# EPF recommendations for the revision of the EU pharmaceutical legislation

July 2023

## INTRODUCTION

EPF welcomes the European Commission's proposals for a Directive and a Regulation to revise and replace the existing general pharmaceutical legislation.

All patients in the EU have the fundamental right to access high-quality, patient-centred, and timely healthcare, including medicines. For many patients living with chronic diseases, medicines are an essential aspect of treatment. Medicines offer the promise of significant boosts in health or quality of life, or sometimes even a cure. Appropriate treatment not only improves patients' health and quality of life but also offsets the significant socio-economic costs of avoidable aggravation of chronic diseases and the existence of co-morbidities.

The European Patients' Forum (EPF) has defined equitable access to medicines according to five principles: **availability, affordability, adequacy, appropriateness, and accessibility[1].** Although many inequalities in access to medicines can be addressed primarily through policies at the national level, the revision of the EU pharmaceutical legislation is a unique opportunity for the patient community and all involved stakeholders to put forward specific proposals to ensure equitable access to medicines across all Member States.

**This revision represents a once-in-a-generation opportunity to make the EU regulatory framework more patient-centred by promoting patient involvement in the regulatory process, improving access to safe, effective, and high-quality medicines, and developing new medicines that better address unmet medical needs.**

**We call for:**

- A comprehensive framework for assessing key terms such as **"unmet medical need"** and **"added therapeutic value", developed and implemented in co-creation with patients.**
- A **fair balance** between incentives for R&D and patient access to new medicines through modulated incentives for addressing unmet needs, improving access across the EU, and facilitating the HTA process.
- Embedding and securing **patients' participation in the regulatory process** for medicines through the inclusion of a legal definition of "patient organisation", participation across EMA scientific working parties and in the Coordination Group for Mutual Recognition and Decentralised Procedures (CMDh), and provisions to establish financial compensation and training for patient representatives.
- The inclusion of **proportionate regulatory flexibilities** to adapt to scientific progress and speed up access to life-saving products without compromising patient safety.
- A **sustained focus on patients' information** including through the continued availability of package leaflets in paper format.

[1] European Patients' Forum (2020). "Position paper: the value and pricing of innovative medicines"

# 1. MEDICINES TARGETING PATIENTS' NEEDS

## ENSURING ADDED THERAPEUTIC VALUE OF MEDICINES

'Added therapeutic value' of medicines for patients is one of the key concepts of this review as it is currently insufficiently and inconsistently taken into consideration in the lifecycle of new medicines. An independent assessment of medicines approved in Europe in 2021 shows that only 17 of the 108 new marketing authorisations represent a major or significant therapeutic advance for patients.[2]

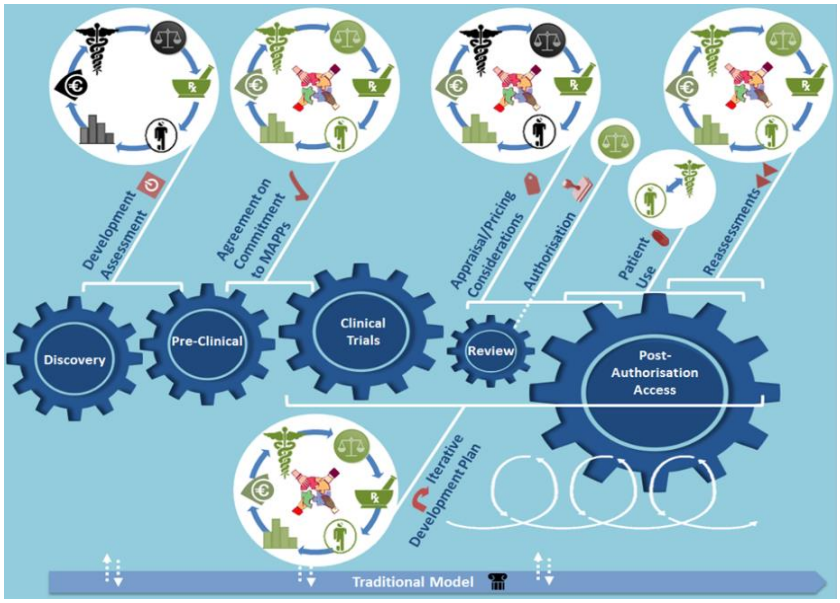
Currently, there is no universally accepted definition of this concept and there are significant differences between Member States as to what constitutes 'added therapeutic value', particularly during national HTA processes. EPF considers that the term 'innovation' often has a normative connotation. **For us, innovative medicines bring real and concrete added benefits to patients – whether it is a new medicine or an old medicine that is repurposed.** Therefore, we consider that not everything new can be considered innovative in this positive sense; what counts is the degree to which the medicine makes a tangible, positive difference to patients.

The revision of the EU pharmaceutical legislation should therefore clearly include a **common and meaningful European-wide definition of 'added therapeutic value'**, developed in partnership with patients. The patient perspective includes patients' perception of quality of life, clinical and quality of life criteria relevant to patients, and patients' views on benefits and risks. It is important that authorised medicines meet the needs of patients.

