveness friendly environment for research, development, and production of medicines in Europe.
4. Make medicines more environmentally sustainable.
5. Address antimicrobial resistance (AMR) through a One Health approach, encompassing human health, animal health and the environment.

[1] Communication from the Commission, Pharmaceutical Strategy for Europe (COM/2020/761 final).
[2] https://commission.europa.eu/strategy-and-policy/priorities-2019-2024/promoting-our-european-way-life/european-health-union_en

To deliver on these objectives, the Commission is proposing to reform the EU's pharmaceutical legislation, including through a proposal for a new Directive and a proposal for a new Regulation, to modernise, simplify and replace the following existing legislation: Directive 2001/83/EC[3] and Regulation (EC) No 726/2004[4] (referred to as the 'general pharmaceutical legislation'), Regulation (EC) No 1901/2006 on medicines for children ('Paediatric Regulation')[5], and Regulation (EC) No 141/2000 on medicines for rare diseases ('Orphan Regulation')[6]. In addition, the Commission is proposing a Council Recommendation on AMR to complement and strengthen the EU's response.

Reforming the pharmaceutical legislation is an opportunity to create a patient-centred, forward-looking, and sustainable framework that brings benefits for patients, our society and healthcare systems in Europe while ensuring the EU industry remains globally competitive. It will require cooperation between different stakeholders to bring about positive change. The role of industry will be fundamental, both for meeting patients' needs and for driving innovation and competitiveness, in an area where the EU must maintain its global leadership and strengthen its resilience. The proposed reform draws on extensive consultations of all relevant stakeholders[7].

This Communication provides an overview of the key elements in the proposed reform of the pharmaceutical legislation and the proposed Council Recommendation on AMR.

2. A reform to deliver better access and affordability of medicines for patients across the EU

Promoting timely and equitable patient access to medicines

A central objective of the reform is to ensure that all patients across the EU have timely and equitable access to safe and effective medicines[8]. Today, this is not always the case, especially for innovative medicines, as patient access varies depending on the Member State in which patients live[9].

To reach patients, medicines require a marketing authorisation and must be launched on the market by the company that holds the authorisation. Most innovative medicines receive a central marketing authorisation in the EU which allows them to be on the market in all Member States at the same time. However, the decision to launch a medicine in a given Member State is a commercial decision by the company based on factors such as market size, promotion and distribution networks, and national pricing and reimbursement policies.

[3] 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.
[4] Regulation (EC) No 726/2004 of the European Parliament and of the Council of 31 March 2004 laying down Union procedures for the authorisation and supervision of medicinal products for human and veterinary use and establishing a European Medicines Agency.
[5] 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.
[6] Regulation (EC) No 141/2000 of the European Parliament and of the Council of 16 December 1999 on orphan medicinal products.
[7] Impact Assessment Report on the revision of the general pharmaceutical legislation, Annex 2: Stakeholder Consultation.
[8] In line with the Principle 16 of the European Pillar of Social Rights, (OJ C 428, 13.12.2017, p. 10).
[9] Impact Assessment Report on the revision of the general pharmaceutical legislation, chapter 2.

Consequently, smaller or less wealthy Member States often face limited or delayed product entries on their markets[10].

The proposed reform aims to facilitate faster patient access to innovative medicines across the EU. The measures include facilitating timely marketing authorisations (see chapter 4), while ensuring a robust evaluation of the quality, safety and efficacy of medicines. Moreover, companies will be incentivised to launch their products in all EU Member States and develop products that address unmet medical needs (see chapter 4 for further details on regulatory protection incentives and regulatory support).

The proposed reform will also facilitate earlier market entry of generic and biosimilar medicines. For new medicines that do not benefit from the proposed conditional regulatory protection periods (see chapter 4), market entry of competing generics and biosimilars will occur earlier than under the current rules. Moreover, procedures to authorise generics and biosimilars will be simplified and thereby accelerated.

Currently, there are already provisions that allow developers of generics and biosimilars to conduct studies for future *marketing authorisation* while the originator product is still covered by patent/Supplementary Protection Certificate (SPC)[11] protection (so-called 'Bolar exemption'). The proposed reform will broaden these provisions and make them more predictable for the generics and biosimilars industry, by harmonising their implementation EU wide. Concretely, it will allow to conduct studies to support future *pricing and reimbursement* as well as the manufacture or purchase of patent-protected active substances for the purpose of seeking marketing authorisations during that period, contributing to the market entry of generics and biosimilars on day one of loss of the patent/SPC protection. For orphan medicines, the reform will also ensure that generics and biosimilars can enter the market as soon as the market exclusivity[12] period ends.

Boosting cooperation and transparency to improve affordability of medicines

Affordability of medicines is a persisting challenge for EU healthcare systems and patients that have to pay for them. For reimbursed medicines, high prices can put the financial sustainability of health systems at risk. For medicines that are not fully reimbursed, high prices can have an important impact on patients' financial situation and lead to direct negative health consequences for patients who cannot afford their medicine.

To make medicines more affordable, the Pharmaceutical Strategy for Europe announced actions to support cooperation of Member States on pricing, reimbursement and payment policies, which is an area of national competence. The Commission has transformed the group of National Competent Authorities on Pricing & Reimbursement and public healthcare payers (NCAPR) from an ad-hoc forum to a platform for continuous voluntary cooperation. The Commission is committed to stepping up this cooperation and further supporting information exchange among national authorities, including on public procurement of medicines, while fully respecting the competences of Member States in this area.

