

# Revision of the EU's general pharmaceutical legislation

*This briefing is one of a series of implementation appraisals produced by the European Parliamentary Research Service (EPRS) on the operation of existing EU legislation in practice. Each briefing focuses on a specific EU law that is likely to be amended or reviewed, as envisaged in the European Commission's annual work programme. Implementation appraisals aim at providing a succinct overview of publicly available material on the implementation, application and effectiveness to date of specific EU law, drawing on input from EU institutions and bodies, as well as external organisations. They are provided by the Ex-Post Evaluation Unit of the EPRS to assist parliamentary committees in their consideration of new European Commission proposals, once tabled.*

## SUMMARY

The European Union has been regulating pharmaceuticals for over 50 years. The legal regulation aims to protect public health and ensure the proper functioning of the internal market in medicinal products. In 2020, the European Commission published a pharmaceutical strategy for Europe aimed at reinforcing the EU pharmaceutical system by making it more patient-centred and resistant to crises (such as pandemics). The achievement of these objectives requires the revision of several pieces of EU legislation regulating pharmaceuticals, including the EU general pharmaceutical legislation (Directive 2001/83/EC and Regulation (EC) No 726/2004). This briefing informs parliamentary decision-making by presenting findings on the implementation of the EU legislation falling within the scope of the revision.

## Background

On 11 November 2020, the European Commission published the [communication](#) 'Building a European Health Union – Reinforcing the EU's resilience for cross-border health threats'. Efforts to build a strong European Health Union aim to better protect citizens' health, improve the resilience of the national health systems, better equip the EU and its Member States to prevent and address future health crises (such as pandemics), and make effective, innovative and safe medicines both available and affordable for patients. Policy initiatives, such as the adoption of [Regulation \(EU\) 2022/2371](#) on serious cross-border threats to health, the establishment of the [Health Emergency Preparedness and Response Authority](#) (HERA), the reinforcement of the [European Medicines Agency](#) (EMA) and the [European Centre for Disease Prevention and Control](#) (ECDC) are among the European Health Union's building blocks.

On 25 November 2020, the Commission published another step in building the European Health Union – [A pharmaceutical strategy for Europe](#). The strategy aims to: i) guarantee patient access to innovative and affordable medicines and address currently unmet medical needs, as regards, for example, cancer, rare diseases and antimicrobial resistance (AMR); ii) support EU industry sustainability, innovative capacity and competitiveness and the development of high quality, effective, safe and more environmentally friendly medicines; iii) strengthen EU crisis preparedness and response mechanisms, including ensuring EU pharmaceutical supply needs are covered by robust supply chains at all times; and iv) ensure the EU promotes a high level of safety, quality and



efficacy standards across the world. Meeting these objectives requires both legislative and non-legislative action, including revision of the EU general pharmaceutical legislation.

## The EU general pharmaceutical legislation – Key features

The EU has been developing a policy on pharmaceuticals for human use for over 50 years. It employs legal regulation as the main policy instrument. The first piece of legislation – [Council Directive 65/65/EEC](#) on the approximation of the law relating to medicinal products – was adopted at EU level in 1965, in the aftermath of the thalidomide tragedy.<sup>1</sup> In the 1990s, the EU life sciences sector experienced negative trends in terms of investment in pharmaceutical research and development (R&D), which affected patients and the competitiveness of the EU pharmaceutical industry on the global market. Furthermore, the perspective for the EU to integrate new Member States (and their markets) created a risk of an even more fragmented pharmaceutical regulatory system across the EU. Addressing these challenges required policy action, which resulted, among other things, in a major revision of the EU legislative framework on pharmaceuticals. In particular, as an essential part of the reform, [Regulation \(EC\) No 726/2004](#) laying down Community procedures for the authorisation and supervision of medicinal products for human and veterinary use and establishing a European Medicines Agency (the regulation) was adopted in 2004 and [Directive 2001/83/EEC](#) on the Community code relating to medicinal products for human use (the directive) was revised. Together, the directive and the regulation are commonly referred to as the 'EU general pharmaceutical legislation' as they regulate medicinal products through their entire lifecycle – R&D, marketing authorisation, and post-marketing authorisation. The 'general legislation' is complemented by 'specialised legislation' on orphan medicinal products intended to treat rare diseases ([Regulation \(EC\) No 141/2000](#)), medicinal products for paediatric use ([Regulation \(EC\) No 1901/2006](#)), and advanced therapy medicinal products that are based on the manipulation of genes, cells or tissues ([Regulation \(EC\) No 1394/2007](#)).

The EU general pharmaceutical legislation aims to protect public health and ensure the proper functioning of the internal market in medicinal products. A key feature of the legislation is that a medicinal product – i.e. a substance or combination of substances – cannot be placed on the market before it has been authorised via the relevant procedure. Manufacturers wishing to market their medicines must provide detailed therapeutic information about the applicant product, including possible adverse reactions. To gain authorisation, the quality, safety and efficacy of the applicant product must be tested and assessed for its benefits and risks. Authorisation might be refused if a medicine's 'risk-benefit' ratio is unfavourable or its therapeutic effect is insufficiently substantiated. There are two types of authorisation procedures – the 'centralised (EU-level) authorisation procedure' (laid down by the regulation and with the EMA and the Commission in the lead) and the 'national authorisation procedures' (harmonised under the directive and with national competent authorities and national scientific advisory bodies in the lead). Once granted, authorisation is valid for five years and is renewable.

