

Revision of the EU pharmaceutical legislation

Impact assessment accompanying a Commission proposal for a directive of the European Parliament and of the Council on the Union code relating to medicinal products for human use (COM(2023) 192), and for a regulation of the European Parliament and of the Council laying down procedures for the authorisation and supervision of medicinal products for human use and establishing rules governing the European Medicines Agency (COM(2023) 193).

This briefing provides an initial analysis of the strengths and weaknesses of the European Commission's [impact assessment](#) (IA) (SWD(2023) 192, SWD(2023) 193 (summary)) accompanying the Commission proposal for a directive on the Union code relating to medicinal products for human use ([COM\(2023\) 192](#)), and for a regulation laying down procedures for the authorisation and supervision of medicinal products for human use and establishing rules governing the European Medicines Agency ([COM\(2023\) 193](#)). The Commission put forward its proposal on 26 April 2023 and it was referred to the European Parliament's Committee on the Environment, Public Health and Food Safety (ENVI). It is one of the flagship initiatives of the EU's 2020 [pharmaceutical strategy](#) – a core building block of the [European health union](#) – and was included in both the 2022 Commission [work programme](#) and in the [joint declaration](#) on legislative priorities for the years 2023 and 2024.

The proposed revision¹ addresses both the EU's general and specific pharmaceutical legislation. The **general pharmaceutical legislation** – introduced in 1965 and last comprehensively revised in 2004² – regulates the marketing authorisation, manufacturing, distribution and monitoring of medicines for human use. Furthermore, it provides for regulatory protection periods (i.e. data protection and market protection that protect a new medicine against competition from generic or biosimilar medicines) to reward pharmaceutical companies for their medicinal innovations.³ It consists of [Directive 2001/83/EC](#) on the **Community code** relating to medicinal products for human use, and [Regulation \(EC\) No 726/2004](#) regarding the **authorisation and supervision of medicinal products** and establishing the European Medicines Agency (EMA).

The **specific pharmaceutical legislation** includes the **Paediatric Regulation** ([\(EC\) No 1901/2006](#)), which regulates medicines for children and obliges companies to screen new adult medicines under development for possible use in children, and the **Orphan Regulation** ([\(EC\) No 141/2000](#)), which provides for medical needs of people with rare diseases.⁴ In principle, marketing authorisation, pharmacovigilance and quality requirements of paediatric and orphan medicines⁵ are governed by the same provisions as those applied to 'general' medicines. The specific legislation aims to incentivise research and development (R&D) in view of the small populations concerned, limitations in scientific knowledge and the industry's generally low interest in developing medicines for a small market (IA, part II, p. 12). Typical incentives include market exclusivity for orphan medicines and a prolonged duration of supplementary protection certificates (SPC)⁶ for paediatric medicines.

The proposed revision of the pharmaceutical framework forms part of a package, comprising

- a [proposal](#) for a **new directive** that would repeal and replace the Community Code Directive 2001/83/EC and Directive 2009/35/EC (regulating colouring matters added to medicinal products), and incorporate relevant parts of the Paediatric Regulation;
- a [proposal](#) for a **new regulation** that would repeal and replace the above-mentioned Regulation (EC) No 726/2004 (regarding medicine authorisation and supervision) and



- the Orphan Regulation, and repeal and incorporate relevant parts of the Paediatric Regulation;
- a Commission [communication](#) outlining the key elements of the proposed reform; and
 - a [proposal](#) for a Council recommendation to step up the fight against antimicrobial resistance, which the Council already [adopted](#) on 22 June 2023.

The legislative proposals are supported by **two separate impact assessments** that were prepared in parallel by the Commission's Directorate-General for Health and Food Safety (DG SANTE), but eventually published as a twin pack under one and the same cover (SWD(2023) 192). **One IA relates to the general pharmaceutical legislation (part I of the SWD), while the other covers the legislation on paediatric and orphan medicines (part II of the SWD).** Their presentation suggests that the revision of the EU's pharmaceutical legislation had initially been conceived as two parallel, coherent initiatives that would 'work synergistically' (IA, part II, p. 12), and that the merger was decided only at a later stage in the process. A justification can be found in the explanatory memorandum of the proposed directive, which reasons that 'the merger of the Orphan Regulation and the Paediatric Regulation with the legislation applicable to all medicinal products will allow for simplification and increased coherence' (COM(2023) 102, p. 3).

Problem definition

Following a succinct outline of the political and legal context, each of the two IAs discusses the problems identified, their underlying drivers and the ensuing consequences in adequate depth. The problem definition appears well developed, underpinned by numerous references to qualitative and quantitative data from Commission internal and other sources. Certain key issues are explained in greater detail in dedicated annexes, such as factors influencing access to affordable medicines (IA, part I, Annex 14 and part II, Annex 10); antimicrobial resistance (AMR) (IA, part I, Annex 15); and the international context (IA, part II, Annex 8).