Without systematic patient involvement, it is impossible to assess the "real" value and obtain a comprehensive, fully accurate picture of the benefit-risk balance of new products. However, meaningful patient engagement is far from being a reality. **Many clinical trials still do not include outcomes that matter to patients, such as quality of life. Patient-relevant outcomes** should be included in the marketing authorisation dossier, which would oblige pharmaceutical companies to genuinely involve patients early in the development and in the research design and to fully integrate those parameters that matter most to patients into their clinical development plans.

Taking the added value of medicine into account is also crucial for reducing **the time between marketing authorisation and effective patient access**. The evidence and data requirements are different between the marketing authorisation, the health technology assessment (HTA) bodies, and the payers. The scientific evidence provided to obtain marketing authorisation is often considered insufficient by HTA agency assessors, which creates delays and inefficiencies.[3] We welcome the incentives for using comparative clinical trial data, which will help national authorities to better assess the cost-effectiveness of new medicines. However, this must be accompanied by measures fostering **early dialogue with health professionals, patients, policymakers, industry, the EMA and HTA bodies, as well as payers**. It would improve alignment on the data requirements, e.g., regarding trial design, patient population and outcomes to be selected, and allow payers to anticipate potential issues or concerns. This was the finding of the ADAPT SMART, a coordination and support project funded under the Innovative Medicines Initiative, which focused on new processes for the implementation of medicines adaptive pathways to patients (MAPPs). It was highlighted that multi-stakeholder dialogues are essential to ensure that all stakeholders agree on the criteria for engaging MAPPs, and an assessment can only be defined on a case-by-case basis.

[2] Prescrire International (2021). 'Drugs in 2021: a brief review'.
[3] KCE (2021). "Evidence gaps for drugs and medical devices at market entry in Europe and potential solutions"




MAPPs Seamless Pathway and Decision Points – ADAPT SMART

**EPF's recommendations:**

- The EMA should encourage marketing authorisation applicants to include data on the added therapeutic value for patients in the marketing authorisation dossier (Annex I of proposed Directive 2023/0132). Adequate guidance should be developed by the EMA in close cooperation with patients.
- The revision of the pharmaceutical legislation should provide a definition of 'added therapeutic value', defined in co-creation with patients (Article 2 of proposed Regulation 2023/0131).
- Patient-relevant outcomes and patient experience data should be included in the marketing authorisation dossier (Annex I of proposed Directive 2023/0132).
- The legislation should provide for an early EU-wide dialogue between health professionals, patients, policymakers, industry, the EMA and HTA bodies, and payers.

## ADDRESSING UNMET MEDICAL NEEDS

The **concept of 'unmet medical need'** is also at the heart of this legislative overhaul, as it is the basis for conditional marketing authorisation, regulatory support, and new incentives. EPF considers that the definition of 'unmet medical need' provided in the proposal is inadequate. By only taking into account morbidity and mortality, it ignores other considerations for the patient community, such as the severity of the disease or quality of life. **This puts into question the appropriateness of the term "unmet medical need", when in fact "unmet patients' needs" – defined by and with patients – should be the main driver of pharmaceutical R&D**.

Rare diseases and paediatric diseases are, for example, unquestionable areas of unmet medical needs. In addition, unmet medical needs may arise from a variety of causes, ranging from a lack of basic research to

understand the disease to the commercial failure of a certain product. Therefore, we believe the legislation should include a more comprehensive and inclusive definition.

Unmet medical needs are not always a yes/no question. Some criteria, defined by patients and catalysing patients' views, should be included in the legislation. They should take into account **all chronic diseases** (including those for which there is already an approved and marketed pharmaceutical product), as well as criteria such as disease severity and frequency, the **impact of the disease on quality of life and life expectancy,** and considerations of current treatment options (e.g., **inconvenience** of current treatment, **adherence** to treatment, **availability**, **appropriateness** for all patients etc.).

Some national healthcare payers (e.g. Belgium[4]) have already applied a kind of 'unmet medical need' concept when negotiating the price and reimbursement of approved medicines and treatments with pharmaceutical companies. **It will be of utmost importance to involve patients in developing and implementing a definition of unmet medical needs, to ensure it is relevant and helps focus R&D on areas that matter to patients.** A patient-driven definition will also help counter the 'orphanisation' of new medicines, where more and more medicines are labelled as addressing unmet medical need to obtain fast-track approval and/or higher prices.

**EPF calls on the co-legislators to ensure that eligibility criteria for accelerated assessment and PRIME based on the concept of 'unmet medical need' are co-created with patients**, to ensure that these schemes target the most promising medicines from a patient perspective.

In addition, patient populations with unmet medical needs are scattered across Europe. Even if a medicine targeting unmet medical needs is approved, there is no guarantee that it will be accessible to patients who need it. This is exacerbated by commercial decisions to launch drugs first in richer countries and in countries with larger patient populations[5]. For this reason, the legislation should require that medicines benefiting from fast-track approval processes because they target an 'unmet medical need' are filed for pricing and reimbursement in all EU Member States within one year of the marketing authorisation.