The centralised authorisation procedure is mandatory in some cases (for example, for orphan medicinal products, advanced therapy medicinal products, or products treating cancer, neurodegenerative disorders, human immunodeficiency virus (HIV), diabetes), and optional in others (for example, if a new active substance is involved, or the innovative product is of patient interest at EU level). Manufacturers wishing to market a product eligible under the centralised authorisation procedure must submit their application directly to the EMA, which takes care of the validation and scientific evaluation of the application. In particular, the agency's committee for medicinal products for human use carries out a scientific assessment of the application and makes a recommendation on whether the product should be authorised by the risk manager (the European Commission). A marketing authorisation granted via the centralised authorisation procedure allows (but does not oblige) the marketing authorisation holder to sell the product and make it available to patients and healthcare professionals across the EU/EEA.

The national authorisation procedures are harmonised under the directive and can take the form of: i) procedures applied to medicinal products marketed in an individual Member State; ii) a 'mutual recognition procedure' (national marketing authorisation has already been granted by at least one

Member State and mutual recognition of the authorisation is sought in others; this is used for the majority of conventional medicinal products), and iii) a 'decentralised procedure', where the application for marketing authorisation is submitted simultaneously in several Member States (one of them acts as the reference Member State).

Article 14(11) of the regulation grants the medicinal products authorised under the regulation an eight-year data protection (data exclusivity) and a ten-year market protection (extendable up to 11 years) period. Intellectual property rights (IPRs) also stem from other pieces of EU legislation, for example, [Regulation \(EC\) No 469/2009](#) concerning the supplementary protection certificate for medicinal products (SPC regulation). However, thanks to the 'Bolar exemption' (Article 10(6) of the directive), the testing required to obtain an authorisation for a 'generic' or 'biosimilar' can take place during the patent/SPC protection period of the 'reference medicinal product' (i.e. the product holding the marketing authorisation or simply, the 'original product'). This allows generic or biosimilars to become available for patients soon after the expiry of the patent/SPC term of the original product.

A '**generic medicinal product**' (a 'generic') is a product that has the same qualitative and quantitative composition in active substances and the same pharmaceutical form as the reference medicinal product, and whose bioequivalence with the reference medicinal product has been demonstrated by appropriate bioavailability studies.

A '**similar biological medicinal product**' (a '**biosimilar**') is a biological medicinal product highly similar to another already approved biological medicinal product. Biosimilars are approved against the same standards for quality, safety and efficacy applicable to all biological medicinal products.

The EU general pharmaceutical legislation also contains detailed requirements on the information (batch number, expiry date, storage precautions) that must be displayed on the outer packaging of the product, as well as on controls on the advertising of medicinal products to the general public (more specifically, the information must be presented objectively, not exaggerate the product's properties and not be misleading). Furthermore, pharmacovigilance systems are used by the marketing authorisation holder and national competent authorities to monitor the effects of medicines, assess any adverse reactions and, ultimately, detect any change to their risk-benefit ratio.

## European Commission

### Ex-post evaluation of the EU general pharmaceutical legislation

The ex-post evaluation of the implementation of the legislation was done in parallel to the ex-ante impact assessment (ex-ante IA) of the revision (i.e. a 'back-to-back' initiative). The process was informed by several support studies prepared for the European Commission. The findings of the [study](#) supporting the ex-post evaluation aspects of the revision are presented below,<sup>2</sup> following the criteria for ex-post evaluations set by the [Better Regulation Guidelines](#) (relevance, effectiveness, efficiency, coherence and EU added value). The findings concern the implementation of the legislation in scope between 2005 and 2020, in European Economic Area (EEA) countries, i.e. all EU Member States, including the United Kingdom (still part of the single market in 2020), as well as Iceland, Liechtenstein and Norway. The study collected data from a large number of secondary (existing) sources as well as from stakeholders through an [open public consultation](#) (run between 28 September and 21 December 2021), a targeted survey and interviews. The stakeholders represent the following groups: public authorities, civil society and patient organisations, industry, healthcare professionals and their associations, academic and public research organisations and experts; individual citizens submitted feedback to the open public consultation.

The study developed an intervention logic of the legislation and its implementation showing how the co-legislators expected it to work when it was adopted.<sup>3</sup> It set main (or general) objectives, stemming from the need to guarantee a high level of public health and the proper functioning of the EU internal market. The **general objectives** identified are to ensure: i) quality, safe and efficacious medical products; ii) regulatory attractiveness in the global context; iii) access to medicines, and iv) a competitive EU internal market.<sup>4</sup>

The study finds that the objectives of the EU general pharmaceutical legislation are still relevant to current needs even 15 years after its adoption and despite the fact that several pieces of EU specialised legislation are applied in parallel. In particular, the legislation has responded well to: the need to stimulate the development of innovative medicines in Europe and authorise high quality, safe, and efficacious medicines; the need to continue monitoring the safety of medicines after their authorisation via a centralised pharmacovigilance system; and the need to ensure compliance with the requirements on marketing, manufacturing and distribution of medicines. However, the current provisions do not fully guarantee that authorised medicines are marketed in all Member States to ensure equitable access for patients across the EU/EEA. The relevance of the legislation to the need for equitable access for patients to medicines is therefore low. Furthermore, new objectives should be formulated to ensure relevance to future needs, such as the legislation's readiness and adaptability to respond to technological developments, or the rapidly increasing presence of digitalisation in new tools generating regulatory evidence and medicinal products that prevent, diagnose and target diseases. The legislative framework also needs to create incentives to ensure development of medicines for high priority unmet medical needs, such as therapies against AMR infection. Complex and advanced therapies need to be recognised as medicinal products under the legislation, which would ensure that their manufacturers could benefit from the authorisation procedures, thereby increasing their relevance.