The problem definition of both IAs builds on the results of the respective evaluation, in line with the 'evaluate first principle'. The 2023 [evaluation](#) of the **general pharmaceutical legislation**⁷ confirmed the continued relevance of the current framework with regard to public health protection and harmonisation of the internal market for medicines, but also identified the following problems:

- 1 **Unmet medical needs:** medical needs of patients are not sufficiently met with currently available treatments, despite the rise in the number of authorised medicines. This concerns, among other conditions, antimicrobial resistance (AMR) and neurodegenerative diseases.
- 2 **Unequal access to medicines across the EU:** notably in smaller EU Member States, access to newly authorised medicines lags behind.
- 3 **Affordability of medicines posing challenges for health systems:** medicines – and in particular innovative medicines – are often costly, while conditions for generic and biosimilar medicines are often unfavourable.
- 4 **Shortages of medicines:** as became apparent during the COVID-19 pandemic, medicine shortages have increased in recent years owing to complex and diversified global supply chains and manufacturing challenges, among many other factors.
- 5 **Regulatory shortcomings:** the regulatory framework does not sufficiently cater for innovation, scientific advances and the digital transformation, and creates unnecessary administrative burden.
- 6 **Medicines in the environment:** residues of medicines enter the environment (during manufacturing, use by patients and disposal), posing a risk to human health (e.g. AMR); in this respect, the current requirements for an environmental risk assessment prior to marketing authorisation was found to have weaknesses.

With regard to **paediatric and orphan medicines** (i.e. the specific pharmaceutical legislation), their [joint evaluation](#) (published in 2020) found that both regulations have enabled and favoured considerable positive developments. Nonetheless, it also pointed to certain problems:

- 1 Medical needs of patients with rare diseases and children are not sufficiently met.
- 2 Affordability of medicinal products is a growing challenge for healthcare systems.
- 3 Patients have unequal access to medicines across the EU.
- 4 The system caters insufficiently for innovation and creates unnecessary burden.

Even if the problems identified in both IAs are very similar in substance, their specific nature and scale can differ greatly. For instance, with regard to affordability of medicines, the cost, and also the willingness to pay, for a new orphan medicine can be very high, especially if it is based on complex technology (IA, part II, pp. 19-20). Moreover, the IA provides evidence that, compared with 'standard' medicines, patient access is worse for orphan medicines (IA, part II, p. 21).

The problem definitions of both IAs include a **foresight dimension**. In this respect, the IAs see the persistence of the problems confirmed by four of the [megatrends](#) identified by the Commission's Joint Research Centre, namely: (i) shifting health challenges; (ii) accelerating technological change and hyperconnectivity; (iii) increasing demographic imbalances; and (iv) climate change and environmental degradation (IA, part I, p. 24, and more elaborated on in part II, pp. 26-27).

Subsidiarity / proportionality

The revision of the EU pharmaceutical legislation is based on Articles 114(1) and 168(4)(c) of the Treaty on the Functioning of the European Union (TFEU). The former provides for the establishment and functioning of the internal market, while the latter sets high standards for the quality and safety of medicinal products.

The proposed directive is accompanied by a [subsidiarity grid](#), as recommended by the Better Regulation Guidelines (BRG) for sensitive or important initiatives (tool #5). The IAs recall the recognised EU added value of the EU pharmaceutical framework, and that the authorisation of medicinal products (including for children and rare diseases) is fully harmonised. They further explain that the internal market and common safety concerns in public health matters fall within the shared competence of the EU and Member States; however, once the EU adopts harmonised legislation in this area, Member States can no longer exercise their own competence. Notwithstanding, the IAs also stress that the initiative respects Member States' exclusive competence in the provision of health services, which includes pricing and reimbursement policies. Concerning proportionality, both IAs state that the proposed revision does not go beyond what is necessary to achieve its objectives. In line with the BRG (tool #17), aspects of subsidiarity and proportionality are duly considered in the comparison of the different policy options.

As the translation of the legislative proposals into the other official EU languages was substantially delayed, the proposals were referred to national parliaments as late as 14 September 2023. The deadline for parliaments' subsidiarity check [expires](#) on 9 November 2023. At the time of writing, no national parliament has issued a reasoned opinion. However, in the context of the political dialogue, the Czech Chamber of Deputies adopted a [resolution](#), in which it asked for clarification regarding the proposed transferable regulatory protection vouchers⁸ and **regulatory sandboxes**. The latter are a structured form of testing innovations in a controlled real-world environment, prior to formal regulation (see BRG, tool #69).