**EPF's recommendations:**

- The legislation should delegate to EMA the development, in co-creation with patients, of a binding framework for assessing 'unmet medical need' (Article 83 of proposed Directive 2023/0132 and Article 162 of proposed Regulation 2023/0131). This framework should be comprehensive and include criteria that matter to patients, including disease severity, quality of life, appropriateness of existing treatments, etc.
- Marketing authorisation holders benefiting from an accelerated approval procedure (PRIME, conditional marketing authorisation, accelerated assessment), because their product meets an unmet medical need, must apply for pricing and reimbursement in the 27 EU Member States within one year of the marketing authorisation (or within two years in the case of SMEs or not-for-profit entities).

[4] INAMI. « Besoin médical non rencontré – Unmet medical need »
[5] Copenhagen Economics (2018). "Study on the economic impact of supplementary protection certificates, pharmaceutical incentives and rewards in Europe", 14.

## 2. INCREASED PATIENT ACCESS TO MEDICINES AND TREATMENTS

### STRENGTHENING INCENTIVES FOR THE DEVELOPMENT OF NEW MEDICINES

An incentives system to foster the research and development (R&D) of new medicines and bring them to the market is a crucial aspect of patient access to medicines. On the one hand, incentives for (R&D) and the marketing of new medicines and treatments encourage innovation, research and pharmaceutical investment (including in areas of 'unmet medical need'). On the other hand, excessively long periods of market exclusivity can lead to late market entry of generics and biosimilars, which delays and hinders patient access. Therefore, EPF considers it crucial to **find the right balance between incentivising R&D of products that provide a real added benefit and access to new medicines and therapies.**

The European regulatory protection system for pharmaceuticals is currently one of the most generous in the world, offering up to 11 years of protection under certain conditions. The United States offers 12 years for biologics, but only 5 years for other small molecules that are new chemical entities[6]. Canada and Japan offer up to 8 years of regulatory data protection for pharmaceuticals, while a significant number of jurisdictions offer 5 to 6 years[7]. Regulatory protection is not the only driver of pharmaceutical innovation. An enabling environment for innovation also includes criteria such as reduced bureaucracy, faster regulatory approvals and strong patient involvement, which improve the quality of medicines and authorisation decisions. The reduction of regulatory protection periods alone cannot explain a flight of R&D to other countries. However, it can speed up the availability of cheaper alternatives, which can help control medicines and overall health care spending.

EPF, therefore, supports the proposed reduction of the baseline regulatory protection periods and especially the modulated incentives for faster launch and earlier access to medicines for patients. We note that the total duration of incentives in the Commission's proposal, if all the conditions are met, is similar to, or may be greater than, current levels, while encouraging earlier patient access. To truly incentivise research, EPF also supports a one year extension of the regulatory protection period granted to medicines that fulfil an unmet medical need, as defined by the EMA in co-creation with patients.

At the same time, improvements can be made to the modulated incentives to achieve rapid and equitable access across all EU countries. An incentive to launch in all Member States must be accompanied by a clear obligation for Member States to comply with the deadlines set out in Council Directive 89/105[8] for pricing and reimbursement decisions, which are 180 days for joint pricing and reimbursement procedures. These deadlines are regularly exceeded by Member States, leading to delays in bringing medicines to market, which slows down the availability of treatments for patients. We also call on Member States to meet their responsibility of ensuring the availability of and access to medicines for patients and providing effective universal health coverage.

We call on the legislator to require that information about the expected market launch is included by applicants in marketing authorisation dossiers. We also support the requirement for transparency in public funding to

[6] Beall, R. F., Hwang, T. J., & Kesselheim, A. S. (2019). Pre-market development times for biologic versus small-molecule drugs. *Nature biotechnology*, 37(7), 708–711.
[7] Copenhagen Economics, op. cit., 54.
[8] Council Directive 89/105/EEC of 21 December 1988 relating to the transparency of measures regulating the pricing of medicinal products for human use and their inclusion in the scope of national health insurance systems.

medicines research. This is a prerequisite for affordable access to innovation and societal confidence in the system.

**EPF's recommendations:**

- The possibility of granting an additional year of regulatory data protection for marketing authorisation holders that obtain authorisation for one or more new therapeutic indications should be more strictly limited (Article 81 of proposed Directive 2023/0132).
- An additional year of data protection could be granted if the product targets an 'unmet medical need', provided that legislation includes, or requires the EMA to develop, a new definition co-created with patients. (Article 81 of proposed Directive 2023/0132).
- Information about expected market launch should be included by the applicant in the marketing authorisation dossier (Annex I of proposed Directive 2023/0132).
- The incentive to launch in all Member States must be accompanied by an obligation for Member States to comply with the deadlines for pricing and reimbursement decisions set out in the Transparency Directive.

## PROMOTING EARLIER MARKET ENTRY OF GENERICS AND BIOSIMILARS

Faster availability of generic and biosimilar medicines is key to patient access to medicines. They increase competition between available medicines, in turn bringing prices down. Generics and biosimilars are cheaper alternatives for healthcare systems and patients, and improve access to medicines. Given their lower price, they also contribute to the sustainability of healthcare systems. However, experience shows that there are still barriers to generics or biosimilars entering the EU market.

EPF supports provisions reducing barriers to market entry for generics and biosimilars, as this means more choices for patients and fostering price competition. This includes proposals to reduce duplications and unnecessary burdens for generic manufacturers while maintaining the highest standards of patient safety. Introducing more flexible use of the centralised procedure, an accelerated mutual recognition procedure, and a more efficient repeat-use procedure could also be considered.