Joint procurement of medicines can be a successful form of increased cooperation to improve affordability as well as access to medicines and security of supply. This has been demonstrated by the joint procurement of COVID-19 therapeutics and monkeypox

[10] Impact Assessment Report on the revision of the general pharmaceutical legislation, chapter 2 and Annex 14.
[11] See chapter 4 for further details on intellectual property rights like patents and SPC.
[12] See chapter 4 for further details on regulatory protection incentives like market exclusivity.

vaccines[13]. Member States interested in joint procurement of medicines can make use of available regulatory tools under the current EU rules, such as the Public Procurement Directive[14], the Joint Procurement Agreement[15] and the Financial Regulation currently under revision[16]. Upon request from the Member States, the Commission stands ready to further support and facilitate access to medicines for European patients, in particular for medicines for rare and chronic diseases.

The proposed reform of the pharmaceutical legislation includes a number of measures that will contribute to greater affordability. Measures to facilitate earlier market entry of generic and biosimilar medicines will increase competition between medicines, reduce their prices and promote affordability for patients and the sustainability of healthcare systems. Moreover, the generation of comparative clinical data will be incentivised to strengthen further the assessment of medicines and support downstream decision-making on pricing and reimbursement. In addition, improved cooperation between authorities responsible for marketing authorisation, health technology assessment (HTA)[17,18] and pricing and reimbursement will promote a more coherent approach on issues such as evidence generation along the medicine's lifecycle (see chapter 4).

Transparency of public funding could also contribute to a reduction in medicine prices. Today, the extent of public financial support that has contributed to the research and development of a given medicine is unclear. This lack of transparency regarding the risks borne by the public, as opposed to the investor, creates an uneven playing field during negotiations between industry and pricing and reimbursement authorities. In response to strong calls from patient organisations and other stakeholders, the proposed reform will introduce measures towards greater transparency around public funding for medicine development. Under the proposed reform, pharmaceutical companies will be required to publish information on all direct financial support received from any public authority or publicly funded body to support activities related to research and development of medicines. This information will be easily accessible to the public on a dedicated webpage of the company and through the database of medicinal products for human use authorised in the Union. Such transparency, in turn, is expected to support Member States in their negotiations with pharmaceutical companies, ultimately making medicines more affordable.

Supporting improved affordability of medicines

- Facilitating earlier market entry of generics and biosimilar medicines, to increase competition and thereby reduce prices.
- Incentivising the generation of comparative clinical data, to support Member States in more timely and evidence-based decision-making on pricing & reimbursement.
- Increasing transparency around public funding for medicine development, to support Member States in their price negotiations with pharmaceutical companies.

[13] The Commission published a study on public procurement of medicines providing recommendations to optimise (joint) procurement. Available at https://data.europa.eu/doi/10.2925/044781.
[14] Directive 2014/24/EU of the European Parliament and of the Council of 26 February 2014 on public procurement and repealing Directive 2004/18/EC.
[15] Regulation (EU) 2022/2371 of the European Parliament and of the Council of 23 November 2022 on serious cross-border threats to health and repealing Decision No 1082/2013/EU.
[16] Proposal for a Regulation of the European Parliament and of the Council on the financial rules applicable to the general budget of the Union (recast) COM/2022/223 final.
[17] Health technology assessments evaluate the added value of new medicines compared to existing medicines.
[18] Regulation (EU) 2021/2282 of the European Parliament and of the Council of 15 December 2021 on health technology assessment and amending Directive 2011/24/EU.

- Supporting, through non-legislative action, cooperation between the national competent authorities on pricing and reimbursement, through exchange of information and best practices on national pricing and procurement policies.

3. Enhancing security of supply of medicines and addressing shortages

Medicines shortages have become a growing public health concern for many EU countries[19], but also globally. They represent potential serious risks to the health of patients in the EU and impact on the right of patients to access appropriate medical treatment. Parliament resolutions[20], Council conclusions[21], Member States and relevant stakeholders have signalled a rise in shortages of medicines in recent years.

The Structured Dialogue on security of supply of medicines[22], as well as recent events such as the COVID-19 pandemic, Russian military aggression in Ukraine and high inflation rates, brought to the fore questions regarding the security of supply of medicines in the EU. As noted in the Commission study on medicine shortages, the root causes of shortages are multifactorial, with certain challenges identified along the entire pharmaceutical value chain, including in relation to manufacturing[23]. In particular, shortages of medicines can result from the increased complexity and specialisation of supply chains, the lack of geographical diversification when sourcing certain key ingredients and medicines, and perceived regulatory complexity. The EU's dependency[24] on a limited number of third countries to produce ingredients and medicines is growing, constituting potential supply chain vulnerabilities.

While key elements set out in the associated Staff Working Document[25] on Vulnerabilities of the global supply chains of medicines are integrated in the proposed reform, a number of additional measures have also been initiated or planned to address challenges that were identified through that process. As noted in the Staff Working Document, the Industrial Strategies[26,27] already provide a strong base for action to improve the security of supply of medicines. Future work will also focus on the promotion of green innovation, digital innovation and enhanced cooperation among key players both within the EU and globally. The Commission is also supporting Member States' effort to pool their public resources via Important Projects of Common European Interest (IPCEI) in the area of health to foster the development of innovative, economically and environmentally sustainable technologies going beyond the current state of the art in the sector, and allowing to address market failures.

[19] See, for instance, European Parliament, Committee on the Environment, Public Health and Food Safety, Report of 22 July 2020, Shortage of medicines – how to address an emerging problem, 2020/2071(INI).
[20] For instance, European Parliament Resolution of 17 September 2020 on the shortages of medicines – how to address emerging problem (2020/2071(INI)), recital G.
[21] For instance, Council Conclusions on Access to medicines and medical devices for a Stronger and Resilient EU (2021/C 269 I/02), recital 5.
[22] https://health.ec.europa.eu/medicinal-products/pharmaceutical-strategy-europe/structured-dialogue-security-medicines-supply_en
[23] https://op.europa.eu/en/publication-detail/-/publication/1f8185d5-5325-11ec-91ac-01aa75ed71a1/language-en/format-PDF/source-245338952
[24] In particular, China and India are becoming major producers of pharmaceutical inputs, constituting the centre of production in Asia. Not only is production regionally concentrated, but for many ingredients also limited to a few manufacturers in these countries.
[25] https://health.ec.europa.eu/system/files/2022-10/mp_vulnerabilities_global-supply_swd_en.pdf
[26] Communication from the Commission. A New Industrial Strategy for Europe. COM(2020) 102 final.
[27] Communication from the Commission. Updating the 2020 New Industrial Strategy: Building a stronger Single Market for Europe's recovery. COM(2021) 350 final.