Objectives of the initiative

Both IAs succinctly explain the objectives of the legislative revision (IA, part I, pp. 26-29 and part II, pp. 29-30). With regard to the revision of the **general pharmaceutical legislation**, the **overall objectives** remain unchanged, namely to guarantee a high level of public health by ensuring the quality, safety and efficacy of medicines for EU patients, and harmonise the internal market for the supervision and control of medicinal products. The IA lists five **specific objectives** (see Table 1).

Table 1 – Specific objectives (revision of the **general** pharmaceutical legislation)

SO #	Specific objective (SO)	Corresponding problem (see. p. 2)
SO 1	Promoting innovation, in particular for unmet medical needs, incl. AMR	problem 1
SO 2	Creating a more balanced system for pharmaceuticals in the EU that promotes affordability for health systems while rewarding innovation	problem 3
SO 3	Ensuring access to innovative and established medicines for patients, with special attention to enhancing supply security across the EU	problems 2 and 4
SO 4	Reducing the environmental impact of the pharmaceutical product lifecycle	problem 6
SO 5	Reducing the regulatory burden and providing a flexible regulatory framework	problem 5

Source: author, based on IA, part I, pp. 27-29.

As Table 1 shows, the specific objectives correspond in substance to the problems identified, even if they are presented in a different order and problems 2 and 4 were merged.

Furthermore, the **overall objective** of the revision of the **specific pharmaceutical legislation** is to ensure that patients with rare diseases and children have access to high-quality medicines and safe and effective therapies to address their medical needs. The four **specific objectives** (SO) derived are fully coherent with the problems identified (see section 'problem definition') and partially identical with those identified above under the general pharmaceutical legislation:

- SO 1: Promoting innovation for rare diseases and for children, in particular for unmet medical needs;
- SO 2: Creating a balanced system for pharmaceuticals in the EU that promotes affordability for health systems while rewarding innovation;
- SO 3: Ensuring timely patient access to orphan and paediatric medicines across the EU;
- SO 4: Reducing the regulatory burden and providing a flexible regulatory framework.

Neither the specific objectives of the general nor those of the specific pharmaceutical legislation are further broken down into operational objectives that would set out more concrete deliverables. They remain rather broad, and their formulation does not appear to meet fully the SMART criteria of being specific, measurable, achievable, realistic and time-bound (BRG, tool #15). However, the indicators included in the monitoring framework allow for measuring the implementation of the preferred policy option.

The objectives of both IAs are in line with Article 35 of the EU [Charter](#) of Fundamental Rights, which confers a right to a high level of human health protection in the definition and implementation of EU policies. Furthermore, the objectives support the achievement of the United Nations **Sustainable Development Goals (SDGs)**, in particular SDG 3 (healthy lives and well-being), SDG 9 (resilient infrastructures and innovation) and SDG 10 (reduced inequalities).

Range of options considered

Each of the two IAs presents a well-substantiated **dynamic baseline scenario** that depicts how the situation would evolve longer-term, over the next 15 years, without any policy intervention. The focus lies on the current framework for regulatory protection and other incentives and obligations. For the general pharmaceutical legislation, the baseline scenario projects a positive outlook solely for medicine innovation. In contrast, the assumptions drawn with regard to research efficiency, investment in R&D, patient access to new medicines, AMR and supply shortages are less favourable. This lets the IA conclude that under the baseline scenario, the current problems would persist. Similarly, drawing on historic EMA data, the evidence-based outlook on how the orphan and

paediatric medicines would evolve over a period of 15 years under the baseline scenario does not suggest the current problems would dissipate.

For the revision of the **general pharmaceutical legislation**, three policy options were examined, in addition to the baseline. Each option contains pivotal and non-pivotal measures, complemented by horizontal measures specifically targeting simplification and innovation.

- Option A builds on the current status quo and would achieve the objectives mainly through new incentives (in terms of regulatory protection periods) and stronger enforcement of existing obligations and information requirements.
- Option B reaches the objectives through more obligations and oversight.
- Option C is geared towards rewards for positive behaviour, while obligations would only be used if no alternatives were available ('*quid pro quo* approach').