Finally, providing comprehensive patient information and promoting ongoing dialogue with healthcare professionals are a priority to ensure informed decisions and acceptance of these products by patients. This is particularly important for biosimilars. Patients want to understand the differences and similarities between biologics and biosimilars, and how they relate to their own treatment.

EPF further calls for maintaining and shortening the "sunset clause", the period for termination of marketing authorisation for medicines that are not placed on the market or withdrawn from the market. There is a continued need for a targeted and harmonised mechanism that encourages competition by avoiding medicines under market exclusivity not actually being placed on the market and not reaching patients.

**EPF's recommendations:**

- The marketing authorisation expiry period for medicinal products not marketed in authorising Member States ("sunset clause") should be maintained and shortened to two years (instead of the current three).
- A targeted review of the competition and regulatory frameworks – and their implementation – to remove barriers to generics and biosimilars entry is needed.

## ADDRESSING DRUG SHORTAGES AND SUPPLY CHAIN VULNERABILITIES

Shortages of medicines, regardless of the cause, can have serious consequences for public health, affecting the entire healthcare system and, first and foremost, patients. There has been increasing evidence of a growing problem of such shortages in Europe in recent years, involving both lifesaving and commonly used medicines. This has an impact on patients, **as shortages can result in deaths, side effects, toxicities, and medical errors** due to the dispensing of substitute medicines, resulting in poorer treatments[9]. Ultimately, **shortages seriously undermine the fundamental right of patients to equitable access to safe and quality health care.** The COVID-19 pandemic has also highlighted Europe's dependence on active pharmaceutical ingredients and other pharmaceutical inputs produced elsewhere, making the EU more vulnerable and less able to address (unforeseen) public health needs. In addition, as globalisation of the pharma supply chain increases, the need for inspection coverage expands and must be strengthened.

EPF strongly supports the focus on shortages in the revision, as the current pharmaceutical legislation is not adequate to tackle shortages of medicines. The few provisions it contains have been implemented by Member States inconsistently[10], including the obligation to supply[11].

Building on the EMA's extended mandate, we welcome the earlier notification of shortages and withdrawals, the possibility for stockpiling, and the strengthening of EU coordination and mechanisms to monitor, manage, and avoid shortages. Greater emphasis should also be placed on stock transparency. Marketing authorisation holders should have both incentives and obligations to ensure the continued availability of medicines on the market and proactively mitigate the impacts of unforeseen supply issues on patients being treated.

However, **we regret the Commission proposal's lack of focus on patients' participation in the management of shortages.** Their involvement in the development of policy solutions is essential, as they are one of the main actors at the end of the supply chain. Patients must be involved in drafting the list of critical medicinal product to be proposed by the EMA, to ensure that it meets patients' needs. Patients and their representatives can also participate, for example, in providing information on alternatives and in reporting shortages to the authorities. Enabling patients to report drug shortages will improve data collection and understanding of their societal impact, thus improving drug shortage management. Member States must put in place a system to enable

[9] Pharmaceutical Group of European Union (2022). "Medicine Shortages. PGEU Survey 2022 Results".
[10] Technopolis Group, Ecorys BV, Milieu Law & Policy Consulting (2021). "Future-proofing pharmaceutical legislation – study on medicine shortages".
[11] Article 81 of Directive 2001/83/EC.

patients and their representatives to report shortages of medicines through the mandatory national shortage databases provided for in the proposals.

In addition, we call for the **introduction of a European database bringing together detailed information from these national databases.** In addition, we believe that the inclusion of data collected as part of the European Medicines Verification System (EVMS) under the EU legislation on falsified medicines should be explored[12]. Since 2019, marketing authorisation holders are required to place two safety features on the packaging of most prescription medicines and some over-the-counter medicines in the EU, namely a barcode and an anti-tampering device, according to Commission Delegated Regulation (EU) 2016/161[13]. Manufacturers upload the information contained in the unique identifier of each medicinal product to a central EU repository. This forms part of an end-to-end medicines verification system in which wholesalers, then pharmacists and hospitals will scan each medicine for authenticity and retrieve them from the repository before dispensing them to patients. While there may be some technical and legal limitations at the moment, these could be overcome to leverage this system as a very valuable source of information for Member States on the use and availability of medicines in the supply chain, thereby supporting better management of medicines' supplies.

Finally, EPF supports the diversification of the supply of active pharmaceutical ingredients to increase the resilience and flexibility of the supply chain and thus ensure continuity and security of supply.

**EPF's recommendations:**

- The European Medicines Agency's (EMA) Executive Steering Group on Shortages and Safety of Medicinal Products should adopt a list of critical medicinal products in collaboration with patient organisations (Article 123 of proposed Regulation 2023/0131).
- The transfer of the marketing authorisation to a third party who has declared their intention to place the medicinal product on the market, or the use of the medicinal product's documentation for the purpose of submitting an application in accordance with Article 14 of proposed Directive 2023/0132, should be extended to all medicinal products, and not just those of a critical nature. The decision must be made public.
- Marketing authorisation holders must introduce transparency measures regarding the number of stocks available to them at any given time for marketed medicinal products (Article 119 of proposed Regulation 2023/0131).
- All EU Member States should be required to establish a system for patients and patient organisations to report shortages of medicines (Article 121 of proposed Regulation 2023/0131).
- A public and user-friendly European database on drug shortages should be created, bringing together the information reported in the national shortage databases and leveraging to the extent possible information included in the central EU repository of the end-to-end verification system established by Commission Delegated Regulation (EU) 2016/161 (Article 124 of proposed Regulation 2023/0131).

