medicines for europe
better access. better health.

Revision of the pharmaceutical legislation

Position paper

July 2023

EXECUTIVE SUMMARY

Medicines for Europe is committed to improving public health through improved access, availability and affordability of medicines, in line with the pharmaceutical strategy for Europe.

Generic, biosimilar and value added medicines play a pivotal role in ensuring sustainable healthcare systems while substantially increasing patient access to medicines. **Generic medicines provide for almost 70% of dispensed medicines in Europe** and have doubled access to medicines for patients with chronic conditions such as diabetes or cardiology. **Biosimilar medicines** are increasing access to biological therapies dramatically for cancer and auto-immune conditions such as rheumatoid arthritis or psoriasis. For diseases like rheumatoid arthritis, Inflammatory Bowel Disease (IBD) or psoriasis, the availability of biosimilar medicines has led to an average of 11% additional prescription across Europe, allowing lift access restrictions for patients. Ireland managed to treat twice as many patients over the course of 6 years"[1]. **Value added medicines** have demonstrated their potential to **increase patient quality of life** for individuals managing chronic diseases while offering significant benefits to the healthcare community. The **repositioning dexamethasone during Covid-19** is one of many examples where off-patent innovation offers potential.

The recent proposal of the Commission to amend the Pharmaceutical Directive and Regulation is a positive first step towards reforming EU pharmaceutical policy for access, availability and sustainability. Building on this proposal and to fully unlock the potential of off-patent medicines, the following changes should be introduced into the legislation:

1- Predictability and legal certainty to deliver on equitable access

The co-legislators can support generic, biosimilar and value-added medicines uptake policies and timely competition by:

- **Ensuring that the modulation of incentives provides legal certainty for generic and biosimilar medicines applications.**

The modulation aims to reward originators for fulfilling key public health objectives such as ensuring equitable access or addressing unmet medical need. Failure to deliver on those objectives should lead to earlier generic or biosimilar medicine competition and access to medicines. Thus, the EU should modulate the market protection rather than data protection. In this way, in case the originator manufacturer does not fulfil the requirement to supply their

[1] source IQVIA Impact of Biosimilar competition in Europe 2022

products to all EU markets, the generic or biosimilar medicinese would be approved in time to supply the underserved market. Since the EU already has the longest data protection period in the world, the cumulative data protection and market protection period should not be extended beyond the current system (8+2+1= 11 years).

-Removing barriers to off-patent medicines competition at loss of protection. The EU should ban the artificial and unlawful barriers to the day-1 entry of generic and biosimilar medicines by clarifying the Bolar provision in the Pharmaceutical Directive. This should include the supply of EU produced active pharmaceutical ingredients (APIs) for obtaining marketing authorisations and conducting studies as well administrative actions needed for pricing and reimbursement and tender procedures.

- **Rejecting transferable exclusivity vouchers (TEV) for novel antimicrobials that will massively increase costs for healthcare budgets, reduce predictability for off patent medicines producers and delay access to medicines in critical therapy areas like oncology**.
The TEV undermines the fundamental tenant of EU innovation policy by delinking the reward from innovation and research and by effectively creating a market to purchase monopoly extensions for most expensive blockbuster drugs. To encourage equitable access to novel and established reserve antibiotics, the EU should develop a solidarity-based market like the Swedish subscription model combined with the transferable regulatory marketing authorisation review voucher that exists in the US. This will ensure a viable market to reward innovation and the secure supply of reserve antibiotics.

2- Make medicines available via a robust and digital supply chain and an efficient regulatory system.

The proposal should include a European Strategy to prevent the risk of medicines shortages and address vulnerabilities in the global production chain by Improving the efficiency and digitalisation of the Medicines Regulatory Network with:

- **A faster pan-European implementation of electronic product information**. This will enable manufacturers to quickly respond to volatile market dynamics and move products more effectively from one EU country to another to address medicine shortages – 90% of which are limited to a single EU Member State according to the Commission study on shortages[2]. Solidarity based allocation of medicines across the EU is one of the critical lessons learned from the Covid pandemic as the European Parliament has reiterated time and time again.

[2] Future-proofing pharmaceutical legislation - Publications Office of the EU (europa.eu)

- **Improving supply chain transparency to enable pre-emptive measures against shortages**. There are over 10 billion packs of medicine prescribed every year and there should be a way to improve the forecast demand and supply through access to existing regulatory and supply chain data, such as the European Medicines Verification System (EMVS), created under the Falsified Medicines Directive. The EU should not duplicate data that already exists in the EMVS by burdening manufacturers with additional reporting requirements.

- **Supporting a risk-based approach for shortages prevention plans (SPP)**, based on a single coherent list of critical medicines or essential medicines with no alternatives. This will ensure that manufacturers and medicines agencies focus their limited resources on preventing and mitigating shortages rather than producing hundreds of thousands of burdensome reports and submissions that no one will ever have the time or human resources to read let alone process.

- Similarly, **the extension of shortages notifications from 2 to 6 months would massively increase shortage "false alarms" as happened in Italy and in Canada**. Manufacturers and regulators should focus resources on preventing and mitigating genuine shortage risks for patients by harmonising and digitalising the reporting of high risks of shortages and using EMVS data, as mentioned above, to predict shortage risks.

- Develop a science driven, risk-based and efficient environmental risk assessment that successfully addresses "Pharmaceuticals in the Environment" while fully maintaining patients' access to essential medicines. We urge extreme caution against any change to the notion of risk/benefit for pharmaceuticals in this context.