Table 2 – Policy options assessed: **General** pharmaceutical legislation

Specific objective	Option A	Option B	Option C
Promoting innovation, notably for unmet medical needs	Regulatory protection: same as status quo (8-year data protection + 2-year market protection) <u>Special incentive:</u> + 1-year data protection for medicines addressing unmet medical needs + 6-month data protection for comparative trials	6-year regulatory data protection + 2-year market protection <u>Special incentive:</u> + 2-year data protection for originators addressing unmet medical needs	6-year regulatory data protection + 2-year market protection <u>Special incentive:</u> + 1-year data protection for medicines addressing unmet medical needs + 6-month data protection for comparative trials
Incentives to promote development of new antimicrobials	Transferable exclusivity vouchers for antimicrobial products	'Pay or play' model for antimicrobial products ⁹	Transferable exclusivity vouchers for antimicrobial products
Creating a balanced system for pharmaceuticals in the EU that promotes affordability for health systems while rewarding innovation	Baseline + additional rewards for innovation and access Incentivising comparative trials	Earlier entry of generics and biosimilars with 2 years shorter protection than baseline + 2-year market protection for medicines with no return of investment Transparency requirements for any public contribution or funding (incl. R&D costs)	Earlier entry of generics and biosimilars if market launch condition not met Transparency requirements for public contribution to R&D costs in relation to clinical trials included in the marketing application Incentivising comparative trials
Ensuring access to innovative and established medicines for patients, with special attention to supply security	+ 6-month additional protection period if centrally authorised product is placed on the market in all Member States within 6 years of the marketing application Allow generic competition if not launched in a majority of Member States within	Obligation to place a centrally authorised medicine on the market launched in the majority of Member States (incl. small Member States) within 5 years	+ 2-year (or + 1-year) data protection extension of medicines placed on the market within 2 years of authorisation and appropriately and continuously supplied Better data on medicine shortages through adequate notification periods; shortage prevention, increased supply chain

	5 years of market application Notification requirement unchanged (+ baseline)	Notification requirement unchanged (+ baseline)	transparency, mitigation plans for all medicines and stockpiling of critical medicines; reinforced shortage monitoring through information exchange mechanism between Member States
Reducing environmental impact of pharmaceutical product lifecycle	No change	Strengthening conditions of use for medicines and environmental risk assessment requirements, incl. environmental risk of manufacturing and its impact on AMR	Same as Option B, with the inclusion of AMR aspects in good manufacturing practice
Reducing regulatory burden; flexible regulatory framework	Horizontal measures (e.g. simplified generic marketing authorisations and regulatory sandboxes)		

Source: IA, part I, p. 32.

The range of options identified respects the BRG requirement of exploring at least two policy alternatives in addition to the baseline. The presentation of the policy options and the envisaged measures under each option appears clear and sufficiently detailed (IA, part I, pp. 30-37). However, it is noteworthy that the development of new antimicrobials has become a priority on its own; it was decoupled from the specific objective 'Promoting innovation, notably for unmet medical needs'.

Eventually, option C is identified as the **preferred option** (marked in orange in Table 2). Put succinctly, this option provides for a variable duration of regulatory data protection: a default option of 6 years (which would be less than the current 8 years), plus conditional additional protection periods as an incentive. Generics and biosimilar medicines could enter the market earlier. Furthermore, companies developing antimicrobials could, under certain conditions, benefit from a transferable exclusivity voucher.¹⁰ Marketing authorisation holders would need to adhere to transparency requirements regarding public funding for clinical trials. The option also provides for reporting of medicine shortages and stricter requirements for environmental risk assessment.

Horizontal measures would complement all three policy options in order to foster innovation and streamline and 'future-proof' the regulatory framework (e.g. through the introduction of **regulatory sandboxes**). The substance of the horizontal measures is outlined in a dedicated section of the IA (IA, part I, pp. 36-37); they relate, inter alia, to the simplification of generic marketing authorisations, adaptive clinical trials, 'full use of health data (real world evidence)' and adjusted EMA working methods. As a further horizontal measure, the environmental risk assessment of medicines that contain or consist of genetically modified organisms (GMOs) would be replaced by specific GMO environmental risk assessment requirements adapted to the specificity of medicines under the general pharmaceutical legislation. This would, however, 'not constitute a complete derogation from the GMO legislation', as the IA stresses (IA, part I, p. 37).

The IA on the **orphan and paediatric pharmaceutical legislation** brings forward – in addition to the baseline – three policy options each, that provide for different degrees of incentives and rewards, plus elements common to all policy options. The latter include, by way of example, measures to stimulate innovation in order to boost R&D especially in areas of (high) unmet medical needs, increased scientific support by EMA for these medicines, and measures to promote faster generic and biosimilar competition. For both initiatives, **option C** has been selected as the **preferred option** (marked below in orange), although for paediatric medicines, the IA is not clear about how this option differs from the current status quo (baseline), aside from the horizontal measures applicable to all options (IA, part II, p. 34 and table on pp. 127-128).

Table 3 – Policy options assessed: **Specific** pharmaceutical legislation

Initiative	Option A	Option B	Option C
Orphan medicines	<p>Keeping 10 years of market exclusivity (= baseline scenario)</p> <p>Additional incentive: transferable regulatory protection voucher for products addressing patients' high unmet medical needs (HUMN)</p>	<p>The current 10-year market exclusivity for all orphan medicines would be abolished</p> <p>Bonus 1-year market exclusivity extension possible for HUMN products and new active substances</p>	<p>Variable duration of market exclusivity of 10, 9 and 5 years, based on the type of orphan medicine</p> <p>Conditional 1-year bonus market exclusivity extension</p>
Paediatric medicines	<p>The 6-month SPC extension remains valid for all medicinal products</p> <p>Extra reward for products benefiting children's unmet medical needs</p>	<p>The paediatric investigation plan (PIP) would remain mandatory, but the reward for its completion would be abolished. This would ensure an early entry of generic products and reduce costs for health systems</p>	<p>The 6-month SPC extension would remain the main reward for the completion of the PIP</p>

Source: author, based on IA, part II, pp. 32-35 and pp. 127-128.