Under the **effectiveness** criterion, the question is whether the objectives of the legislation are being met (or progress is being achieved) as a result of its implementation. The study's general conclusion on effectiveness is that the EU general pharmaceutical legislation is a successful EU intervention in the sense that it achieved all four high-level objectives, although to a varying extent.

The study finds that the legislation has been 'most effective' with regard to the objective of **ensuring quality, safety and efficacy of medicinal products**. The centralised authorisation procedure is considered to be a major enabler of this achievement, as it allows for effective and robust authorisation of medicines at EU level. The centralised authorisation procedure together with the mutual recognition procedure and decentralised procedure, services offered by the EMA (such as pre-authorisation scientific advice), accelerated assessment and the streamlining of processes, are considered 'key achievements' by stakeholders across all categories. These regulatory features also stimulated innovation and ultimately have improved quality standards, thereby ensuring the availability of efficacious and safe medicines for patients in the EU. Further improvements are required however as regards, for example, the assessment of microbiome products, genetically modified organisms (GMOs), environmental risk, and better integration of digitalisation and emerging science and technology developments in the current regulatory system, to stimulate innovation in particular.

The centralised authorisation procedure is also assessed as contributing to a coherent and **attractive EU regulatory system** for developing pharmaceuticals. This increases the EU's attractiveness in the global context in terms of both market and location for pharmaceutical development and manufacturing. However, the study finds that the objective of ensuring the EU's attractiveness was achieved only to a moderate extent. The EU remains the second-largest market for pharmaceuticals, after the USA with more than twice the size of the EU market. The US regulatory system (where the US Food and Drug Administration (FDA) is the regulatory agency) is still preferred by developers when submitting applications for innovative products. Requests for new active substance authorisations are largely first submitted (including by EU-based developers) to the US FDA (first-choice jurisdiction) followed by a submission to the EU regulatory system (second-choice jurisdiction).<sup>5</sup> Nevertheless, the proportion of substances authorised by the US FDA that are not authorised by the EMA has fallen over time, which, according to the study, is a sign of a globally attractive EU regulatory system. Although the EU legislation has proven flexible in accommodating much development and innovation in the pharmaceutical sector (such as advanced therapy medicinal products), it has not been fully effective in accommodating emerging technological developments (such as substances of human origin or new manufacturing methods (for example, decentralised or continuous manufacturing)).<sup>6</sup> Stakeholders suggest this is due to the lack of coherence in some aspects of the EU regulatory system, which can make it less attractive for

developers, in particular for small and medium-sized enterprises (SMEs). Some stakeholders note that the legislation has not been successful in increasing the EU's regulatory attractiveness in specific areas, due to a lack of adequate incentives for innovation by SMEs, academic/industrial collaborations, innovation addressing unmet medical needs, and innovation in generics, biosimilars, and antimicrobials. This observation correlates with the fact that, although growing, R&D investment in the EU (more than €40 billion in 2019) still lags behind the US (€74 billion in 2019). In the EU, R&D is concentrated mainly in universities and other public research organisations. However, their developments (including cell and gene therapies for cancer and some genetic diseases) often fail to reach the market because academics do not necessarily have the required regulatory knowledge and capacity, have little experience of product development, or do not have the right production capacity. All this negatively affects EU pharmaceutical sector competitiveness and patient access to new products.

The study assesses that the legislation has been least effective in terms of ensuring **access to affordable medicines** and addressing the associated affordability and shortage of medicines issue. Access to medicines across the EU remains uneven. It is of note, however, that access to medicines is the result of factors that go beyond the scope of the legislation.<sup>7</sup> The legislation affects access via its market authorisation procedures. The study therefore warns that granting market access, even if via the centralised authorisation procedure, does not automatically guarantee the authorised product will be available for all EU/EEA patients, because access might be hindered, for example, by reimbursement issues in the country concerned. Furthermore, the centralised authorisation procedure does not oblige the market authorisation holder to market the medicinal products on all, or a minimum number, of EEA/EU Member State markets. Uneven and delayed access to medicines might also be the result of differences in Member State interpretation and implementation of the EU general pharmaceutical legislation (and related EU law). Nor is **affordability**, which is an essential aspect of access to medicines, directly addressed by the EU general pharmaceutical legislation. However, the data exclusivity and market protections granted by Article 14(11) of the regulation as well as other IPR protections (such as patent/SPCs)<sup>8</sup> and the protection afforded to orphan and paediatric medicines delay the entry of generics and biosimilars that are otherwise expected to decrease prices and increase medicine affordability for patients. **Medicine shortages** is another issue negatively affecting access to medicines, as patients are at risk of sub-optimal care and higher healthcare costs. The rising number of shortage notifications is seen (by the health professionals stakeholder group) as a sign of ineffective implementation of the legislation in scope. The study notes however that the rising number of notifications may also mean that more countries are tracking and hence reporting more shortages, or simply doing it more effectively; furthermore, the predominant number of notifications resulting from 'quality and manufacturing' issues<sup>9</sup> could be seen as a success in increasing the observance of manufacturing standards and ultimately as a sign of effective implementation of the legislation. In any case, the legislation has not yet sufficiently addressed the reasons behind the observed shortages or mitigated their impact. Generics are reported to be at higher risk because of the greater relative fragility of their supply chain.