As part of the building blocks of the European Health Union and addressing some of the weaknesses exposed during the COVID-19 pandemic, the mandate of the European Medicines Agency (EMA) was extended[28] to allow for the coordination and management of specific medicines shortages during crises. In addition, the European Health Emergency Preparedness and Response Authority (HERA)[29] was established to ensure the availability of medical countermeasures needed for public health emergencies and address market challenges, through measures such as supply chain monitoring, stockpiling[30] or procurement. As an element in relation to supply chains, the proposed Critical Raw Material Regulation[31] will secure the availability of certain materials relevant for the production of medicines.

While efficient processes have been established within this framework, there is a clear need for greater EU-wide coordination and appropriate measures to safeguard the supply and availability of medicines for EU citizens not only during public crisis but also in normal times.

The reform proposes measures to address supply and availability challenges beyond those in EMA's extended mandate and HERA's role, which are limited to crisis preparedness and response. It will address systemic shortages and improve security of supply of critical medicines at all times by introducing stronger obligations on supply, earlier notification of shortages and withdrawals, and a stronger role of EMA in coordinating actions against shortages. In addition, under the proposed reform, medicines that are considered most critical for EU health systems will be identified in an EU list. This will allow for an analysis of supply chain vulnerabilities of those medicines, followed by recommendations on measures to be taken to improve security of supply (e.g. contingency stocks to be maintained) by marketing authorisation holders, Member States, or other entities. In this context, Member States will also have to report to EMA the measures that they have been taking to strengthen the supply of that medicine.

This way, the EU can efficiently pre-empt supply challenges and ensure continuity of supply of those medicines to EU citizens.

Addressing medicines shortages and supply chain challenges at all times

- The proposed reform introduces requirements for continuous monitoring of shortages of medicines by competent authorities at national level and EMA. Obligations on marketing authorisation holders will be strengthened, including earlier and harmonised reporting of shortages of medicines and maintenance of shortage prevention plans.
- EMA will be empowered with a strengthened coordination role, to monitor and manage critical shortages of medicines at EU level at all times, together with the Executive Steering Group on Shortages and Safety of Medicinal Products. In this context, Member States will also have to report to EMA any foreseen or taken actions at the national level to mitigate or resolve the shortages of a given medicine. Transparency on shortages will

[28] https://eur-lex.europa.eu/legal-content/EN/TXT/?toc=OJ:L:2022:020:TOC&uri=uriserv:OJ.L_.2022.020.01.0001.01.ENG

[29] https://health.ec.europa.eu/system/files/2021-09/hera_2021_decision_en_0.pdf

[30] HERA has a budget of 1.2bn EUR to stockpile medical countermeasures under rescEU. Part of this budget will be used to stockpile antibiotics, while taking care not to exacerbate existing shortages. The stockpiled antibiotics could be deployed to Member States in case of need through the Union Civil Protection Mechanism.

[31] Proposal for a Regulation of the European Parliament and of the Council establishing a framework for ensuring a secure and sustainable supply of critical raw materials and amending Regulations (EU) COM/2023/160 final

be achieved through the publication of information on shortages of medicines at national and EU level.

- An EU-wide list of critical medicines will be established by the Commission and supply chain vulnerabilities will be assessed for those medicines.
- For critical shortages, marketing authorisation holders of medicines will have to work to resolve those shortages, taking into account recommendations and report the results of measures taken. Examples of such recommendations could be to increase or reorganise manufacturing capacity or adjust distribution to improve supply.

4. A reform boosting innovation and EU competitiveness

An effective incentives framework for innovation, access and addressing unmet medical needs

The EU is after the US the second largest market in the world for pharmaceuticals and the pharmaceutical industry in the EU is strong and competitive. It is one of Europe's top performing high-technology sectors, directly employs 840 000 people and three times more indirectly in upstream and downstream employment. Europe (the EU, UK and Switzerland) is the second biggest R&D investor in pharmaceuticals with EUR 39.7 billion in 2020, trailing only US investments of EUR 63.5 billion[32]. In terms of manufacturing high-tech medicines, the EU is a clear global leader, also evidenced by the EU's leading role in supplying the world with COVID-19 vaccines. In 2021 the EU exported pharmaceuticals worth EUR 235 billion, which is EUR 136 billion more than its imports[33]. The EU spends around 1.5% of its GDP on medicines, or EUR 230 billion in 2021, of which more than 80% goes to innovative products[34]. The EU pharmaceutical market accounts for 17% of the global market, making it the second most attractive market for industry, especially for innovators.

The reform of the pharmaceutical legislation aims to maintain and reinforce the position of the EU pharmaceutical industry, both within the EU and globally. The regulatory framework will continue to support innovation and ensure that patients in the EU can benefit from state-of-the-art healthcare and medicines. As COVID-19 has shown, innovation is essential to develop new and better therapies, including new medicines and new uses for existing medicines.

Conducting research on medicines is a complex process, incurring significant costs and risks for developers (e.g. related to the cost and scientific complexity of pre-clinical and clinical research). Moreover, there is international competition to attract pharmaceutical research and development by providing not only a future-proof and stable legal framework but also a favourable environment. Issues like access to capital, available infrastructure and a skilled and qualified labour force are key enablers for medicine development and driving innovation. The revision of the pharmaceutical legislation takes account of the EU competitiveness dimension both from a regulatory and an industrial policy perspective. A proper balance is established between the promotion of innovation, access to medicines and their affordability. The development of new medicines and the availability of medicines that our health systems need depend on a thriving pharmaceutical industry which is a key asset to the EU economy.