- Go a few steps further in a**chieving greater regulatory efficiency** and to introduce better solutions in the case of some MA procedures (e.g. improving opting -in to the decentralised procedures (DCP), reducing the need for duplicate Marketing Authorisations Applications in the Centralised Procedure (CP) due to use patents, no limiting the Mutual Recognition Procedure (MRP) within a year from the granting of marketing authorisation), while retaining the current flexibility of choosing MA procedure (allowing generic, hybrid and fixed dose combination of known molecules' applications to access both the Centralised (CP) and the Decentralised DCP (national)procedures).

Last but not least, for robust and resilient supply chains, the revision of the pharmaceutical legislation should be complemented by a **Medicines Security Act that echoes the Member States Critical Medicines Act**. An EU medicines manufacturing strategy could incentivise investment in secure essential medicine supplies for the EU while fixing the broken generic medicine market with European Guidelines on sustainable public procurement of medicines and an improved implementation of the Transparency Directive.

3- Affordable innovation that addresses patient needs

Supporting affordable innovation to address patient needs via a clear pathway for repurposed medicines (value added medicines).

To encourage investment in affordable innovation, the co-legislators should include in the article devoted to repurposing all relevant changes which deliver significant benefit to patients, provided they are based on appropriate pre-clinical or clinical evidence. These include new indications, pharmaceutical forms, methods, or routes of administration as well as updates in posology, which can all bring meaningful improvements to health outcomes and help reduce the burden of disease for patients and healthcare systems.

To avoid misuse of this article for evergreening, this should fully respect the letter and spirit of the global marketing authorization which limits the possibility to extend data and market protection beyond the maximum of 10 years for any product or company.

The legislation should encourage commercial investment in repurposing which can support the efforts done by charitable/non-profit entities to bring this kind of innovative medicine to patients in the future. The dedicated pathway established for not-for-profit entities to submit data to support a new indication to the regulatory authorities, recognises these efforts. Approached in a rational manner, considering limitations imposed by intellectual property and ensuring a simple regulatory procedure for manufacturers, this can become a pragmatic solution for addressing inconsistencies between available evidence and authorised uses.

Content

1.

Predictability and legal certainty to deliver on equitable access

1. Predictability and legal certainty to deliver on equitable access

The European pharmaceutical framework is designed to both stimulate innovation as well as guarantee timely access to well-established medicines at day-1 after the intellectual property expires. This will ensure that pharmaceutical policy delivers on promised public health objectives (access, availability and affordability), and supports a competitive industry that delivers for both on patent and off-patent medicines. **To ensure timely and equitable access to off-patent medicines, predictability and legal certainty are of utmost importance**.

1.1 Modulation of incentives: revision of the regulatory exclusivities

(Directive Chapter VII – articles 81, 82, 83)

Medicines for Europe supports the proposal for conditional exclusivities for better access to medicines in all EU countries. However, it is fundamental to **ensure predictability and legal certainty to prevent delays in access to generic and biosimilar medicines compared to the system of today**.

The proposal[3] recommends a baseline of 6 years of data protection and 2 years of market protection. Companies may receive additional protection if certain criteria are fulfilled which increases the total potential period of protection to a maximum of 12 years (13 years in case a Transferrable Exclusivity Voucher (TEV) were added). **This goes well beyond the current legislation which provides for a maximum of only 11 years of market protection**. The criteria for additional protection are to launch and supply the medicine in all Member States (+2 years), to address an unmet medical need (+6 months), and/or to conduct comparative clinical trials (+6 months). A further year of data protection can be granted if the medicine can treat other disease(s).

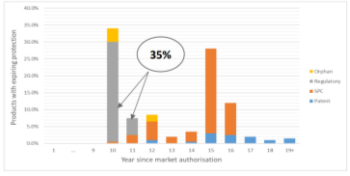
[3] *It is important to have in mind that according to the European Commission's draft proposal* ***the suggested modulation will concern only 35% of products*** *(Impact Assessment, page 38) "It differs case by case which instrument provides the longest protection period after entering the market, as demonstrated by Figure 3 on a representative sample of 200 medicines. Medicines protected by patent or SPC not only enjoy a longer protection, but on average they generate 2-3 times higher revenues than those protected only by RP (Table 3). We expect this ratio among protection types to remain in the next 15 years, therefore the changes to the RP would concern around 1/3 (i.e. 35%) of the new medicines, which have a 23% share among all originator medicine sales in the EU."*

Table 3 Medicines' protection period and revenues by their last layer of protection

Last line of protection	Number of products	Avg. protection duration	Avg peak annual sales[1]
Regulatory protection	69	10.1 years	€ 158.7 m
Market Exclusivity	12	10.7 years	€ 41.7 m
SPC	95	14.3 years	€ 368.3 m
Patent	23	16.7 years	€ 300.5 m
Grand Total	**199**	**12.9 years**	€ 268.2 m

We expect this ratio among protection types to remain in the next 15 years, therefore the changes to the RP would **concern around 1/3 (i.e. 35%) of the new medicines**, which have a **23% share among all originator medicine sales in the EU**.