#### Applicants' choice of regulatory system

The study notes that the choice of a regulatory system for submitting an authorisation application depends mainly on the market size to which authorisation would give market access. Data requirements, the time needed for the assessment of the marketing authorisation application by the relevant agency, and specific local epidemiological situations might also be decision drivers as to where to apply first. The fact that applicants need to interact with several EMA committees, for instance in the case of advanced therapy medicinal products, reduces the EU regulatory system's attractiveness.

The study notes that the objective of **ensuring the competitive functioning of the EU internal market was achieved to a moderate extent**. Given that there is no competition between the different therapeutic areas (as treatment substitution is not possible), markets can only be understood if the therapeutic areas are analysed separately. Some stakeholders (among the groups of public authorities, healthcare professionals and civil society) question whether there is an EU

internal market for pharmaceuticals at all, insisting that, in practice, there are several national or even regional markets. Stakeholders agree that competition in the EU pharmaceutical sector is sub-optimal. Nevertheless, many stakeholders agree that, thanks to the 'Bolar exemption', the legislation was instrumental in increasing competition in the sector by easing the entry of generics and biosimilars into the market immediately upon expiry of the protection of the original product. Furthermore, the EU is a frontrunner in the adoption of biosimilars, creating authorisation pathways earlier than other countries. Between 2006 and 2021, 84 biosimilars were authorised for use in the EU, while the US FDA only approved the first biosimilar in 2015 and has approved only 29 biosimilars (only 18 of which are sold on the US market) since then. This accelerated EU uptake of biosimilars has a positive effect on patients, who have easier access to medicines, and ultimately increases competition (between the biosimilar and the original product).

Under **efficiency**, the question is whether the costs and benefits stemming from the implementation of the EU legislation are proportionate. The study outlines costs and benefits for citizens (consumers), businesses and regulatory bodies (the EMA and national competent authorities). In quantitative terms, the study finds that the changes introduced by the 2004 revision have likely resulted in a net increase in regulatory costs to society ranging between €1.1–€1.8 billion over a 15-year period. As regards quantified benefits, the 2004 revision is estimated to have resulted in more innovative medicinal products (25-30) and a better-quality regulatory system, which is likely to have led to a positive health impact for patients treated with such products, as these would otherwise not have been available, or would have been available only later. Using the 'quality-adjusted life year' (QALY) approach for assessing health impacts prescribed by the EU Better Regulation [toolbox](#) – where one QALY is one year lived in perfect health – the 25-30 innovative medicines produced 170 000-210 000 QALYs in total, ranging from €4.8–€17.2 billion. While the quantification of costs and benefits was challenging (given that it results in large ranges for the cost and benefit monetary estimates), stakeholders (across all groups) are generally positive that the costs of implementation of the EU general pharmaceutical legislation (as revised in 2004) are proportionate to the benefits. There are however notable differences in the opinions of the various stakeholder groups. For businesses and regulatory bodies, costs and benefits are balanced. Patients however are not so convinced; patient groups believe that the legislative changes introduced in 2004 (and subsequent rounds of minor revisions) were 'strongly beneficial to the industry, offering valuable incentives that have supported investment in innovative medicines but have increased prices for those products' that affect patients' interests. Patients are thus far less positive about the cost-benefit balance (from their own perspective) and are concerned about uneven access, affordability, shortages of medicines, and unmet medical needs.

Under **coherence**, the question is how well aligned the directive and the regulation (and their implementation) are between themselves; with other pieces of EU specialised pharmaceutical legislation; and with other relevant EU legislation. The study did not identify contradictions, overlaps or other inconsistencies between the regulation and the directive. There are however 'potential' coherence issues between the EU general and specialised pharmaceutical legislation, namely with the Orphan Regulation and the Paediatric Regulation, identified by the 2020 [joint evaluation](#) of the latter. There are also coherence issues between the EU general pharmaceutical legislation and other pieces of EU legislation whose implementation and enforcement may affect the objectives of the former. Pieces of EU legislation touching upon healthcare issues concern, for example, blood, tissues and cells ([Directive 2002/98/EC](#) and [Directive 2004/23/EC](#)), medical devices ([Regulation \(EU\) 2017/745](#)), health technology assessment ([Regulation \(EU\) 2021/2282](#)), GMOs (several pieces of legislation),<sup>10</sup> basic safety standards in the context of radiopharmaceuticals ([Council Directive 2013/59/Euratom](#)), transparency and sustainability of EU risk assessment in the food chain ([Regulation \(EU\) 2019/1381](#)). EU legislation that does not directly relate to healthcare concern, for example, data protection ([Regulation \(EU\) 2016/679](#) and [Regulation \(EU\) 2018/1725](#)), the registration, evaluation, authorisation and restriction of chemicals (REACH – [Regulation \(EC\) No 1907/2006](#)), and policy areas, currently under revision, such as SPCs, ground water ([Directive 2006/118/EC](#)), urban waste-water treatment ([Council Directive 91/271/EEC](#)) and environmental quality standards in the field of water policy ([Directive 2008/105/EC](#)).