[32] The Pharmaceutical Industry in Figures, Key Data. EFPIA, 2022.
[33] Trade surplus in medicinal products records high. Eurostat, 2022.
[34] IQVIA MIDAS database

In the EU, a strong system of intellectual property rights (patents and Supplementary Protection Certificates (SPC)[35]) is complemented by regulatory protection incentives provided by the pharmaceutical legislation. Both intellectual property rights and regulatory protection incentives safeguard and foster innovation and compensate for the risks and costs that developers of innovative medicines incur. At the same time, this system also provides a clear framework for generics and biosimilars to enter the market once the relevant intellectual property rights and regulatory protection periods end.

Medicines can be protected by patents and SPC under national, European and international legal frameworks, including the EU Regulation on SPC[36]. This protection can last for more than 20 years from the time the first patent is filed, usually at an early stage of medicine development. In addition, from the time of marketing authorisation, the EU pharmaceutical legislation provides innovative medicines with 10 years of regulatory protection, which includes 8 years of regulatory data protection[37] and 2 years of market protection[38]. This period can be extended up to 11 years if a new therapeutic indication is added after the initial marketing authorisation. In the case of medicines for rare diseases (orphan medicines), innovative medicines are granted 10 years of market exclusivity[39]. In addition to the above protections, medicines which have conducted the paediatric development plan agreed with EMA receive a six month extension of their SPC.

Together, intellectual property rights and regulatory protection create a strong system for innovation in the EU which is very competitive compared to that of other countries around the world.

However, current investments in developing medicines do not always prioritise the greatest unmet medical needs. This is particularly true for diseases that face scientific challenges (e.g. limited understanding of the disease, limited fundamental research) or limited commercial interest (e.g. rare diseases). As a result, there are serious diseases, such as certain cancers or neurodegenerative diseases, where satisfactory treatments are still lacking. In addition, there are over 6 000 known rare diseases[40], with 95% currently having no treatment option[41]. Concerning medicines for children, there has been good progress in areas where paediatric and adult needs overlap, as development is still steered by the needs of adults. However, in cases where diseases are biologically different in adults and children, like paediatric cancers, mental and behavioural disorders or neonatal conditions, only a limited number of medicines has been developed.

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[35] The supplementary protection certificate is an intellectual property right that serves as an extension to a patent right.

[36] Regulation (EC) No 469/2009 of the European Parliament and of the Council of 6 May 2009 concerning the supplementary protection certificate for medicinal products.

[37] Regulatory data protection refers to the period after the initial authorisation of a medicine during which companies wishing to develop generic or biosimilar versions of the medicine cannot refer to the results of preclinical tests and clinical trials on the medicine included in the initial dossier.

[38] Market protection refers to a period during which generic and biosimilar marketing authorisation applications can already be filed and assessed and the respective marketing authorisations be granted. However, the generic or biosimilar product can only be placed on the market after the expiry of that period.

[39] Market exclusivity refers to a period after marketing authorisation during which similar medicines for the same indication cannot be placed on the market.

[40] https://www.orpha.net/consor/cgi-bin/Education_AboutRareDiseases.php?lng=EN

[41] Joint evaluation of Regulation (EC) No 1901/2006 of the European Parliament and of the Council of 12 December 2006 on medicinal products for paediatric use and Regulation (EC) No 141/2000 of the European Parliament and of the Council of 16 December 1999 on orphan medicinal products SWD(2020) 163.

Moreover, even when innovative medicines have been developed and authorised, not all patients across the EU have access to them in a timely manner.

The proposed reform of the pharmaceutical legislation will move the regulatory protection system from 'one size fits all' to a more targeted approach that promotes patient access to affordable medicines across EU Member States and addresses unmet medical needs. Moreover, innovation in areas of unmet medical needs will also be promoted by targeted EMA regulatory support (see strengthened PRIME scheme discussed in the next section).

Under the proposed reform, innovative medicines will benefit from a standard period of regulatory protection, which is slightly shorter than today, but which can be extended if the product delivers on certain public health objectives (see box below). With the additional conditional protection periods, the maximum period of regulatory protection that can be granted will be even higher than today: Under the proposed reform, the regulatory protection periods can add up to a maximum of 12 years for innovative medicines (if a new therapeutic indication is added after the initial marketing authorisation), while today the maximum is 11 years. For orphan medicines that address a high unmet medical need, regulatory protection periods can add up to maximum of 13 years, while today the maximum is 10 years.

The EU will thus continue to offer one of the most attractive regulatory environments worldwide. Other countries offer from 6 years (Israel, China) to 8 years (Japan, Canada) of regulatory protection on average.

More targeted incentives for innovation with a focus on patient access and unmet medical needs

- Under the proposed reform, the minimum period of regulatory protection for innovative medicines will be 8 years, which includes 6 years of data protection and 2 years of market protection. Companies can benefit from additional periods of regulatory data protection if they launch the medicine in all Member States (+2 years) or if they develop a medicinal product addressing unmet medical needs (+6 months) or conduct comparative clinical trials (+6 months). An additional year of data protection can be granted for a new therapeutic indication.
- These above new rules on regulatory protection will also apply to paediatric medicines. In addition, medicines which have conducted the paediatric development plan agreed with EMA will continue to receive an extension of 6 months of their SPC. Moreover, rules on paediatric development plans will be adapted to further stimulate research and development of medicines for diseases that affect only children.
- Specific provisions will apply to orphan medicines, to boost research and development in rare diseases. The standard duration of market exclusivity for orphan medicines will be 9 years. Companies can benefit from additional periods of market exclusivity if they address a high unmet medical need (+1 year), launch the medicine in all Member States (+1 year), or develop new therapeutic indications for an already authorised orphan medicine (up to 2 extra years).
- The additional regulatory protection for market launch in all Member States will be granted if the medicine is continuously supplied in sufficient quantity in all Member States within two years of marketing authorisation, or within three years for companies with limited experience in the EU system e.g. small and medium-sized enterprises (SMEs). If a Member State issues a waiver (e.g. because it wishes for market launch to take place only at a later point in time), the additional regulatory protection will still be granted.