Assessment of impacts

Duly considering the available evidence, including stakeholder views, the IA dedicates much space to assessing the **economic impacts** of key policy measures identified under all policy options, including the horizontal measures (qualitative and quantitative data). The impact analysis is substantiated by several comparative tables and annexes. Annex 11 (IA, part I), in particular, provides, spread over 120 pages, a qualitative impact analysis (multi-criteria analysis) for the proposed key policy measures across all policy options, and a cost-benefit analysis of the proposed horizontal measures suggested under the revision of the general pharmaceutical legislation. These horizontal measures alone are expected to generate net benefit of up to €100 million a year, shared among businesses and authorities (IA, part I, p. 50).

To reduce complexity and improve readability, the combined economic impacts of each policy option under the revision of both the general and specific EU pharmaceutical legislation are summarised succinctly (IA, part I, pp. 51-54, and part II, pp. 56-59, the latter including tables on costs and benefits). The expected impacts of all options are then compared in relation to the baseline scenario in terms of their effectiveness, efficiency, coherence, EU added value, as well as proportionality and subsidiarity, in line with the BRG.

For the revision of the **general pharmaceutical legislation**, the **preferred option** is deemed 'a modulated trade-off' between the different specific objectives (IA, part I, p. 64). It examines impacts on patients, companies, national health systems and regulators. The – very detailed – assessment of **economic impacts** provides calculations of how the different incentive scenarios and other policy measures would impact on the main stakeholder groups (patients, healthcare systems, and the pharmaceutical sector split into originators – which would see a profit loss – and the generic industry, which is expected to benefit from generics' accelerated market entry). Based on further quantifications, it expects overall positive effects on the functioning of the internal market and on the conduct of businesses. However, it concedes that certain measures would entail additional administrative burden for businesses (in particular marketing authorisation holders). Furthermore, the preferred option expects benefits for research and innovation (increased return on investment; additional investment in R&D for unmet medical needs and AMR).

In comparison, social and environmental impacts receive less attention. In terms of **social impacts**, the IA focuses on public health and safety, considering the interests of both patients and health systems. The IA estimates that, under the preferred option, 67 million more EU citizens would potentially have access to a typical new medicinal product over a period of 10 years (i.e. the protection period) (IA, part I, p. 55). Moreover, the transferable exclusivity voucher is expected to help develop novel antibiotics and thus contribute to fight AMR.

The preferred option is also expected to have a positive **environmental impact** (though not quantified) thanks to less medicine residues and strengthened rules for the environmental risk assessment. The inclusion of AMR aspects into good manufacturing practice is expected to decrease the volume of antibiotics entering the environment during the manufacturing process.

Similarly, the **economic impact** of the preferred option under the proposed revision of the **orphan and paediatric framework** is highly detailed, relying on quantitative and qualitative data. A positive impact is expected for the EU internal market and the conduct of business, and the stimulation of innovation. Overall, procedural simplifications would reduce administrative burden. With regard to **social impacts**, patient access to orphan medicines would be improved, owing to the earlier market entrance of generics and biosimilar medicines and the proposed changes for market exclusivity. Similarly, access to paediatric medicines is expected to improve (more medicines and faster market access). The **environmental impacts** would be similar to those under the general pharmaceutical legislation.

Both IAs look into the initiatives' simplification and burden-reduction potential for businesses in the context of regulatory offsetting (**one in, one out approach**). With regard to the general pharmaceutical legislation, the IA estimates the proposed streamlining procedures to yield savings for pharmaceutical businesses in the range of €412.5 million to €825 million over the next 15 years. Digitalisation measures are expected to bring about additional savings for the industry, amounting to between €112 million and €225 million over 15 years. The reduction of administrative costs for companies is estimated at €3.6 million per year under the proposed orphan legislation and at €1.5 million per year under the paediatric legislation.