Figure 3 – Ratio of medicines by the length of last layer of protection and type of protection



1. Predictability and legal certainty to deliver on equitable access

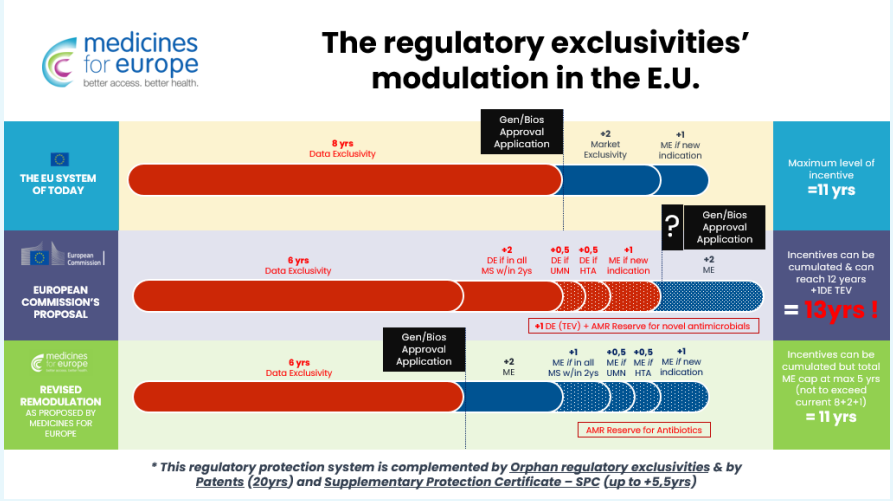
While the intentions of the modulated system are good, there is a lot of uncertainty for follow-on medicines developers.

Medicines for Europe supports the 6 years of fixed data protection, but to ensure that generic or biosimilar medicine developers can fulfil their role in reducing access gaps, the rules for the grant of conditional exclusivities must ensure predictability and legal certainty. Specifically, the proposed modulation of data protection intends to provide clarity to follow-on developers as to the expiry of the protection only less than 3 years before a generic/biosimilar could apply for a marketing authorisation. For one of those criteria (+1 for new indication), competitors would know about the protection extension just one day before the expiry of the data protection, which would block the generic/biosimilar application very last minute, creating inefficiencies not only for industry but also for the Agency. This is certainly not in line with the needed time for making investment decisions, as well as for development of generic (4-5 years) and biosimilar (7-10 years) medicines. Therefore, it would be preferable to modulate the period of market protection rather than the period of data protection to ensure that the filing date for a generic or biosimilar marketing authorisation application would always be clear and fixed at year six after the originator marketing authorisation. Otherwise, there would be no certainty that the generic or biosimilar medicine will be able to enter the market once protections drop.

MEDICINES FOR EUROPE RECOMMENDATIONS

1) To ensure equitable access to medicines for all EU Member States, a **modulation of the market protection instead of the data protection** would enable off-patent manufacturers to develop and apply for a marketing authorisation after six years and then to market the product when the other exclusivities run out. This would dramatically improve the predictability of the system by allowing developers to properly plan regulatory filings. This would have no impact on the originator industry unless they failed to meet the criteria such as supplying all markets.

With **modulated data protection**, there will be uncertainty about the date of protection expiry and once the protection drops (if the conditions for reward have not been met or maintained) the generic or biosimilar would not be approved, and its launch would be delayed. This would nullify the incentive for the originator to comply with the criteria as there would be no threat of generic or biosimilar competition.



2) **Guardrails to prevent evergreening abuses of the incentive system**:

- There is well documented evidence of the abuse of existing incentive schemes to artificially extend monopolies for blockbuster drugs which the new legislation seeks to correct. Therefore, it is important to ensure that the modulated protection system cannot be misused to create legal uncertainty and to delay competition from b **generic and biosimilar medicines**.
- **Decisions to extend protections should be made transparently**, through the timely publication of the variation process for obtaining the conditional additional years of protection, and there should be an administrative procedure for follow-on developers to challenge those additional protection where there is manifest misuse of the system for additional protection periods.
- Since the EU has the longest period of regulatory data protection in the world, (See table 2, European Commission Impact Assessment, page 38) which delays access, affordability and availability, the cumulated period of data protection and market protection should be capped at the current **maximum level of protection (11 years) and not extended to 12 or 13 years.**

Table 2 Basic regulatory protection periods for medicines globally[128]

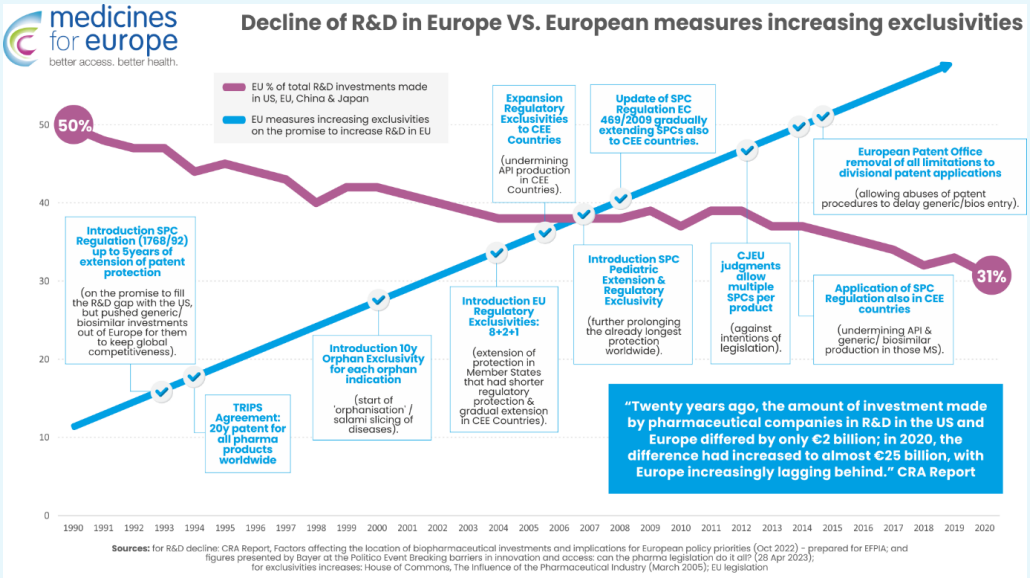
Country	Protection	Duration
Canada	New Chemical Entity+ Market Protection	6+2 years
EU	New Chemical Entity+ Market Protection	8+2+1 years
Switzerland	New Chemical Entity	10 years
USA	New Chemical Entity (small molecule)	5 years
USA	Biosimilar Application Approval Exclusivity (biologic)	4+8 years
Israel	Market Protection	6 or 6.5 years
China	New Chemical Entity	6 years
Japan	New Chemical Entity	8 years

3) Will the pharmaceutical legislation harm EU competitiveness?