- New therapeutic uses of established medicines (repurposing) can benefit from a four year data protection period. Furthermore, non-profit entities will be able to submit to EMA evidence supporting new therapeutic indications addressing unmet medical needs for already authorised medicines.

It is important to note that the proposed reform of the pharmaceutical legislation will not affect intellectual property (patent and SPC) protection. In this respect, the Commission is presenting in parallel a reform of the SPC regulation, which will create a centralised examination procedure for the granting of national SPCs and a unitary SPC for medicines, without changing the substance of the applicable rules (e.g. eligibility conditions, duration, etc.). For SPC applicants, the proposed reform will considerably alleviate the costs and administrative burden of the current SPC regime, which is currently implemented at a purely national level. By improving the legal certainty and transparency of the SPC regime, this initiative will also be beneficial for generics producers. Importantly, the initiative will also ensure that innovative pharmaceutical industry can reap the benefits of the unitary patent through a corresponding unitary SPC.

In conclusion, the combination of patents/SPC and regulatory protection will continue to safeguard the EU's competitive edge globally in pharmaceutical development, while steering research and development towards the greatest patient needs and ensuring more timely and equitable patient access to medicines across the EU.

Rewarding innovation in areas of unmet medical need by boosting regulatory support for the development of promising medicines

EMA offers scientific support to medicine developers on the most appropriate way to generate robust evidence on a medicine's benefits and risks (e.g. scientific guidance on the design of clinical trials), with the aim to support the timely and sound development of high-quality, effective and safe medicines for the benefit of patients.

The proposed reform will further strengthen EMA's scientific support, particularly for promising medicines under development for unmet medical needs, building on the experience gained with the priority medicines scheme (so called PRIME)[42]. Such priority medicines will receive enhanced scientific and regulatory support and benefit from accelerated assessment mechanisms. This strengthened PRIME scheme will boost innovation in areas of unmet medical needs, allow pharmaceutical companies to speed up the development process and promote earlier patient access.

In addition, the reform will make it easier to repurpose off-patent medicines for new therapeutic uses, with a dedicated EMA support scheme for SMEs and not-for-profit developers.

The reform will also expedite the assessment of promising medicines by leveraging the possibility of a 'rolling review' approach that reviews data in phases as they become available. This approach has proven effective during the COVID-19 pandemic and the reform seeks to extend it to promising medicines that offer an exceptional therapeutic advancement in areas of unmet medical needs. A temporary emergency marketing authorisation at EU level will be introduced for public health emergencies where there is a major interest in developing and authorising safe and effective medicines as quickly as possible.

[42] https://www.ema.europa.eu/en/human-regulatory/research-development/prime-priority-medicines

Improving the regulatory system for Europe to remain an attractive place to invest and innovate

An efficient and agile EU regulatory system plays a crucial role in supporting the development and timely authorisation of medicines and their availability to patients. It also creates a favourable environment for boosting the innovation capacity and competitiveness of the pharmaceutical industry.

Currently, the scientific evaluation of medicines for an EU marketing authorisation involves significant 'clock-stops' during which companies prepare responses to EMA requests for information missing from the initial application. The proposed strengthening of EMA' scientific support to medicine developers, before the submission of applications for marketing authorisation, will improve the quality of initial applications, reduce delays caused by 'clock-stops' and expedite evaluations for marketing authorisation. Incomplete applications will be invalidated during the evaluation, if applicants fail to provide the missing data within set deadlines. This will free resources and optimise the evaluation system. Additionally, the reform proposes to reduce the scientific assessment time from 210 days today to 180 days and the time for the Commission to authorise the medicine from 67 to 46 days. For medicines which are of major interest from the point of view of public health the assessment time will be 150 days. These reduced timelines together with the above mentioned support measures will ensure that medicines reach patients faster.

Moreover, the proposed reform will improve EMA's structure and governance, by simplifying the structure of its scientific committees and by increasing its expertise-based capacity. It will avoid duplication of work, increasing efficiency and reducing evaluation times of medicines, while maintaining the high standards and scientific expertise. Additionally, the reform includes various measures to simplify regulatory procedures and foster digitisation, thereby reducing the administrative burden for medicine developers and competent authorities (see box below).

Small and medium-sized enterprises (SMEs) and not-for-profit entities involved in medicine development will benefit particularly from the proposed reform, as it will reduce their regulatory burden. EMA will also offer targeted scientific and regulatory support, including fee reductions or waivers schemes, to SMEs and not-for-profit entities.

Regulatory support and simplification measures to reduce regulatory burden

- Strengthening the early regulatory support by EMA, particularly for promising medicines under development for unmet medical needs.
- Introducing, for promising medicines that offer an exceptional therapeutic advancement in areas of unmet medical needs, the possibility for EMA to reviews data in phases, as they become available.
- Setting up a temporary emergency marketing authorisation at EU level for public health emergencies where there is a major interest in developing and authorising safe and effective medicines as quickly as possible.
- Optimising EMA's structure (e.g. fewer scientific committees), with a focus on expertise and capacity-building within the network of competent authorities.
- Simplifying regulatory procedures (e.g. abolishing marketing authorisation renewal in most cases, and simplifying requirements for authorising generic and biosimilar medicines).
- Reducing the assessment time by EMA from 210 days (in practice, on average 400 days) today to 180 days and the time for the Commission to authorise the medicine from 67 to

46 days. In addition, products addressing unmet medical needs and bringing major contributions to public health needs could benefit from an accelerated procedure and be assessed in 150 days.