Based on the consensual opinion of stakeholders across all groups, the study notes that the implementation of the EU general pharmaceutical legislation has a large **EU added value**. Stakeholders consider that, without action at EU level, Member States would have been able to put in place appropriate measures only to a 'small or moderate extent'. The legislation has created a robust framework for harmonising regulations, incentives, standards, administrative requirements and procedures for medicinal products across the EU/EEA. For stakeholders, the centralised authorisation procedure and pharmacovigilance have improved the availability of high-quality, safe, and efficacious medicines in the EU/EEA. The EMA is prized as a key player in this process. The EU regulatory networks coordinated by the agency create a space for valuable exchange of experience and access to a wide range of scientific and technical expertise that would not be available in one country or region alone. Furthermore, the centralised authorisation procedure, in which the EMA is a key actor, is assessed as 'particularly valuable' for smaller Member States that do not possess the necessary resources and expertise to establish their own systems. The EU added value of the legislation was also demonstrated during the COVID-19 pandemic. More specifically, the action triggered at EU level, for example, the EMA's granting of conditional marketing authorisation for the first COVID-19 vaccine only nine months into the pandemic) enabled a faster and coordinated action compared to what Member States would have been able to achieve if acting alone. For stakeholders, this response results from regulatory flexibilities and optimisations enabling resources, capacities, expertise, and information technology capabilities to be rapidly mobilised across EU.

## Revision of the EU general pharmaceutical legislation

On 26 April 2023, against the background of the results from the ex-post evaluation, the EU and national experience gained during the pandemic, the ambition to build a European Health Union, and its pharmaceutical strategy in particular, the European Commission submitted a [proposal](#) for a directive and a [proposal](#) for a regulation. These long-awaited proposals constitute the first major reform of the EU general pharmaceutical legislation (and complementary legislation) since 2004. They would repeal the EU general pharmaceutical legislation (the directive and the regulation currently in force) and the regulations on orphan and paediatric medicines; and amend related legislation on colouring substances that may be added to medicinal products ([Directive 2009/35/EC](#)), clinical trials on medicinal products for human use ([Regulation \(EU\) No 536/2014](#)), and the Advanced Therapy Medicinal Products Regulation. The objectives of the reform defined by the [Commission](#) are to: i) create a single market for medicines ensuring that all patients across the EU have timely and equitable access to safe, effective, and affordable medicines; ii) continue to offer an attractive and innovation-friendly framework for R&D and production of medicines in Europe; iii) reduce the administrative burden drastically by speeding up procedures to significantly reduce authorisation times for medicines, so that they reach patients faster; iv) enhance availability and ensure medicines can always be supplied to patients, regardless of where they live in the EU; v) address AMR and the presence of pharmaceuticals in the environment through a 'One Health' approach; and vi) make medicines more environmentally sustainable. The achievement of these objectives relies on a number of measures. For example, marketing of innovative medicines would have a minimum regulatory protection of eight years – six years (data exclusivity protection) and two years (market protection). Manufacturers may benefit from additional protection periods increasing the total period up to a maximum of 12 years (compared to 11 years today). These additional protection periods can be granted if the manufacturers launch the medicine in all Member States (plus two years), if the medicine concerns an unmet medical need (plus six months), etc. An additional year of data protection could be granted if the medicine can also treat other disease(s). The Commission expects the additional regulatory protection of two years (if medicines are launched in all Member States) to increase access by 15 %, i.e. 67 million more EU patients could potentially benefit from a new medicine.

## European Parliament

On 26 April 2023, a few hours after the European Commission submitted its proposed reforms, the European Parliament's Committee on the Environment, Public Health and Food Safety (ENVI) held

an [exchange of views](#) with Commissioner Stella Kyriakides, who presented the new policy measures. The European Parliament's commitment to improving the EU regulation of pharmaceuticals and its implementation is also evidenced by the active non-legislative parliamentary work briefly introduced below.

## European Parliament resolutions

In November 2021, the European Parliament adopted an own-initiative (INI) [resolution](#) on a pharmaceutical strategy for Europe.

As regards **access to medicines**, Parliament underlines that healthcare is a human right enshrined in the United Nations [Universal Declaration of Human Rights](#) and regrets the disparities in access to high-quality healthcare services, including access to medicinal products between Member States and different regions within Member States. In this context, Parliament calls for national and EU measures, including legislative measures where appropriate, to address these disparities and guarantee patients' rights to universal, affordable, effective, safe and timely access to essential and innovative medicines. It is also 'concerned that ... innovative medicines are expensive or in certain Member States not even brought to the market for commercial reasons'. Parliament welcomes the Commission's intention to review the EU pharmaceutical legislation with the aim of promoting robust and fair competition, supporting Member States in stabilising and balancing national drug pricing systems, promoting fair national drug pricing systems and ensuring equal access to medicines and medical products across the Member States. Parliament's sustained commitment to the issue of access to medicines is also evidenced in a topical own-initiative [resolution](#) of March 2017 on EU options for improving access to medicines.