We do not agree that the EU pharmaceutical legislation reform will necessarily undermine the competitiveness of the EU pharmaceutical industry.

The decline in global competitiveness of the European pharmaceutical sector in R&D is not related to intellectual property erosion since, as demonstrated in the graph below, **the EU has consistently increased regulatory incentive and IP monopolies since the 1990s. Each new IP or regulatory protection** (product patents under TRIPs, SPCs, the world's longest regulatory and market exclusivities, orphan exclusivity, paediatric exclusivity and SPC extension) **was introduced with the stated objective to make Europe the world leader in R&D innovation. Yet this ratcheting up of monopoly protections corresponds exactly with Europe's relative R&D decline compared to China and the US**. This shows that the claim 'more monopoly leads to more R&D' is false. To make matters worse, these monopoly measures have directly contributed to the delocalisation of medicine manufacturing outside of Europe, although we commend the EU's efforts to correct this with reforms such as the SPC manufacturing waiver or the Bolar exemption.

In contrast, **policy measures that have stimulated competition from the off-patent sector have fully delivered on their promise**. Generic licencing rules have stimulated much needed competition, doubled access to medicines in Europe and reduced pressure on healthcare budgets. Biosimilar licencing rules have made Europe the global leader in this technology and driven substantial investment in EU biologic manufacturing. It is therefore imperative that the Pharmaceutical Strategy for Europe continues to foster this sector.



This Impact assessment of the pharmaceutical legislation underlines (page 43) that *"[a] direct link between EU incentives and EU competitiveness is hard to establish because **while the incentives make the EU markets more attractive, they are agnostic to the medicines' geographical origin**. Around 20% of new medicines authorised in the EU are from the EU, the others are mainly from US, UK, Switzerland and Japan that are equally eligible to all EU incentives. Equally EU based innovative companies can benefit from incentives elsewhere, if they sell their products there. In June 2016, the Council requested the Commission to conduct an evidence-based analysis of the impact of incentive mechanisms, notably SPCs. Two studies have been commissioned. One from Max Planck Institute[4] questions whether the availability of patent or SPC protection affects companies' decisions to locate research facilities in one jurisdiction or another, **emphasising that other factors are likely of greater importance**. The Copenhagen Economics study[5] argued that SPCs could play a role in attracting innovation to Europe, **pointing out that taxation, education, and other factors are probably more significant in that respect**." (Emphasis added)*

[4] Max Planck Institute. Study on the legal aspects of supplementary protection certificates in the EU, 2018.
[5] Copenhagen Economics. Study of the economic impact of supplementary protection certificates, pharmaceutical incentives and rewards, 2018.

Impact on competitiveness and SMEs

For SMEs, the Impact assessment states: (page 60) *"In terms of effect on competitiveness,* ***the proposed incentives do not make a geographic distinction, they equally offer regulatory protection for products developed in the EU, or anywhere in the world*** *which ensures a level playing field between EU-based and third country-based companies. While the EU regulatory framework is attractive for developers,* ***competitiveness also depends on many other factors e.g. tax system and incentives; available grants, loans and other funding (e.g. the European Innovation Council Accelerator); pool of talents; proximity of top academia; clinical trials infrastructures; market size; security of supply chains; favourable reimbursement decisions****." (Emphasis added)*

(page 61) "Similarly, incentives for UMN would benefit SMEs, which are generally willing to make early-stage investments in areas of high risk, by giving more value to their assets even if they are acquired by big pharma in late-stage development. SMEs already enjoy fee exemptions and reductions for regulatory procedures and through the new horizontal measures SMEs will benefit from optimised scientific support with a greater likelihood of success for authorisation. Overall, with the increasing investment in biopharmaceutical R&D and the increasing share of SMEs among developers, biopharma SMEs in the EU and elsewhere would have excellent prospects for the future. Overall, Option C scores the highest in the multi-criteria analysis, this option addresses the most effectively the specific objectives of the revision, and has the most positive economic, social and environmental impacts."

1.2 Transferable exclusivity voucher (TEV) for novel antimicrobials

(Regulation, Chapter III "incentives for the development of 'priority antimicrobials', articles 40-41-42-43)

As the main provider of antibiotic medicines, representing 75% of the antibiotic market, the generic medicines industry is committed to playing an active role in developing policy solutions to tackle antimicrobial resistance (AMR). We recognise the magnitude of the problem and are engaging with our members, stakeholders and policy makers to reduce the spread of AMR.

The Commission is proposing a system of transferable exclusivity vouchers for antimicrobials (which covers a broad scope of medicines including antibiotics, antivirals and antifungals) under certain conditions. **Medicines for Europe agrees with the need to tackle access to reserve antibiotics but strongly opposes the creation of a market to buy monopoly extensions for blockbuster drugs.** This would massively increase costs for healthcare budgets by delaying access to medicines in critical therapy areas, such as oncology. As demonstrated in multiple independent studies [6]and scientific

[6] "Improving access to essential antibiotics" Study by the Slovenian Presidency of the EU and the EU-JAMRAI, reported in the EPSCO Conclusions on strengthening the European Health Union.

articles[7] confirmed by the October European Parliament workshop[8], as well as a vast number of Member States in their non paper published in December 2022[9] ahead of the Health Council (EPSCO), the introduction of transferable exclusivity extension vouchers in the EU would:

Fig. 2. Additional costs calculated by Medicines for Europe on some blockbuster molecules of recent years considering 1 additional year of exclusivity.