SMEs/ Competitiveness

Both IAs acknowledge the fundamental role small and medium-sized enterprises (**SMEs**) play in the 'EU pharmaceutical ecosystem', which covers activities from pre-clinical research to manufacturing (e.g. IA, part I, Annex 7 and part II, Annex 9). While the exact number of SMEs active in the sector is not indicated, reference is made to more than 1 900 EU-based SMEs registered in EMA's corporate database (IA, part II, Annex 11), and to the fact that nearly half of the authorised medicinal products for rare diseases were developed by SMEs (IA, part II, p. 16). Although it would appear that no full and formal SME test was carried out (in line with BRG tool #23), and that SMEs were not specifically consulted, potential impacts on SMEs are duly considered throughout both IAs.¹¹ The IA underpinning the revision of the **general pharmaceutical legislation** expects burdens and benefits for SMEs under the preferred option. On the one hand, the strengthened requirements for the environmental risk assessment might increase administrative burden for SMEs, and SMEs could also be more affected than larger pharmaceutical companies by the expanded obligations and requirements for reporting and management of withdrawals and shortages. On the other, according to the IA, SMEs would benefit from the introduction of regulatory sandboxes to support the development of innovative products, scientific support from EMA, and fee reductions. Biopharmaceutical SMEs in particular are expected to benefit from the incentives scheme for unmet medical needs and AMR, as they are more likely to engage in the 'risky early-stage drug discovery' (IA, part I, p. 54). The latter argument is also brought forward in the IA supporting the **orphan and paediatric legislation**. In addition, SMEs are believed to benefit both from simplified procedures and from the period of market exclusivity for products addressing 'high unmet medical needs' (HUMN) – i.e. diseases for which currently no treatment exists. More generally, the preferred option is deemed to boost research and innovation in orphan medicines and improve the **competitiveness**

of the EU pharmaceutical sector, including SMEs (IA, part II, p. 67). Also for the general pharmaceutical legislation, the IA considers the impact on the pharmaceutical sector's competitiveness to be positive, not least because of the horizontal measures and the additional incentives relating to unmet medical needs, AMR and comparative trials (IA, part I, pp. 53-54).

Simplification and other regulatory implications

For both IAs, simplification of the regulatory framework is a key objective. A dedicated REFIT section (IA, part I, pp. 69-70) points to simplification potential in the general pharmaceutical legislation, notably with regard to streamlining and accelerating procedures and digitalisation (e.g. integration of national regulatory systems; re-use of data). Simplification is also expected to result from the proposed transfer of the responsibility for orphan designation from the Commission to EMA (the EU authority for the evaluation and supervision of medicinal products). The proposed regulation would alter the structure and working methods of EMA and the European medicines regulatory network.

Monitoring and evaluation

Both IAs provide for a comprehensive monitoring framework. The sets of indicators that allow for measuring the impact of each specific objective appear to be adequate. The IA underpinning the revision of the specific pharmaceutical legislation holds that data collection would not impose any additional administrative burden, as all relevant data are already gathered by EMA, and reporting could (at least partly) be factored in the Commission's [annual reports](#) on medicines for children. In comparison, the IA on the general pharmaceutical legislation is more prudent, stating that 'much of the data' are already collected by EMA, and collecting new data 'would result in only a minor additional burden' (IA, part I, p. 71). Both IAs stress that medicine development is a lengthy process spanning years. Therefore, for measures like incentives and rewards, 'a meaningful evaluation of the revised legislation can take place only 15 years from its application' (IA, part I, p. 71).

Stakeholder consultation

The Commission undertook ample stakeholder consultation activities for both IAs. Their results are summarised in comprehensive and detailed synopsis reports annexed to the IAs, as required by the BRG. They are presented in an informative manner, broken down by salient topical issues and the groups of stakeholders primarily targeted by the Commission, in particular:

- public authorities competent in health, medical and pharmaceutical matters;
- pharmaceutical industry (including SMEs);
- representatives of civil society (including patients and public health organisations);
- healthcare providers (including professional associations); and
- academics and research organisations.

It appears that stakeholder input was duly considered throughout the IA reports. Broadly, the preferred options are backed by stakeholders' views, although the pharmaceutical industry expressed scepticism towards a potential modulation or shortening of incentives.

For the revision of the **general pharmaceutical legislation**, the Commission first collected, in spring 2021, feedback on the combined evaluation roadmap/inception IA. The ensuing public consultation was open for contributions between 28 September and 21 December 2021 (thus meeting the 12-week requirement set out by the BRG). Input from the public was complemented by targeted stakeholder surveys, semi-structured interviews (138 in total), and two validation workshops on the findings of the evaluation and the IA, respectively.

Similarly, for the revision of the **specific pharmaceutical legislation**, the Commission carried out a public consultation, open between 7 May and 30 July 2021 (equally respecting the minimum 12 weeks). In addition, it undertook targeted surveys, namely an options survey and a costing survey, addressed to the pharmaceutical sector and public authorities. Data obtained through the costing survey fed into the cost-benefit analysis, although only few responses were received (3 from the pharma sector and 7 from public authorities). Furthermore, the Commission gathered input

through an interview programme (conducting 60 interviews with 'the most relevant representatives' of the stakeholder groups (IA, part II, p. 79)), and held a meeting with focus groups.