Parliament recalls that the EU's open strategic autonomy is linked to a constant and sufficient availability of medicines in all Member States. It calls on the Commission, Member States and EMA to develop an early warning system for **medicine shortages**, based on an innovative, user-friendly, transparent and centralised European digital platform to exchange information and data on shortages and focus on supply problems. Such a system should be capable of determining the volume of existing medicine stocks and demand and provide data that helps in detecting, predicting and preventing shortages of medicinal products. The Commission is called upon to increase public-private collaboration and monitor all relevant supply stakeholders' obligation to provide early and transparent information on the availability of medicines, demand for medicines, parallel trade activities, export bans and market distortions, without undue regulatory and administrative burdens. The resolution also recalls that the root causes of the issue should be addressed and tackled as a matter of urgency, considering the links between the supply chain and production challenges. Parliament therefore calls on the Commission to ensure that the revision of the EU general pharmaceutical legislation builds on a good understanding of the root causes of medicine shortages. It highlights that the Union's pharmaceutical industry needs a diversified supply chain and a medicine shortage risk mitigation plan to cope with any vulnerabilities and risks. However, sustainable systemic policies need to be put in place before resorting to disproportionate regulatory requirements, an obligation to supply, penalties, or ill-conceived stockpiling that could fragment the single market or threaten products' economic sustainability, which may lead to further shortages. Parliament's views on the issue of medicine shortages and means to address them are expressed in detail in an own-initiative [resolution](#) adopted in September 2020.

As regards the need for **innovative (including research in pharmaceuticals) capacity and (global) competitiveness of the EU pharmaceutical industry**, Parliament calls on the Commission to, among other things, assess and revise where appropriate the system of incentives to promote R&D of new medicines for UMNs, prioritising public interest and patient safety when assessing projects promoted by the pharmaceutical industry to combat cancers, including paediatric cancers, in particular to incentivise first-in-child development of paediatric anticancer medicines; rare diseases; neurodegenerative and mental illnesses; and AMR; with the aim of finding more therapeutic options and meeting patient and health system needs. Furthermore, when revising pharmaceutical legislation, the Commission is called upon to draw up a regulatory framework geared to the deployment of radiological and nuclear technologies for therapeutic (and not solely



diagnostic) purposes. Parliament insists further that a competitive, self-sufficient and sustainable EU pharmaceutical industry is of strategic importance for the EU, as it fosters innovation, research and high-quality employment and is more responsive to patients' needs.

The EU industry's innovative capacity and competitiveness are, among other things, assessed in the context of the **quality of the regulatory environment and the need for digitalisation**. The resolution points out that the industry needs a stable and predictable regulatory environment, which limits the administrative burden and safeguards the principle of prevention and the availability of safe, effective and high-quality medicines on the EU market. Parliament underlines that the marketing authorisation system should build on the existing legislative framework and prevent duplication and any additional administrative burden. It welcomes the strong focus and several initiatives included in the pharmaceutical strategy on the need to optimise and modernise the existing regulatory framework, such as through revision of the various pieces of EU legislation on pharmaceuticals, more digitalised and efficient regulatory processes, implementation of electronic product information (ePI), streamlined active pharmaceutical ingredient (API) assessment, and better 'good manufacturing processes', manufacturing management and resources. Parliament also welcomes the revision of pharmaceutical legislation to reduce red tape and to adapt it to cutting-edge products, scientific advances and technological transformation. It thus urges the Commission to make swift progress on this agenda, making the best use of existing digital tools at EU level (for example, telematics). Parliament calls on the Commission to further facilitate access to global markets for the EU pharmaceutical industry, including SMEs, through a level playing field and a robust and clear regulatory framework promoting the highest standards of quality and safety at international level and facilitating trade agreements that prize innovation-based competitiveness, to make the pharmaceutical sector a strategic pillar of the EU. In this context, it highlights the importance of removing trade and non-tariff barriers in third countries, and ensuring fair access to international markets for companies operating in the EU.

Parliament stresses, among other things, the need for an **environmentally friendly and climate-neutral** pharmaceutical industry covering the whole lifecycle of medicinal products, while ensuring patient access to safe and effective pharmaceutical treatments. It also calls on the Commission to strengthen inspection and auditing throughout the production chain, particularly outside the EU. The Commission is urged to ensure quality environmental sustainability standards for APIs imported from non-EU countries. Parliament also calls upon the Commission to respond to the demands expressed in its own-initiative resolution on a strategic approach to pharmaceuticals in the environment adopted in September 2020. The Commission should revise the pharmaceutical legislation to strengthen the environmental risk assessment requirements and conditions for the approval and use of medicines, provided that marketing authorisations are not delayed or refused solely on the grounds of adverse environmental impacts.