- Digitisation (e.g. electronic submission of applications, electronic product information).

The improved EMA structure combined with the strengthened EMA scientific support, simplified procedures and digitisation will reduce the time needed to evaluate and authorise medicines. This will contribute to improving the competitiveness of the EU regulatory system, while also facilitating timely patient access to innovative medicines, generics and biosimilars.

Moreover, a number of future-proofing measures will ensure that the regulatory system can keep pace with scientific and technological progress, and create an enabling regulatory environment for promising new therapies and breakthrough innovation, in line with the Innovation Principle[43]. This also comprises promoting innovative methods, including those aimed at reducing animal testing. The reform will enable for the first time the possibility for regulatory sandboxes in the field of medicines. They provide a structured testing environment in which innovative methods and novel medicinal products can be tried out under the supervision of regulators. Regulatory sandboxes offer an opportunity to learn not just about innovation, but also about the rules and regulations underpinning it and how they are best applied to future technologies. The learnings from those sandboxes can be over time translated into adapted regulatory frameworks, another new element of the reform, thereby creating tailored horizontal rules that meet the required regulatory standards, while fully accommodating innovative elements.

The secondary use of health data has the potential to enhance the efficiency and effectiveness of medicines development, reduce costs, and improve patient outcomes. For instance, health data can be used to identify unmet medical needs, to optimise clinical trial design, and to support evidence generation for marketing authorisation. Additionally, real-world data can be used to monitor the safety and efficacy of medicines post-authorisation and to support continuous learning and improvement in healthcare. The reform of the pharmaceutical legislation together with the European Health Data Space will facilitate access to and use of health data, while protecting patient privacy. Opening the way for the secondary use of health data for regulatory purposes will offer a unique opportunity for innovation and boost the competitiveness of the pharmaceutical industry in the EU.

Future-proofing the regulatory framework

- Facilitate use of real-world evidence, and of health data for regulatory purposes, while protecting patient privacy.
- Improved clarity on the interplay between EU legislative frameworks for medicines and for other health technologies (e.g. medical devices, substances of human origin).
- Regulatory sandboxes for testing new regulatory approaches for novel technologies before formal regulation.
- Adapted frameworks with specific regulatory requirements tailored to the characteristics of certain novel medicines.
- Promote use of new methodologies to reduce animal testing.

[43] https://research-and-innovation.ec.europa.eu/law-and-regulations/ensuring-eu-legislation-supports-innovation_en

The proposed reform will promote cooperation among the various public authorities in the EU involved in different aspects of a medicine's lifecycle. For example, EMA will coordinate a mechanism to facilitate exchange of information and knowledge on scientific and technical issues of common interest among authorities responsible for marketing authorisation, clinical trials, health technology assessment (HTA), and pricing and reimbursement of medicines in the EU. This will enable a more coherent approach to issues such as unmet medical needs and evidence generation along the medicine's lifecycle. The reform will also facilitate cooperation between EMA and other EU agencies, such as those in the field of chemicals, in line with the 'one substance, one assessment' approach.

The Pharmaceutical Committee[44] will serve as a forum for discussing policy issues related to medicines, such as the application of the rules on the regulatory incentive for market launch, to ensure enhanced dialogue, close interaction, and a proactive exchange of information between the Member States and the Commission. Other national authorities (e.g. for HTA, pricing and reimbursement) may be invited to participate in discussions of the Pharmaceutical Committee. The measures for cooperation among public authorities will improve policy coherence and create a more predictable and consistent environment for investors and innovators in the EU.

Overall, these reforms represent an important step towards a more efficient and effective regulatory framework, better equipped to address emerging challenges and to support the competitiveness of the pharmaceutical sector and innovation that benefits patients in the EU.

5. Making medicines more environmentally sustainable

To achieve the environmental sustainability ambitions of the Pharmaceutical Strategy and other initiatives in the European Green Deal[45] (e.g. the EU Action Plan 'Towards a Zero Pollution for Air, Water and Soil'[46]), the pharmaceutical industry needs to curb the negative impact of its products and processes on the environment, biodiversity and human health.

Scientific evidence shows that pharmaceuticals are present in the environment because of manufacture, patient use, and improper disposal of unused or expired products[47]. The fact that antimicrobials have been detected in wastewater treatment, manufacturing effluent, surface and ground waters is of particular concern, as their presence boosts antimicrobial resistance (see chapter 6). Pharmaceuticals present in the environment are affecting not only the environment; if they enter the water cycle or the food chain, they also affect human health directly.

Such negative effects have been considered in the recently adopted Commission proposal for the Urban Waste Water Treatment directive[48], which includes an Extended Producer Responsibility scheme that also applies to pharmaceuticals and in the Commission proposal for amending the water directives,[49] which is addressing pharmaceuticals that are present in surface and groundwaters.

[44] Council Decision 75/320/EEC of 20 May 1975 setting up a pharmaceutical committee.
[45] Communication from the Commission. The European Green Deal. COM (2019) 640 final.
[46] Communication from the Commission. Pathway to a Healthy Planet for All EU Action Plan: 'Towards Zero Pollution for Air, Water and Soil' COM (2021) 400 final.
[47] OECD: Pharmaceutical Residues in Freshwater Hazards and Policy Responses, 2019.
[48] Proposal for a Directive of the European Parliament and of the Council concerning urban wastewater treatment (recast) COM (2022) 541 final.
[49] https://environment.ec.europa.eu/publications/proposal-amending-water-directives_en

The proposed reform of the pharmaceutical legislation responds to a number of commitments in the Strategic Approach to Pharmaceuticals in the Environment[50]. It strengthens the environmental risk assessment (ERA) of medicines to ensure a better evaluation and limit the potential adverse impacts of medicines on the environment and public health. Today, the ERA is mandatory for all pharmaceutical companies placing their medicines on EU markets and covers the use and disposal of medicines into the environment. Moreover, in the future, work on promoting EU environmental standards internationally will continue.[51]

Strengthening the environmental risk assessment under the marketing authorisation

- Enhancing ERA by introducing a refusal ground for the marketing authorisation where companies do not provide adequate evidence for the evaluation of the environmental risks or if the proposed risk mitigation measures are not sufficient to address the identified risks.
- Setting clearer ERA requirements, including compliance with scientific guidelines, regular ERA updates, and post-authorisation obligation for additional ERA studies.
- Extending the ERA scope to cover the risks to the environment from the manufacturing of antibiotics.
- Extending ERA to all products already in the market and potentially harmful to the environment.