[12] European Medicines Agency. "Falsified medicines: overview"

[13] Commission Delegated Regulation (EU) 2016/161 of 2 October 2015 supplementing Directive 2001/83/EC of the European Parliament and of the Council by laying down detailed rules for the safety features appearing on the packaging of medicinal products for human use.

- A list of excipients for which a sufficient production level must be maintained in each EU Member State should be established.
- While respecting the principle of subsidiarity and recognising that public procurement policies for medicinal products are a national competence, the legislation should invite Member States to consider where products' active pharmaceutical ingredients and/ or excipients have been produced as criteria for their national/regional/local public procurement procedures for medicines.

## BOOSTING INCENTIVES FOR THE DEVELOPMENT OF AND ACCESS TO ANTIMICROBIALS

In view of the global threat of antimicrobial resistance (AMR), the review of the EU pharmaceutical legislation provides **a unique opportunity to encourage research and development of new antimicrobials** and support sustainable and affordable access to both old and new antimicrobials.

New antibiotics are failing to generate sufficient revenues to sustain the interest of multinational players and small developers risk failing to cover their costs. At the same time, for antibiotic stewardship it is better to use antimicrobials appropriately and reserve new antimicrobials while older ones are still effective.[14] In parallel, shortages of older antibiotics are increasing[15].

While the proposed transferable exclusivity extension (TEE) vouchers may have some incentive potential**, their effectiveness and potential cost to national healthcare systems raise questions**. Firstly, TEE vouchers are a one-off reward, which does not guarantee that companies will launch these new antimicrobials in all Member States or that they will continue to market them in the future[16]. The current criteria solely require manufacturers to demonstrate the capacity to supply the priority antimicrobial in sufficient quantities for the expected needs of the EU market. In addition, there is a strong likelihood that pharmaceutical companies will apply the granted TEE to their most profitable products and/or to products that would not otherwise "deserve" additional regulatory protection. In this sense, TEE vouchers would unduly delay the market entry of generics and biosimilars.

Finally, the introduction of TEE vouchers would be associated with substantial costs for EU healthcare systems[17]. Depending on the study, estimates for a 12-month TEE range from €1[18] to €3 billion[19] in additional costs for EU health systems.

EPF considers that facilitating the development of new antimicrobials and promoting access to old and new antibiotics requires **a combination of 'push' and 'pull' incentives**, not all of which can be implemented in the

[14] Årdal, Christine et al., op. cit., 1994-1999.
[15] EU-JAMRAI (2021). Policy brief: Incentivizing antibiotic access and innovation.
[16] Anderson, Michael & Wouters, Olivier & Mossialos, Elias (2022). Transferable exclusivity extensions to stimulate antibiotics research development: What is at Stake? The Lancet. doi: https://doi.org/10.1016/S2666-5247(22)00336-6
[17] Ibid.
[18] Berdud M, Ferraro J, Mestre-Ferrandiz J, Towse (2019). A Study of the potential use of an EU Transferable Exclusivity Extension (TEE) to incentivize antibiotic R&D. ; Medicines for Europe (2022). 'Note on Transferable Vouchers'
[19] Årdal, Christine et al. (2020). Financing Pull Mechanisms for Antibiotic-Related Innovation: Opportunities for Europe. Clinical infectious diseases: an official publication of the Infectious Diseases Society of America vol. 71,8. 1994-1999. doi:10.1093/cid/ciaa153

EU pharmaceutical legislation. Incentives should take into account the specificities of antibiotics and the need for better antibiotic stewardship. In the context of the revision of the pharmaceutical legislation, EPF calls for pull incentives that decouple antimicrobial revenues from sales volumes: **the minimum annual revenue guarantee.**

Sweden and the United Kingdom (UK) launched pilot projects in this direction. A study shows that Swedish and UK patients now have access to more newly marketed antimicrobials than any other country except the United States[20]. Evidence generated by the pilot projects and research conducted by the EU Join Action on Antimicrobial Resistance and Healthcare-Associated Infections (EU-JAMRAI) provide a good basis for an EU-coordinated approach. Such a solution should be applied in a broader European context to improve access for all patients and stimulate innovation. From the designation of antimicrobials to the definition of access and stewardship stipulations, patient involvement will be crucial to ensure that this mechanism truly meets their needs.

In addition to this minimum annual revenue guarantee, **a "play or pay" model** could be introduced to stimulate the development of new antimicrobials and complement national funding. Through this model, pharmaceutical companies that do not have an antimicrobial in their portfolio would pay a proportionate share of their revenues into a fund towards the development of new antimicrobials. This measure would impose additional costs and obligations on pharmaceutical companies operating in the EU. However, it could encourage large companies to integrate antimicrobial development into their portfolio. The redistribution of funds by the European Commission should be based on the advice of an expert group, including patient representatives. Specific requirements and transparency rules of this “play or pay” model should be fine-tuned by a panel of independent experts to prevent gaming, namely pharmaceutical industries investing minimally in antimicrobial R&D to meet the required threshold but not intending to bring the product to the market.