- break the founding principle of the relationship between innovation and reward;
- dramatically increase costs for healthcare budgets, with significant risk of overcompensation especially if the development for instance of an antimicrobial would have taken place anyway
- extend monopolies on the most profitable blockbuster drugs delaying access and burdening healthcare budgets.
- unduly delay access to generic and biosimilar medicines for patients;
- Transfer the cost of funding antimicrobials to patients with already limited and unequitable access to blockbuster drugs across Europe;
- increase legal uncertainty and unnecessary litigation for generic and biosimilar medicine developers and manufacturers which need predictability for their investment plans by artificially extending exclusivity periods based on a company's ability to pay for a voucher;

MEDICINES FOR EUROPE RECOMMENDATIONS

The co-legislators should replace the unnecessarily expensive and disruptive TEV with a cost-effective market policy as mentioned in the paragraph 29 of the proposed Council Recommendation on "stepping up EU actions to combat antimicrobial resistance in a One Health approach" to create the design and governance of a Union multi-country pull incentive scheme to improve innovation, development and access to antimicrobials. For novel antibiotics, the policy could take the form of a guarantee revenue as proposed by leading experts on AMR, with a system mirroring the proposal in the EU-JAMRAI study published by the Slovenian Presidency of the EU, also quoted in Dec 2021 EPSCO

Table 8 – Changes to baseline with the voucher and value of voucher

Stakeholder	change	change %
Originator gross profit	**+€387 m**	+10.1%
Generic gross profit	**-€54 m**	-23%
Cost to public payer	**+€283 m**	+4.7%
Patients monetised gain/loss	-€158 m	-3.8%
Patient + payer monetised gain/loss	-€441 m	-7.3%

Fig. 3. European Commission impact assessment that summarises the effects to the various stakeholders, page 47

[7] Transferable exclusivity voucher: a flawed incentive to stimulate antibiotic innovation, The Lancet, Feb 2023 & Transferable Exclusivity Vouchers and Incentives for Antimicrobial Development in the European Union, Cambridge University, May 2023.

[8] European Parliament workshop organised by the ENVI Health Working Group on "Antimicrobial resistance -New incentives to improve the accessibility and availability of antimicrobial medicinal products", October 2022, report accessible here.

[9] Non paper – Novel stimuli for the development and keeping on the market of antimicrobials –Based on an initiative from the Netherlands, and is supported by Austria, Belgium, Finland, France, Hungary, Ireland, Latvia, Lithuania, Luxembourg, Poland, Portugal, Slovakia, and Slovenia

Conclusions (see EU-JAMRAI proposal below). For existing antibiotics, a commitment to keep a reserve for all EU countries would ensure equitable access, along the lines of the model adopted in Sweden.

EU-JAMRAI proposed European pull incentive for essential antibiotics

Step 1: Eligible antibiotics	Newly approved antibiotics would be recommended by European Medicines Agency (EMA) based upon their ability to meet unmet public health need, as assessed by WHO and national governments through existing health technology assessments. Existing antibiotics would be nominated by European countries that are concerned with vulnerable supply.
Step 2: Tendered antibiotics	The European Commission (EC) would gather countries' willingness to participate in the revenue guarantee for each eligible antibiotic. A minimum number of countries would need to express interest for the antibiotic to be included in the tender. National financial responsibility for the guarantee would be apportioned and agreed.
Step 3: Negotiation	The EC would perform a tender for all of the antibiotics defined in step 2. To participate in the tender, a company would need to have either marketing approval through the European centralised procedure or marketing approval in at least one European country (which could be expanded through mutual recognition). Companies must commit to access and stewardship stipulations for all participating countries. For older antibiotics, ideally multiple companies would be selected. The revenue guarantee would be adjusted based upon the countries served.
Step 4: Fulfilment	Participating countries would continue to price, procure, and reimburse the antibiotics as per normal national practices. Companies would meet the access requirements as per the revenue guarantee.
Step 5: Payment	After the close of each year (or other specified time period), companies would report their total unit sales amount for each participating country to the EC. Governments would validate these figures. Each country would then pay the difference between its apportioned guarantee amount and actual sales to the company. If actual sales exceeded the guarantee amount, no further action would be taken.
Step 6: Repeat	This process would be repeated dependent upon the nomination of additional antibiotics, or at the expiry of the revenue guarantees. Ideally revenue guarantees would last 3-5 years.

1.3 Harmonisation of the Bolar clause for timely competition of off-patent medicines

(Directive Chapter VII – article 85)

The social contract of the EU pharmaceutical market is to provide a market protection period to recoup the costs of investing in innovation and then to encourage strong competition at day-1 of expiry. Unfortunately, there is ample evidence of originator companies artificially extending protection periods well beyond the social contract by misusing the patent system in conjunction with regulatory and administrative procedures. This must now be corrected in the pharmaceutical legislation.

The *Bolar* clause allows companies, during the patent/Supplementary Protection Certificate (SPC) protection of the innovative product, to conduct studies, trials and the subsequent practical requirements necessary to obtain regulatory approvals for generic and biosimilar medicines, without this being considered patent/SPC infringement. The Bolar also exempts from infringement certain experimental research activities to develop new medicines.