For investigational medicines containing or consisting of genetically modified organisms (GMOs), the reform establishes one single EU ERA procedure for clinical trials. As a result, a single harmonised, EU-wide assessment will replace Member State assessments, meaning that sponsors of clinical trials will no longer have to submit multiple authorisation requests. Additionally, the ERA requirements for the assessment of medicines containing or consisting of GMOs for the purpose of authorisation will be based on the principles set out in Directive 2001/18/EC[52], but will be adapted to take into account the specificities of medicines. These changes will remove significant and time-consuming regulatory hurdles, facilitate clinical trials in the EU and optimise evaluation and authorisation of innovative, life-changing treatments.

6. Combating antimicrobial resistance

Antimicrobials[53] are among the most essential medicines. However, over the years, their overuse and misuse have led to an increase in antimicrobial resistance (AMR), meaning that they become ineffective, and infections are becoming increasingly difficult, if not impossible, to treat. AMR, the 'silent pandemic', is responsible for more than 35 000 deaths every year in the European Union[54] and leads to high costs for healthcare systems[55]. AMR is considered one of the top three health threats in the EU[56].

[50] Communication from the Commission. European Union Strategic Approach to Pharmaceuticals in the Environment. COM (2019) 128 final.
[51] For more information see Section 7 of the Staff Working Document on Vulnerabilities of the global supply chains of medicines, https://health.ec.europa.eu/system/files/2022-10/mp_vulnerabilities_global-supply_swd_en.pdf.
[52] Directive 2001/18/EC of the European Parliament and of the Council of 12 March 2001 on the deliberate release into the environment of genetically modified organisms and repealing Council Directive 90/220/EEC (OJ L 106, 17.4.2001, p. 1).
[53] Antimicrobials include antibiotics, antivirals, antifungals and antiprotozoals.
[54] https://www.ecdc.europa.eu/sites/default/files/documents/Health-burden-infections-antibiotic-resistant-bacteria.pdf

To address increasing AMR, it is essential to ensure both access to existing antimicrobials and the development of novel effective ones. To avoid that microorganisms develop resistance against those antimicrobials, measures for their prudent use are also proposed.

However, curbing the use of antimicrobials has an impact on sales volumes and on the return on investment for marketing authorisation holders, which is responsible for the market failure. That is why incentives for developing innovative antimicrobials and securing access to antimicrobials are needed.

Development of, access to, and prudent use of antimicrobials

Incentives for development of and access to antimicrobials

The EU needs both push incentives (i.e. funding for antimicrobial research and innovation, primarily via research grants and partnerships) and pull incentives (both regulatory and financial) to reward successful development and secure access to effective antimicrobials. The Commission is proposing the following pull incentives:

- Temporary mechanism consisting of transferable data exclusivity vouchers, for the development of novel antimicrobials to be granted and used under strict conditions.
- Procurement mechanisms for access to new and existing antimicrobials that would guarantee revenue for antimicrobials marketing authorisation holders, regardless of sales volumes.

The EU needs to find smart ways to enable the development of novel antimicrobials as a matter of urgency. This is why the reform proposes to test for 15 years a transferable data exclusivity voucher scheme for novel antimicrobials. The voucher will grant an additional year of regulatory data protection[57] to the developer of the antimicrobial, which the developer can either use for one of its own products or sell to another marketing authorisation holder. The eligibility to the scheme will be restricted to game-changing antimicrobials that address antimicrobial resistance and the priority pathogens recognised by WHO. Strict conditions will govern the use of the voucher, so that the main reward goes to the developer of the innovative antimicrobial. The proposed scheme also includes conditions for the supply of the antimicrobial to ensure its delivery when required.

A voucher scheme creates an attractive business case for the development of innovative antimicrobials for which the current research pipeline is very limited. This scheme will ultimately transfer the costs of the vouchers to the Member States' health systems, by delaying the market entry of generics of the products covered by the vouchers. To curtail the costs for the health systems, the reform will restrict the number of vouchers reserved for novel antimicrobials to maximum 10 vouchers that can be granted over a period of 15 years. Therefore, the vouchers, if applied under strict conditions, represent a credible measure against AMR as their benefits and costs need to be weighed against the cost of inaction and the impact of AMR on public health and the economy. After the 15 years period, the voucher scheme will be evaluated.

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[55] https://www.oecd.org/health/health-systems/AMR-Tackling-the-Burden-in-the-EU-OECD-ECDC-Briefing-Note-2019.pdf , 2019.

[56] The other two key priority threats are according to the assessment carried out by Commission services, together with the Member States, pathogens with high pandemic potential as well as chemical, biological, radiological and nuclear (CBRN) threats.

[57] The concept of regulatory data protection is explained in more detail in chapter 4 of this document.