Parliament considers that **AMR** constitutes a serious threat to public health and calls on the Commission and Member States to fund projects aimed at improving diagnostics and developing new antibiotics, as well as developing a protocol for the prudent use of antibiotics and an awareness campaign for health professionals to encourage more targeted treatment based on patients' actual needs. It is imperative that a common EU therapeutic guide for antimicrobials be introduced to set up traceable antimicrobial use reduction targets at EU level, and that communication campaigns on AMR be coordinated through a single calendar at EU level to increase the awareness of AMR, resistant variants and their consequences. The one health approach, on which Parliament adopted an own-initiative [resolution](#) in September 2018, should guide the reduction and optimisation of antimicrobial use, as well as the development of new medicines, including antimicrobial agents. Parliament calls on the Commission and Member States to assess the existing legislative framework relevant to AMR and, where appropriate, the Commission should make a proposal for revision.

Other specific policy aspects addressed by the 2021 parliamentary resolution on the pharmaceutical strategy for Europe include the pricing and costs of pharmaceuticals; the role of generic and biosimilar medicines; delayed availability of medicines on the market; public-private partnerships and innovation; HERA; procurement practices; clinical trials; health technology assessment; increasing resilience in terms of sustainable medicines, crisis preparedness and response

mechanisms; a European health data space, health data and general data protection requirements; structured dialogue with stakeholders; and patents and agreements on trade-related aspects of IPRs. On IPRs, Parliament calls on the Commission to provide for a possibility to temporarily authorise the granting of compulsory licences in the event of a health crisis when preparing the revision of the regulation, to allow for production of generic versions of life-saving medicines.

## Written questions from Members of the European Parliament

Members of the European Parliament have submitted a large number of written questions to the Commission on various aspects of the implementation of the EU general pharmaceutical legislation, including in the context of the coronavirus pandemic, and specifically on the issues falling in the scope of the revision of the current legislation. One example of a recent written question concerning shortage of medicines is presented below.

### [Written question](#) submitted by Loucas Fourlas (EPP, Cyprus) on 13 February 2023

According to the author, disruption to the production and supply chain caused by the pandemic and the Russian invasion of Ukraine have led to shortages of medicines in recent years. The issue has been exacerbated further by problems of supply and inadequate notification of shortages and withdrawal from the market. Effort must therefore be made to ensure full transparency regarding stocks, guarantee access to medicines for all patients in need of them and avoid any disruption of the EU market in this sector. In this context, the author asks: i) what measures is the Commission taking to ensure adequate supplies of medicinal products on the EU market; and ii) how are the stocks of different types of medicines verified?

### [Answer](#) given by Stella Kyriakides on behalf of the Commission on 4 April 2023

The Commissioner replies that the root causes of medicines shortages have been identified by a 2021 [study](#) for the Commission on medicine shortages and the 2022 Commission [staff working document](#) on the security of medicines supply. These documents map areas of focus at EU level, including both new and ongoing action to improve the security of supply and availability of critical medicines, APIs and raw materials. The Commissioner refers to the forthcoming (as of 4 April 2023) revision of the EU general pharmaceutical legislation, which would envisage stronger obligations on market authorisation holders and a harmonised approach for reporting shortages. In addition, following the 2022 reinforcement of its role in crisis preparedness and management ([Regulation \(EU\) 2022/123](#)), the EMA can better monitor shortages of medicines across the EU and can take measures to mitigate shortages. The agency also coordinates the work of national competent authorities with the aim of monitoring and mitigating shortages. In case of cross-border health emergencies, HERA can help in ensuring the development and equitable distribution of key medical countermeasures to address supply chain vulnerabilities and help prevent shortages. Finally, the root causes of shortages are multifactorial, relating to, for example, increased demand, manufacturing and quality issues, supply chain disruptions and pricing and reimbursement policies.

## Petitions and citizens' enquiries

Individual EU citizens and representative organisations are concerned by the implementation of the EU general pharmaceutical legislation, including issues within the scope of the revision or issues specific to the coronavirus pandemic. This is evidenced by the individual citizens' enquiries and petitions<sup>11</sup> received by the European Parliament.

## Council of the European Union

On 5 May 2023, an [informal meeting](#) of the EU Member States' health ministers took place in Stockholm (under the Swedish Presidency of the Council of the EU) with a focus on access to medicines. The Council has also addressed pharmaceuticals on several previous occasions. In its [conclusions](#) of 15 June 2021 on access to medicines and medical devices for a stronger and resilient

EU, the Council stresses, in the context of the revision of the pharmaceutical legislation, the need to adapt the EU regulatory framework to improve market **access for medicines** of the highest quality, efficacy and safety. The ministers support sustainable **innovation** and access to generics, biosimilars, and other well established products, as well as **health sector sustainability and European pharmaceutical industry competitiveness**. As regards **medicines shortages**, the Council invites the Commission and Member States to support collaboration and coordination within the regulatory network, early communication strategies on possible supply disruptions between all stakeholders within the supply chain and identification of additional sources of supply. To ensure patients' needs are met, the Commission and Member States are also invited to collaborate on identifying unmet medical needs and their causes, as well as areas of public health concern, such as **AMR** and the **environmental impact** of pharmaceutical manufacturing.

Pharmaceuticals are also addressed in the Council's 2021 [conclusions](#) on the strengthening the European Health Union.