Supporting data and analytical methods used

The IA on the **general pharmaceutical legislation** was carried out in parallel ('back-to-back') with an evaluation of the existing legislation (BRG, tool #51).¹² The process was informed by two external studies supporting the [impact assessment](#) and the [evaluation](#), respectively. Contrary to the BRG (tool #50), the Commission's evaluation report (SWD) was not published as an annex to the IA, but remains hidden on a DG SANTE [webpage](#). This is also true for other mandatory annexes, such as the annex on procedural issues, the synopsis report on stakeholder consultation, methodological information, and quantifications of costs and benefits. This clerical omission infringes the BRG's transparency requirements (see tool #11, section 'annexes that must be included in the IA report').

According to Annex 4 (methodology), multiple data sources and related analytical methods were used to strengthen the IA's evidence base. These include a literature and document review; country reports; a comparative legal analysis of pharmaceutical legislation in certain third countries; quantitative data analysis; and case studies (for instance, on criteria for unmet medical needs and regulatory support for SMEs). Overall, the methodological framework appears solid. The IA is also frank about limitations, notably challenges with regard to quantitative data that made it impossible to 'quantify all relevant impacts of every policy measure discussed in the policy options' (IA, part I, Annex 4, p. 31).

In an attempt to mitigate these data gaps, a multi-criteria analysis was applied, based on triangulation of qualitative and (where available) quantitative data. According to the IA, this method helped to assess the different policy options. Furthermore, quantitative modelling of various policy scenarios (e.g. changes in regulatory data and market protection) was undertaken, mainly based on [IQVIA Ark Patent Intelligence data](#)¹³ (for details see IA, part I, Annex 4, pp. 33-37).

The IA on the **specific pharmaceutical legislation** drew substantially on the Commission's 2020 [joint evaluation](#) of the paediatric and orphan regulations and on supporting studies. In addition, the IA relied on a wide range of published literature, including a contracted [study](#) on the economic impact of SPCs, pharmaceutical incentives and rewards (2018), and a 2021 [study](#) on future-proofing pharmaceutical legislation, addressing medicine shortages. The IA is transparent about data gaps and concedes, for instance, that evidence on R&D costs 'was particularly difficult to gather' (IA, part II, p. 76), owing to the low response rate to the above-mentioned costing survey.

Follow-up to the opinion of the Commission Regulatory Scrutiny Board

The Regulatory Scrutiny Board (RSB) examined the two IAs in question separately, but its opinions were eventually published in [one document](#). In both cases, the Board first issued a negative opinion (dated 22 June 2022 and 19 July 2022, respectively); following the resubmission of both revised IAs on 28 October 2022, it gave them a positive opinion with reservations in a written procedure.

While the RSB noted certain improvements in both IAs, it still required a number of shortcomings to be addressed. Regarding the **general pharmaceutical legislation**, it raised the following issues.

- The criteria and conditions of the AMR voucher system were found to be too vague.
- The content, functioning and effectiveness of certain safeguards and incentives were not deemed sufficiently clear.
- The impacts of reduced regulatory protection periods on the sector's capacity to finance future innovations and global competitiveness should be better assessed.

Turning to **paediatric and orphan legislation**, the Board reiterated its comment regarding the impact of reduced regulatory protection periods, and insisted on the following improvements:

- better clarify the safeguards for market access measures and explain whether these are the same as those envisaged for the general pharmaceutical legislation;
- better develop some of the impact analyses and the sensitivity of the analysis;

- complement the comparison of options with quantitative information (e.g. new medicines compared to the baseline, and costs for patients, health systems, etc.).

It appears that the RSB comments have been addressed.

Coherence between the Commission's legislative proposal and IA

In substance, the proposals (for a new directive and regulation) and the IA appear coherent. However, the difference in the way the IA and the proposals are presented somewhat hamper a coherent reading: while the IAs examine the general and the specific pharmaceutical legislation separately, the proposals follow an integrated approach. Overall, the proposals appear to follow the preferred sets of options laid out in the IA. However, some of the specific objectives (SO) are phrased differently, suggesting a slightly different focus. To give an example: the SO set out in the IA reads 'promote innovation, in particular for unmet medical needs', while the SO in the proposal's explanatory memorandum is more geared towards competitiveness ('offer an attractive, innovation- and competitiveness-friendly environment for research, development, and production of medicines in Europe').

The proposed revision of the EU's pharmaceutical framework covers the EU's general pharmaceutical legislation and the paediatric and orphan medicines regulations ('specific pharmaceutical legislation') in an integrated manner. The merger of the orphan and paediatric regulations with the legislation applicable to all medicinal products is explained with 'simplification and increased coherence' in the explanatory memorandum of the proposed directive. The proposed revision is supported by two impact assessments that were prepared in separate processes, but striving for utmost coherence, and eventually published under the same cover: one focusing on the general and the other on the specific pharmaceutical legislation. The ease of assessing the IAs in conjunction with the proposed legislation is somewhat hampered by the differences in structure described above.