Finally, the regulatory framework should create the conditions for faster approval of new antimicrobials. The approval of new antimicrobials should go through the centralised procedure and be eligible for an accelerated assessment, reducing the time from 210 to 150 days, which would both improve patient access and encourage applications for approval of new antimicrobials.

**EPF’s recommendations:**

- Based on the EU-JAMRAI proposition[21], an EU pull incentive mechanism for essential antimicrobials based on an annual revenue guarantee should be incorporated into the revised legislation.
- A "pay or play" model proportional to income should be introduced, in which funds obtained for research into new antimicrobials are collected and redistributed by the European Commission with the advice of a panel of experts including patients and under strict transparency rules.
- The centralised authorisation procedure should be the mandatory procedure for new antimicrobials. New antimicrobials should be eligible for accelerated assessment, which reduces the assessment time to 150 days instead of 210 (Article 6(7) of the proposed Directive 2023/0132).

[20] Outterson, K., Orubu, E. S. F., Rex, J., Årdal, C., & Zaman, M. H. (2022). Patient Access in 14 High-Income Countries to New Antibacterials Approved by the US Food and Drug Administration, European Medicines Agency, Japanese Pharmaceuticals and Medical Devices Agency, or Health Canada, 2010-2020. Clinical infectious diseases: an official publication of the Infectious Diseases Society of America, 74(7), 1183–1190. https://doi.org/10.1093/cid/ciab612

[21] Årdal, Christine et al. (2021). Policy brief: Improving access to essential antibiotics.

- While respecting the principle of subsidiarity and acknowledging that medicines prescribing policies are a national competence, the European Commission, in cooperation with patients and healthcare professionals' organisations, should draft European guidelines on antimicrobial prescribing practices, in line with international standards and recommendations.
- As AMR is recognised as a serious cross-border threat, leverage the creation of the Health Emergency Response Authority (HERA) to coordinate EU action in this area, including efforts to stimulate the antimicrobials' pipeline.

# 3. A PATIENT-CENTRED REGULATORY PROCESS

## EMBEDDING PATIENT INVOLVEMENT IN THE LEGISLATION

The EU should **lead the way in patient involvement** and make it mandatory throughout the regulatory process for medicines.

Patient involvement **improves the outcome of regulatory decisions**, which ultimately contributes to the quality of drug evaluation and outcomes[22]. Patients and their representatives also contribute to the dissemination of EMA Committees' results when they become public and ensure the quality of patient information and communication on medicines. Patient involvement should be recognised and integrated into the revised legislation with the inclusion of a **definition of 'patient organisation'**, as defined by patients[23]. This would be an indispensable starting point for patient-centred legislation and ensure that patient involvement is not sidelined, as was sometimes the case during the COVID-19 pandemic.

We strongly **welcome the inclusion** of four patient representatives and four alternates on the Committee for Human Medicinal Product (CHMP) and the increased representation of patients on the Pharmacovigilance Risk Assessment Committee (PRAC). We would like to note however the importance of retaining the expertise of patients involved in the committees that are set to disappear under the updated legislation and to ensure patients' participation in the scientific working groups to be created by the CHMP. Patients have a thorough understanding of their disease or condition, the benefits and side effects of treatment, and their impacts on their daily lives. Patient involvement can bring immense value to the discussion of benefits and risks.

In addition, patients and their representatives must be **included in decentralised or mutual recognition procedures** via the Coordination Group for Mutual Recognition and Decentralised Procedures – Human (CMDh). Patient organisations, especially those operating at the EU level, have practical knowledge of medicines requiring harmonised product information. Therefore, including representatives from patient organisations would bring value to this Coordination Group. It will further ensure that patients are involved throughout the regulatory cycle of medicines that have not been centrally approved.

[22] Murphy, Aisling & Bere, Nathalie & Vamvakas, Spiros & Mavris, Maria. (2022). The Added Value of Patient Engagement in Early Dialogue at EMA: Scientific Advice as a Case Study. Frontiers in Medicine. 8. 10.3389/fmed.2021.811855.
[23] See EPF, "What is a patient organisation?"

This increased involvement of patients in the regulatory life cycle of medicines must **go hand in hand with reasonable compensation** from the EU budget for the time and efforts spent in preparing, travelling for, and attending meetings. Patient representatives are in a particularly important yet vulnerable position: they are often volunteers and spend a considerable amount of time contributing to the EMA activities. In addition, we call on the European Commission to develop and fund specific training and capacity building programmes to support patients and encourage their meaningful and active participation in regulatory processes and product-specific discussions.