The stated **primary Bolar objective** is to **ensure immediate day-1 generic and biosimilar competition after expiry of patent/Supplementary Protection Certificate (SPC) protection**[10]. **It can also limit patent linkage strategies to delay generic/biosimilar launches** (which occurs regularly and occurred recently for HIV medicine Truvada). The *Bolar* has been interpreted in different ways by Member States, leading to vast legal uncertainty for developers of generic medicines, biosimilar medicines, and active pharmaceutical ingredients (API), forcing investments on API development outside of Europe. The Commission has finally decided to act in the revision of pharmaceutical legislation to stop unnecessary delays to competition as already announced in 2015[11].

The revised ***Bolar*** clause should therefore **(1) clarify the inclusion in its scope of all regulatory and administrative steps (marketing authorisations, price and reimbursement listing, tender bids, etc.) needed to ensure effective market entry of off-patent products on day-1** and **(2) clarify all the actions allowed by API suppliers (application for the ASMF Certificate, offer, manufacture, supply, storage, import, export, use, sale)**. Moreover, given its distorting impact on competition and the fact that it is against the purposes of the *Bolar* and the principles of the EU pharmaceutical system, **patent linkage[12] should be formally banned** in the legislation, as stated in recital 65, **regarding**

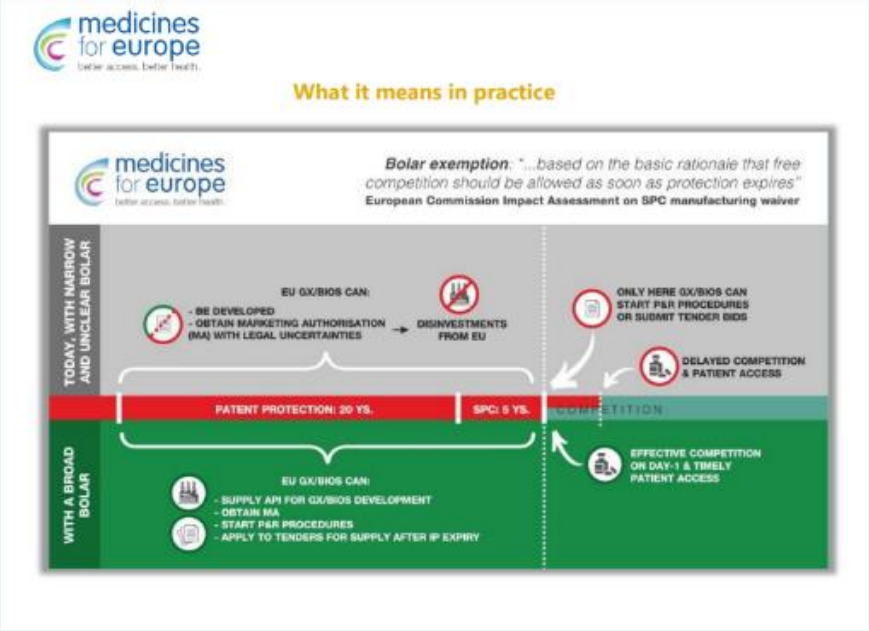
[10] European Commission Impact Assessment on the SPC manufacturing waiver, p. 15

[11] The 2015 Single Market Strategy for Europe identified enlargement & harmonisation of Bolar as a priority. In 2016, the EC published a Charles River Associate study that highlighted the huge benefits for the entire pharmaceutical sector of an extension of the scope of Bolar. In 2017, the EC Roadmap to optimise the IP legal framework explored the Bolar reform and its benefits. In 2018 the Commission issued a Max Planck Institute study describing the willingness of EU Member States to harmonise the Bolar interpretation; The 2020 pharmaceutical strategy includes Bolar as a priority issue for reform to deliver on equitable and timely access. The European Parliament Report on the IP Action Plan urges to address Bolar.

[12] Patent linkage occurs when generic & biosimilars' Marketing Authorisations/P&R decisions/tender bids are blocked due to existing patents covering the reference product. The EC considers it "unlawful" and anti-competitive in its Sector Inquiry Report of 2009, as it delays generic/biosimilar medicines systematically. The 2012 EC Proposal for Revised Transparency Directive included a prohibition of patent linkage. The European Parliament Resolutions on Access to Medicines in 2017 & on the Pharmaceutical Strategy in 2021 urged the

marketing authorisation as well as pricing and reimbursement and tender procedures.

MEDICINES FOR EUROPE RECOMMENDATIONS



As clearly stated in the proposal recitals (63-64-65), the intentions of the Commission are to allow generic and biosimilar medicines to execute all the regulatory and all the administrative phases to ensure immediate generic/biosimilar entry at IP expiry. This means the need to obtain marketing authorisation, pricing and reimbursement decisions and tender bids timely. Consequently **article 85 of the Directive should be drafted in a very clear way to avoid confusion, legal uncertainty and abusive litigation when transposed at national level to *de facto* deliver on equitable and timely access through competition**.

Critically, the legal text of the legislation should include a **clear ban of patent linkage** in relation not only to marketing authorisation, as explicitly included in recital 65 of the revised directive, but also to pricing and reimbursement procedures and tender bids, all necessary steps to effectively allow day-1 competition.

Commission to end patent linkage to ensure immediate market entry for generic/biosimilar competitors. A June 2021 study of the European Parliament confirms the issue, and the European Parliament Report on the IP Action Plan urges to ban patent linkage and to address Bolar.

2.

Make medicines available via a robust and digital supply chain and an efficient regulatory system

2. Make medicines available via a robust and digital supply chain and an efficient regulatory system

The negative consequences of shortages on patient health and healthcare systems highlight the urgent need for policies to ensure the security of supply of medicines. Those policies should avoid a complex and burdensome regulatory environment that could lead to further consolidation of manufacturing and ultimately undermine the benefits of the off-patent sector in increasing access to medicines and preventing shortages.