## EU advisory bodies

In its [opinion](#) of 7 May 2021 discussing the pharmaceutical strategy, among other things, the European Committee of the Regions welcomes the Commission's intention to revise the legislation with a view to addressing needs in terms of **access to medicines for patients (including affordable prices), medicines shortages, research and innovation, EU pharmaceutical industry competitiveness, environmental risk assessment of medicines and AMR**. The European Committee of the Regions stressed that local and regional authorities, especially in Member States where they have primary responsibility for public health policy, play key roles in the funding, evaluation, procurement and provision of medicines and in crisis management and preparedness. It is therefore essential for the local and regional level to be involved in the forms of cooperation proposed in the pharmaceutical strategy.

In its [opinion](#) on the pharmaceutical strategy of 27 April 2023, the European Economic and Social Committee (EESC) also comments on needs related to **access (including affordability and availability), medicine supply shortages, innovative research and development, EU pharmaceutical industry competitiveness, support for the objectives of the European Green Deal, and AMR**. The EESC notes that 'under the current framework conditions, the European pharmaceutical sector has in recent years evolved in a direction that has led in part to misuse of the various incentive schemes, that lacks transparency in many respects and that has resulted in a concentration on business areas with high profit margins and in some cases excessive price demands. The EESC therefore feels that there is an urgent need to revise and adapt the current regulatory framework for medicines and to link it more closely to conditionalities relating to affordability and availability'.

## Court of Justice of the European Union

The Court of Justice of the European Union has delivered several judgments relevant to the legislation. These judgments provide guidance on the interpretation of provisions on, for example, the mutual recognition procedure ([C-452/05](#)) and the definition of a 'reference medicinal product' ([C-527/07](#)).

## ENDNOTES

- <sup>1</sup> In the late 1950s, the consumption of thalidomide by pregnant women in many countries resulted in the birth of thousands of babies with limb malformations.
- <sup>2</sup> The back-to-back initiative was announced by the Commission on 7 April 2021. According to the proposals for a directive and a regulation published on 26 April 2023, the Commission findings from the ex-post evaluation had to be published under Annex V to the staff working document (SWD) presenting the results of the ex-ante impact assessment (see p. 7 of both proposals). However, at the time of publication of the Commission proposals, Annex V to the SWD did not contain the results of the ex-post evaluation, but information related to the ex-ante IA instead. On 27 April 2023, the Ex-post Evaluation Unit of EPRS asked the Commission to submit the results of the ex-post evaluation. At the time of completing this briefing on 11 May 2023, this document had not been submitted; the Commission submitted the document on 12 May 2023. To ensure timely publication, therefore, this implementation appraisal presents findings of the study prepared by an external contractor in support of the Commission ex-post evaluation and not the Commission's findings. However, these latter may be consulted [here](#).
- <sup>3</sup> At the time the proposals for a directive and a regulation were submitted by the Commission, in 1999 and 2001 respectively, the development of an intervention logic was not yet a formal regulatory requirement. Nor were the proposals accompanied by a comprehensive ex-ante IA.
- <sup>4</sup> The intervention logic also developed the following specific objectives stemming from the general ones: i) to accommodate innovation; ii) reduce administrative burden, improve adaptability of the regulatory environment; iii) reduce disparities across Member States and duplication of efforts; and iv) facilitate free movement of medicines.
- <sup>5</sup> The study notes that new active substances (authorised by all agencies) are first submitted to the US regulatory system and only a few days later (on average) to the EU regulatory system. Submissions to the other regulatory systems (Japan, Canada, Switzerland, Australia) takes place 63-150 days later (on average) after the submission to the US.
- <sup>6</sup> According to the pharmaceutical strategy (p. 19), these methods create new manufacturing models, with a shift from industrial to 'bedside' manufacturing (i.e. shift from the production of personalised medicines from being exclusively in the factory towards a fine-tuning at the patient's bedside). These methods may speed up the production, but may also create challenges in terms of quality, inspection and oversight.
- <sup>7</sup> The study warns that access is defined by fulfilment of the following criteria: i) a medicine has been (conditionally or fully) approved for marketing, ii) has been placed on the market by the marketing authorisation holder; and iii) is made available to patients as part of (partially) reimbursed care. The EU legislation has to do only with the first factor, while the second and the third are beyond its direct reach.
- <sup>8</sup> See details on the implementation of the SPC Regulation in Huemer, M.-A. Revision of the supplementary protection certificates regulations for pharmaceutical and plant protection products, [Implementation appraisal](#), EPRS, 2023
- <sup>9</sup> Other root causes for medicines shortages listed on p. 39 of the study are: commercial reasons; unexpected increased demand; distribution issues; regulatory issues; unpredicted major events and natural disasters; and other issues.
- <sup>10</sup> Some of the building blocks of the EU GMO legislation are [Directive 2001/18/EC](#) on the deliberate release of GMOs into the environment, [Regulation \(EC\) 1829/2003](#) on genetically modified food and feed, [Directive \(EU\) 2015/412](#) as regards the possibility for the Member States to restrict or prohibit the cultivation of GMOs in their territory.
- <sup>11</sup> See, for example, [petition No 0875/2018](#) by Jesús Mallol Escobar (Spanish) on the failure by Spain to comply with Directive 2001/83/EC; [petition No 0006/2021](#) by F.B. (Greek) on the authorisation of the Pfizer BioNTech vaccine against COVID-19; and [petition No 0513/2017](#) by R. N. S. (German) on multidrug-resistant pathogens and the (alleged) lack of responsibility of the European pharmaceutical sector.

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