In addition to the voucher scheme, financial pull incentives – in the form of procurement mechanisms – could be brought in. A Commission study on bringing AMR medical countermeasures to the market[58], assessed four major types of procurement mechanisms that may help increase the expected revenue for developers: revenue guarantee, market entry rewards combined with revenue guarantee, lump-sum market entry rewards and milestone payments. With the annual revenue guarantee mechanism, the public authorities 'top up' revenue for developers to reach the 'guaranteed' amount. If sales reach the threshold amount, no further 'top up' is awarded. Market-entry rewards consist of a series of financial payments to an antibiotic developer for successfully achieving regulatory approval for an antibiotic that meets specific pre-defined criteria. Milestone-Based Reward is an early-stage financial reward upon achieving certain R&D objectives prior market approval (e.g. successful completion of phase I). While these mechanisms would serve primarily to provide access to existing antimicrobials, they could also support new antimicrobials in the development phase. The initial pre-feasibility assessment determined that all options may be implemented as procurement transactions – notwithstanding some notable restrictions and considerations that require further in-depth investigation. Both EU and Member State contributions will probably be required.

Global support for the development of antimicrobials is greatly needed. The EU will have to step up cooperation through existing fora, notably the G7, G20, the Transatlantic Task Force on Antimicrobial Resistance, the Quadripartite (World Health Organization, UN Food and Agriculture Organization, World Organisation for Animal Health and United Nations Environment Programme), the AMR Multi-Partner Trust Fund and in the negotiations on a potential World Health Organization international agreement on pandemic prevention, preparedness and response[59] and with regional institutions such as the African Union.

Measures for prudent use of antimicrobials

- Through the reform of the pharmaceutical legislation, measures for prudent use will become part of the marketing authorisation process, covering the prescription status, adequate pack size, specific patient/healthcare professional information, an antimicrobial stewardship plan including risk mitigation measures, and monitoring and reporting of resistance to the antimicrobial.
- Through the proposal for a Council Recommendation, additional support measures will be proposed, including recommended targets and measures to promote high levels of infection prevention and control, to improve awareness, education and training and to foster cooperation between stakeholders from all relevant sectors.

Recommended targets for antimicrobial consumption and resistance

The proposed Council recommendation provides for concrete measurable targets to reduce antimicrobial consumption (AMC) and the spread of AMR in the human health. These targets were designed with the support of the European Centre for Disease Prevention and Control taking into account national situations and the different levels of AMC and spread of key resistant pathogens across the Member States. They allow for targeted support and for monitoring the progress in the coming years.

[58] European Commission, European Health and Digital Executive Agency, Study on bringing AMR medical countermeasures to the market : final report, Publications Office of the European Union, 2023, https://op.europa.eu/en/publication-detail/-/publication/51b2c82c-c21b-11ed-8912-01aa75ed71a1/language-en

[59] https://www.who.int/news-room/questions-and-answers/item/pandemic-prevention--preparedness-and-response-accord

Other recommended measures to combat antimicrobial resistance

The proposed Council Recommendation also aims to boost national One Health action plans on AMR, foster research and innovation, reinforce surveillance and monitoring of AMR and antimicrobial consumption, enhance global actions and incentivise the development of other AMR medical countermeasures such as vaccines and rapid diagnostics, which are also pivotal. The proposed Council Recommendation will also contribute to a stronger framework to fight AMR, combining a One Health approach with other EU policies, the Common Agricultural Policy[60], the Farm to Fork Strategy[61] , the Zero Pollution Action Plan[62] aiming at reducing by 50% the overall EU sales of antimicrobials for farmed animals and in aquaculture by 2030, the EU's Horizon Europe programme[63] and the recent Commission proposals leading to stricter environmental monitoring of AMR[64].

7. Conclusion

The proposed reform of the pharmaceutical legislation will pave the way for a stronger and more resilient European Union that better protects the health of its citizens. It will promote timely and equal access to a continuous supply of safe, effective and affordable medicines that meet the medical needs of patients across the EU. At the same time, it will stimulate further innovation and support the pharmaceutical industry's competitiveness. And it will enhance the environmental sustainability of medicines throughout their lifecycle.

In parallel, the proposed Council Recommendation on antimicrobial resistance, together with the related measures proposed under the reform of the EU pharmaceutical legislation, will complement and extend actions under the 2017 EU One Health Action Plan against AMR. Together they will equip the EU with the tools it needs to combat this silent pandemic.

As a result, the ambitious package of proposals that are part of the reform will bring lasting health, social, economic and environmental benefits to EU citizens. It will support the innovation capacity and competitiveness of the pharmaceutical sector in the EU. It will help address global challenges like AMR and environmental sustainability, while strengthening the EU's global leadership in the pharmaceutical field, complementing the EU's role in global health and supporting the rollout of the EU Global Health Strategy.

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[60] https://agriculture.ec.europa.eu/common-agricultural-policy/cap-overview/cap-glance_en

[61] Communication from the Commission to the European Parliament, the Council, the European Economic and Social Committee and the Committee of the Regions A Farm to Fork Strategy for a fair, healthy and environmentally-friendly food system, COM/2020/381 final.

[62] Communication from the Commission to the European Parliament, the Council, the European Economic and Social committee and the Committee of the Regions Pathway to a Healthy Planet for All EU Action Plan: 'Towards Zero Pollution for Air, Water and Soil', COM/2021/400 final.

[63] Regulation (EU) 2021/695 of the European Parliament and of the Council of 28 April 2021 establishing Horizon Europe – the Framework Programme for Research and Innovation, laying down its rules for participation and dissemination, and repealing Regulations (EU) No 1290/2013 and (EU) No 1291/2013 (OJ L 170, 12.5.2021, p. 1).

[64] Commission proposal of 26 October 2022 for a Directive of the European Parliament and of the Council amending Directive 2000/60/EC establishing a framework for Community action in the field of water policy, Directive 2006/118/EC on the protection of groundwater against pollution and deterioration and Directive 2008/105/EC on environmental quality standards in the field of water policy. COM(2022) 540 final 2022/0344 (COD) and Commission proposal of 26 October 2022 for a Directive concerning urban wastewater treatment (recast) COM(2022) 541 final, 2022/0345 (COD).