Both IAs draw on the results of the respective Commission evaluations, in line with the 'evaluate first principle'. They appear solid in substance, underpinned by a seemingly sound evidence base. Despite the complex nature of the topic, the main parts of the IAs are drafted in a way that is accessible to non-experts. Much of the data is further substantiated in (partly rather detailed and technical) annexes. Each IA presents three well-developed options in addition to the dynamic baseline scenario. The assessment of the specific policy measures' impacts under each option appears comprehensive; in particular, the section on economic impacts is developed thoroughly, substantiated by qualitative and quantitative data (including, inter alia, a cost-benefit analysis). In terms of transparency, the IA on the general pharmaceutical legislation (IA, part I), as published on EurLex and the Commission's public register of documents, is incomplete in the sense that it lacks all annexes, including the Commission's [evaluation](#) of the general pharmaceutical legislation, prepared back-to-back with the IA. Although the annexes were (later) published on a dedicated DG SANTE [webpage](#), they remain difficult to trace and lack stable hyperlinks.

ENDNOTES

- ¹ For details on the legislative procedure, see L. Amand-Eeckhout, [Revision of EU pharmaceutical legislation](#), EPRS, European Parliament, June 2023.
- ² In addition, targeted revisions took place in 2010 and 2011 and concerned pharmacovigilance and falsified medicines.
- ³ For details regarding the current regulatory protection periods, see section 3.3. of the [evaluation](#) (pp. 11-13).
- ⁴ Strictly speaking, the EU's specific pharmaceutical legislation also covers a third element, namely advanced therapy medicinal products. The '[ATMP Regulation](#)' provides for the technical requirements for the authorisation of medicines based on genes, tissues or cells and is out of scope of the current revision.
- ⁵ In line with Article 3 of the Orphan Regulation, EMA defines an [orphan medicine](#) as a 'medicine for the diagnosis, prevention or treatment of a life-threatening or chronically debilitating condition that is rare (affecting not more than five in 10 000 people in the EU) or where the medicine is unlikely to generate sufficient profit to justify R&D costs'. According to the IA (part II, pp. 12-13), over 6 000 rare diseases are currently recognised, and 36 million EU citizens are estimated to be affected by rare diseases.
- ⁶ Supplementary protection certificates (SPCs) are an intellectual property right, applying, inter alia, to patented pharmaceutical products that have been authorised by regulatory authorities. Governed by [Regulation \(EC\) No 469/2009](#), SPCs aim to encourage medicinal innovation. See also M.-A. Huemer, [Revision of the Supplementary Protection Certificate Regulations for medicinal and plant protection products](#), EPRS, European Parliament, May 2023.
- ⁷ For details on the implementation of the general pharmaceutical legislation see also E. Karamfilova, [Revision of the EU's general pharmaceutical legislation](#), EPRS, European Parliament, May 2023.
- ⁸ A transferable regulatory protection voucher allows for a 1-year extension of the regulatory protection period. It can be sold to another company and used for a product in that company's portfolio.
- ⁹ In the pay or play model, 'a company finances the innovation and either holds an antimicrobial in its portfolio or it pays into a fund to finance the development of novel antimicrobials' (IA, part I, p. 47).
- ¹⁰ A transferable exclusivity voucher (or: transferable regulatory protection voucher) allows the developer of a novel antimicrobial that reduces AMR to benefit from an additional year of regulatory protection on another product in their portfolio, or to sell the voucher to another company (IA, part I, p. 33).
- ¹¹ The IA on the general pharmaceutical legislation contains a reference to an SME test in 'Appendix D of Annex 12' (IA, part I, p. 51), but it does not appear to be included in any of the annexes. In contrast, the IA on the specific pharmaceutical legislation includes a brief annex on SMEs (Annex 11), which presents interesting facts on pharmaceutical and biotechnology SMEs, but cannot be considered a full SME test (BRG, tool #23).
- ¹² In its [resolution](#) of 7 July 2023, the European Parliament expressed serious concerns about the increasing number of back-to-back revisions (point 52).
- ¹³ IQVIA is a contract research and analytical services organisation that collects data including global pharmaceutical sales data. These data are not public. The model referenced is not included in the Commission's model database [MIDAS](#), and it is not clear whether it qualifies as a model under the BRG.

This briefing, prepared for the ENVI committee, analyses whether the principal criteria laid down in the Commission's own Better Regulation Guidelines, as well as additional factors identified by the European Parliament in its Impact Assessment Handbook, appear to be met by the impact assessment. It does not attempt to deal with the substance of the proposal.

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