The Covid-19 pandemic showcased the failings of national and European policies in preventing medicines shortages and encouraging a sustainable competitive off-patent medicines market. The situation has been exacerbated by skyrocketing inflation rates and the dramatic increase of all input costs for medicine manufacturing such as energy prices, raw materials (risen by between 50%-160%), packaging, transport (up to 500%), and logistics which cannot be absorbed by manufacturers in the off-patent sector due to strict price regulation, budget austerity measures, and lowest-price tender rules, causing substantial price erosion and an unsustainable situation for manufacturers.

This paper analyses the provisions within the scope of the revision of the pharmaceutical legislation, but it is important to underline that the structural root cause of shortages lies in the pricing and procurement of these medicines, as evidenced in Commission studies such as the Technopolis Study on medicines shortages[13] or the study on best practices in the public procurement of medicines. Both studies identify the absence of supply security criteria in market policies as a major risk for the EU. [14]

Therefore, as described in a proposal for a Medicines Security Act, an action plan to prevent and mitigate shortages should be implemented by the European Union. To complement the pharmaceutical legislation some critical policy measures are needed, such as the upgrading of the medicines procurement system via European guidelines to support Member States in the implementation of the Public Procurement Directive, with a strong focus on incorporating requirements for more diversified, multi-winner tenders and inclusion of MEAT criteria, to reward companies that invest in the twin (green and digital) transition, and security of supply. The latter, according to Commission studies is included in only 24% of tenders, mostly for vaccines[15]. Canada[16]

[13] Technopolis Study ''Future-proofing pharmaceutical legislation Study on medicine shortages: final report''
[14] Study on best practices in public procurement of medicines (Gesundheit Österreich GmbH).
[15] Study on best practices in public procurement of medicines (Gesundheit Österreich GmbH) page 40-41.
[16] Medicines for Europe CreativCeutical study on "New pricing models for generic medicines (infographic and full study).

and Australia[17] introduced security of supply criteria into medicine tenders with successful results that could serve Europe as well and giving the off-patent medicines sector access to European funds to boost investments in APIs and essential medicines and requested by the Belgian government along with 20 Member States.

In the pharmaceutical legislation, we call on:

* European measures to improve the digital collection of data to monitor medicine shortage risks.
* A clear European strategy to prevent and mitigate shortages.
* An efficient regulatory system that delivers on medicine availability.

2.1 European measures to monitor medicine shortages

Definitions

"Shortage"
(Regulation, Article 2 Definitions, para 14)
Medicines for Europe supports the harmonised definition of a shortage: the supply of a medicinal product that is authorised and placed on the market in a Member State does not meet the demand for that medicinal product in that Member State.

A common definition is crucial to standardise and automate shortage reporting across the EU. Additionally, the Covid-19 pandemic underlined the critical importance of defining a shortage based on patient needs. This was acknowledged in the definition of "demand" of Regulation 2022/123 on a reinforced role of the EMA, where demand includes the request of a healthcare professional or patient in response to clinical need. Patient needs should similarly be included in the definition in the Regulation. This will ensure that speculation does not exacerbate hoarding and profiteering by traders in a shortage.

"Critical shortage in Member State"
(Regulation, Article 2 Definitions, para 15)
Medicines for Europe supports the harmonised definition of "critical shortage in Member State" which means a shortage of a medicinal product, for which there is no appropriate alternative medicinal product available on the market in that Member State, and that shortage cannot be resolved.

[17] Landmark new medicines agreements to bring significant benefits for Australian patients.

Medicines for Europe supports this definition, which is crucial to facilitate European coordination, and will streamline the process of addressing critical shortages. This harmonisation will also facilitate the move towards automation and digitalisation of shortage reporting.

Definition "Critical medicinal product"
(Regulation, Article 2, para 13 + Article 127, 130)

Building on the European Commission's structured dialogue on the security of medicines supply[18], Medicines for Europe supports the Commission text to define critical medicinal products at the EU level and the development of a common methodology in consultation, where appropriate, with relevant stakeholders to identify those critical products which includes the evaluation of vulnerabilities within the supply chain of those medicines, in consultation, where appropriate, with relevant stakeholders. In line with the outcomes of the structured dialogue, this methodology should consider both the therapeutic indication and importance of the medicines as well as the availability of appropriate alternatives. Given the role that critical medicinal products play in bolstering the resilience of healthcare systems and ensuring public health and patient care, it is imperative that their supply is consistently secured, with targeted measures:[19] critical medicines should be taken as a reference list for specific shortage prevention requirements, such as shortage prevention plans.

Medicine shortages reporting requirements

The European Commission has extended the notification periods for marketing authorisation holders:

- For withdrawals and permanent cessation of the marketing obligation, the notification period is of 12 months.
- For temporary disruptions (i.e. expected shortages lasting more than 2 weeks), the notification period is of not less than six months before the start of such temporary disruption of supply or, if this is not possible and where duly justified, as soon as manufacturers become aware of such temporary disruption. This approach is relatively similar to that of the US Food and Drug Administration (US FDA).

The 6-month notification period for shortages will create a massive increase in false-alert shortage notifications as demonstrated by the experience in Canada and in Italy. This will create overwhelming burdens for manufacturers and National Competent Authorities (NCAs) responsible for shortage monitoring without any benefit for patients. This has been clearly displayed in countries which opted

[18] This structured dialogue has been established on February 2021 to identify supply chain vulnerabilities and propose solutions to make medicines and APIs supply chain more resilient.