**EPF's recommendations:**

- Patient involvement should be embedded in the legislation with a legal definition of "patient organisation" (Article 4 of proposed Directive 2023/0132), defined by patients.
- Patients and their representatives who are members of the CHMP and PRAC must receive financial compensation from the EMA budget and have access to appropriate training programmes (Article 148 and 149 of proposed Regulation 2023/0131).
- The legislation should provide greater clarity on patient organisations' involvement in other scientific working parties (Article 150 of proposed Regulation 2023/0131).
- Patients and their representatives should also be represented in the Coordination Group for Mutual Recognition and Decentralised Procedures – Human (CMDh) (Article 37 of proposed Directive 2023/0132)

## STREAMLINING PROCEDURES WITH HIGH STANDARDS OF EVIDENCE AND PATIENT SAFETY

A key priority is to ensure that EMA and the EU Medicines Regulatory Network have the appropriate funding and resources to carry out their mission, to keep pace with emerging scientific and technological developments, and to be prepared to address potential future health threats.

This legislative overhaul further represents an opportunity to review and streamline the EU framework for the marketing authorisation of medicinal products to improve patient access to medicines while maintaining stringent standards to ensure patient safety. For example, EPF supports a simplification of EMA's committee structure to make the decision-making process more efficient, as long as the new structure safeguards the quality and independence of EMA's assessments. We also welcome the proposal to reduce the time required for the CHMP's assessment and the Commission's decision, which will speed up the approval of medicinal products and promote rapid access to medicines for patients.

Regarding the new requirements for marketing authorisations, it is necessary to clarify further the conditions for refusal of marketing authorisations. EPF welcomes the efforts to strengthen the Environmental Risk Assessment (ERA) process for all medicines, including those already authorised, in order to limit the potential adverse effects of medicines with a One Health approach, and make the ERA mandatory for all marketing authorisation holders in the EU. However, this should not compromise patients' access to the medicines they need. This new provision opens the door to ethical questions when it comes to life-changing medicines that are highly polluting, such as some oncology products.

Finally, EPF strongly supports the regulatory route dedicated to the repurposing of old medicines and the possibility for not-for-profit organisations, including patient organisations, to submit data on repurposed medicines. Repurposing medicines reduces development costs and makes life-changing treatments available to patients in a shorter timeframe. It has been particularly successful recently in the fight against COVID-19. Not-for-profit organisations have a major interest in drug repurposing because of the lower costs involved. In particular, patient organisations play a key role as data generators. Patient organisations are increasingly active collaborators in research, especially in setting research priorities and collecting data, in several disease areas. We call for the extension of the possibility for not-for-profit organisations to submit data for a new therapeutic indication to all medicines, not just those that meet unmet medical needs.

**EPF's recommendations:**

- Greater clarity on how the new grounds for refusal of marketing authorisation will apply in the case of life-saving but highly polluting medicines (Article 47 of proposed Directive 2023/0132 and Article 15 of proposed Regulation 2023/0131).
- The possibility for non-for-profit organisations, including patient organisations, to submit data for a new indication should be extended to all medicinal products, beyond those that address an unmet medical need (Article 48 of the proposed Regulation 2023/0131).
- Scientific advice for not-for-profit organisations should be extended to all medicines (Article 58 of the proposed Regulation 2023/0131).

## ADAPTING TO SCIENTIFIC PROGRESS

Precision therapies, personalised or stratified medicines, combination products[24], advanced therapies, artificial intelligence medicines, etc. will require new evaluation approaches. EPF calls on EU institutions and Member States to ensure that the pharma regulatory framework remains fit for purpose, adaptable, and consistent with other EU legislation, to facilitate patient access to new products while keeping patient safety at its core.

Many new products, especially those developed for small populations, involve uncertainty regarding their long-term effectiveness at the time of marketing authorisation – available evidence shows a positive risk-benefit, but more data is required.

EPF supports the introduction of new regulatory procedures to adapt to scientific progress, such as regulatory sandboxes or temporary marketing authorisations. Adaptive pathways, where evidence is accumulated post-marketing, can be beneficial to patients, as they allow faster access to potentially life-saving medicines and treatments, especially for niche products. Similarly, rolling reviews and conditional marketing authorisations have enabled the EMA to authorise COVID-19 vaccines and therapeutics in record time. However, these options should **not undermine patient safety** . Strict requirements for post-marketing studies should be included in the

[24] Products where it is not clear if they fall under the definition of medicinal product or some other category (for example medical device or food supplement) for regulatory purposes.

revised legislation, as studies[25] have shown that the generation of post-marketing evidence is usually completed with a significant delay.

In addition, EPF calls on EU institutions to clarify the regulatory framework for combination products and ensure that the system prioritises patient safety. Currently, the absence of clear provisions to establish coordination of the information flow across sectors and appropriate oversight is concerning. As more complex drug-device products are expected to come onto the market, the EU needs a clear and fit-for-purpose pathway to ensure access to safe, effective and high-quality products.

While it cannot replace clinical trial data, the **collection of real-world data (RWD) and the generation of real-world evidence (RWE) can play a critical role** in deepening regulators' understanding of the benefit-risk balance of a medicine and in assessing its value for patients and healthcare systems. RWD can fill evidence gaps and provide insight into "real-life" effectiveness. Patients' full involvement is essential in RWD collection, as they can capture the real world experience. Patient organisations also play a crucial role in RWD collection on the ground and should be recognised as such. To fully leverage the potential of RWD/RWE, patients should be fully involved in future initiatives aimed at providing guidance on e.g. RWD sources, data elements they should include, and data quality standards.

Sharing of health data cannot be separated from patients' access to their own data. Implementation of the Regulation on the European Health Data Space and its synergy with the new pharmaceutical legislation will therefore be crucial to allow patients to have systematic free access to their electronic health records where they can add information, notably on side effects or suspected adverse events.

**EPF's recommendations:**

- The obligation to complete post-authorisation safety and efficacy studies within a certain timeframe and measures in case of non-compliance should be included. Detailed information on the studies should be published in a publicly accessible register (Article 20 of proposed Regulation 2023/0131).
- If a specific condition is not fulfilled in time or if the marketing authorisation holder fails to resolve existing concerns regarding the efficacy or safety of the medicinal product by conducting the study referred to in Article 20 of proposed Regulation 2023/0131, the marketing authorisation should be withdrawn.
- RWD and RWE should complement clinical trial data but not replace it.
- Building on DARWIN EU, the collection and use of RWD to evaluate the effectiveness of authorised medicines continuously should be encouraged.
- Patient organisations should be fully involved in initiatives to further leverage the use and usability of RWD/RWE, including guidance on data standards for RWD.

[25] Hoekman, J., Klamer, T. T., Mantel-Teeuwisse, A. K., Leufkens, H. G., & De Bruin, M. L. (2016). Characteristics and follow-up of postmarketing studies of conditionally authorized medicines in the EU. British journal of clinical pharmacology, 82(1), 213–226. ; and Banzi, R., Gerardi, C., Bertele', V., & Garattini, S. (2015). Approvals of drugs with uncertain benefit-risk profiles in Europe. European journal of internal medicine, 26(8), 572–584.

## INFORMATION TO PATIENTS

Information to patients is a crucial issue for the patient community. Not only does it empower patients and enable them to play an active role in their personal health and care, but **access to high-quality information is also an important aspect of health equity**. The revision of pharmaceutical legislation should therefore move towards more information that is objective, reliable, relevant and user-friendly. It should also support ongoing efforts to increase transparency of data supporting marketing authorisations.

EPF is concerned about the timeline for the full transition to **electronic product information** (ePI) for the package leaflet that is foreseen in the revision. We support ePI as part of an overall strategy to ensure that all patients in the EU have access to comprehensive, high-quality, up-to-date and understandable information on medicines. Information is the cornerstone of patient empowerment that enables health literacy, shared decision-making, and effective self-management. However, ePI should not be seen as a substitute for the paper leaflet, but rather as an opportunity to expand available formats. Paper-based information will continue to be needed for people who do not have online access or whose digital literacy is limited. Similarly, the AMR awareness card must also be available in paper format so as not to exclude patients.

In addition, EPF calls for the inclusion of a **key information section** in the summary of product characteristics and package leaflet, which would allow patients and healthcare professionals to quickly identify key safety messages with information on the benefits of the medicines. According to a study[26] prepared for the European Commission, patients' understanding of the package leaflet and its readability can be improved. The summary of product characteristics is less problematic, although there is still room for improvement, particularly in terms of readability.

The role of patient involvement in the development of the **European Public Assessment Report** also needs to be improved. Patient review at the EMA comes too late in the process, so suggestions for change are difficult to include. Meaningful patient involvement should be incorporated into legislation to ensure that this commitment is not side-lined and that patients are systematically invited to give their views. Similarly, patient organisations should be involved in drafting **the AMR awareness card** to ensure that it meets patients' needs.

Finally, the environmental impact and climate change footprint of medicines are of great concern to patients. The outcomes of the ERA and the overall environmental impact of medicines should not only be limited to the application dossier. **Patients should have easy access to information on how to dispose of the product, and about the environmental footprint of its manufacturing**. This would increase awareness of products that directly contribute to AMR, pollution or global warming. Many patients are not able to play a full role in their care and the environmental impact of their treatments, while they represent a subpopulation uniquely vulnerable to environmental disruptions. Medicines should not be a source of pollution, and every effort should be made to minimise their environmental impact without compromising patients' access to the medicines they need.

[26] European Commission (2017) "Report from the commission to the European Parliament and the Council in accordance with Article 59(4) of Directive 2001/83/EC of the European Parliament and of the Council of 6 November 2001 on the community code relating to medicinal products for human use"

**EPF's recommendations:**

- Electronic product information should not replace paper-based information. Package leaflet should be made available in paper format and electronically (Article 63 of proposed Directive 2023/0132).
- A key information section should be included in the package leaflet and a summary of product characteristics developed together with patients (Annex VI of proposed Directive 2023/0132).
- The involvement of patients in the development of the European Public Assessment Report (EPAR) should be specifically included in the legislation (Article 16 of proposed Regulation 2023/0131).
- Patient organisations must be involved in drawing up the AMR awareness card (Article 69 of proposed Directive 2023/0132).
- Appropriate information about the environmental impact of a medicinal product – and how to dispose of it - should be included on the package leaflet of a product, with a view to raising awareness and empowering patients to access less polluting alternatives when possible.

## About EPF

The European Patients' Forum (EPF) is an umbrella organisation of patient organisations across Europe and across disease areas. Our 79 members include disease-specific patient groups active at the EU level and national coalitions of patients representing 19 countries and an estimated 150 million patients across Europe. www.eu-patient.eu