[19] Final Report Workstream 2 on critical medicines. The purpose of this workstream is to consider available methodologies and criteria and identify medicinal products that are considered to be critical to public health and discuss methodology to trace EU manufacturing capacity for those critical products.

for longer notification requirements such as Italy and Canada, where the number of shortages reported exceeded the previous levels by tenfold. In Italy, the burden has been so high, including for the regulatory authority, that the 4-month notification period is being reversed to 2 months.[20] It is therefore important to ensure that the system remains targeted so that MAHs can make informed notifications when they anticipate real shortage risks rather than focusing on the risks of penalties. To this end, the adoption of an FDA-like approach (notification where possible as opposed to at all times) will be beneficial in decreasing the incidence of false alarms.

To ensure that the implementation of such a comprehensive and complex reporting system is feasible for MAHs and NCAs, the shortage reporting system **must be fully digitalised and automated with a one-stop reporting system** leading to a streamlined centralised reporting based on single notification. This should enable two-way communication, with standardised requirements (notification criteria, template, vocabulary…) to which both the European Medicines Agency and the National Competent Authorities have access. This harmonised approach, which should apply to both nationally and centrally authorised products, will also offer a complete picture of the shortage risks and enable solidarity across member states.

In the proposal, the data from **the European Medicines Verification system** is deemed appropriate to monitor the supply status of products for data protection prolongation for market launch (Article 82.1 of the Directive proposal). The proposal, however, does not extend the use of the EMVS data for shortage reporting and monitoring. To ensure an automated system, leveraging the EMVS will be necessary, and notably already to input the European shortages monitoring platform (ESMP), where 70-80% of the information required from MAHs is readily available from EMVS. This will also improve the EU's ability to detect shortage risks as the system contains all information related to supply and demand for prescription medicines. A sudden surge in demand or a mismatch between supply and demand can be detected with this data.

MEDICINES FOR EUROPE RECOMMENDATIONS

Shortages reporting requirements

The generation of a thousands of false alerts resulting from a 6-month notification period should be avoided. Instead, a digitalised and automated reporting system would allow MAHs to report shortages a soon as they are aware without placing an unnecessary burden on either them or the competent authorities.

[20] Decreto legge Semplificazioni, Schillaci: "Ricetta elettronica a regime e modifica a norma carenza farmaci" (federfarma.it)

2.2 A clear European strategy to prevent and mitigate shortages

Introduce the use the data of existing IT systems for supply chain transparency and shortages prevention

The proposed legislation correctly identifies the need to harmonise the definition of medicine shortages across the EU so that in the future, it will be possible to digitalise shortage notifications to the authorities. This is essential as it is not possible today to understand from shortage notifications where shortages are occurring in the EU. This significantly delays the possibility for manufacturers to resolve shortages through more efficient allocation across member states. In addition, this should enable the EU to tackle the distortions caused by medicines trading and hoarding that undermine the possibility of ensuring solidarity-based healthcare in the EU.

(To be added in the Directive, art 67, para 6, safety features)

Unfortunately, the proposal fails to build on this harmonisation to introduce a shortage prevention system within the pharmaceutical legislation. In addition to addressing the market failures with European guidance on medicines public procurement (this would build on the outcomes of the study on best practices in the public procurement of medicines), policymakers should use the potential of existing IT tools to forecast demand and supply to prevent medicine shortages.

Today the EMA and national regulatory authorities could already increase the visibility and transparency of the supply chain by using the data of existing IT systems, such as the data stored in the interoperable network of national repositories being set up in the context of the European Medicines Verification System (EMVS), introduced by the Falsified Medicines Directive (2011/62)[21]. The data stored in the interoperable network of national repositories being set up in the context of the Falsified Medicines Directive (Directive 2011/62/EU) and its Delegated Regulation 2016/161/EU on safety features can be used to provide additional intelligence to monitor shortages. Indeed, this data could provide useful intelligence regarding the number of packs for all prescription products being supplied by manufacturers on the various EU markets, the number of packs dispensed in national pharmacies, the number of packs exported (and/or imported), as well as on the level of stocks present in the

[21] Medicine Shortages: From Assumption to Evidence to Action - A Proposal for Using the FMD Data Repositories for Shortages Monitoring.

supply chain at country level. The real-time information in the repositories can be analysed according to very granular time frames (per day, per week, per month etc.) as well as per region (postal codes). That wealth of data would supplement information already provided by Marketing Authorisation Holders on manufacturing and quality-related supply disruption to National Competent Authorities, and in providing information on the causes and extent of shortages beyond manufacturing-related issues, would facilitate the detection and mitigation of genuine shortages. This system would also facilitate cooperation and solidarity between Member States when a shortage occurs by giving visibility to the availability of stocks across the Member States.

Regulatory efficiency and harmonisation measures are also essential to improve supply chain resilience, with measures such as the replacement of paper leaflets with electronic product information (ePI) and the harmonisation of packs and requirements at national level can dramatically reduce complexity, stockouts and misallocation across countries. Additionally, the removal of the requirement for an official language for products not intended to be delivered to the patient for self-administration would improve the availability of medicines and facilitate the reallocation of products across Member States. During the Covid-19 pandemic, this concept was proven to be very efficient, specifically on the flexibility in distribution, therefore by having a positive impact on the availability of medicines.

Union list of Critical medicinal products

(Regulation, Article 131, The Union List of Critical Medicinal Products)

Building on Covid-19 lessons learned, Medicines for Europe supports the creation of a European list of critical medicinal products for which coordinated Union-level action is required. The proposal does not provide enough harmonisation and simplification as it encourages the identification of critical medicines by the Member States, which could lead to the development and multiplication of national lists of critical medicinal products. We are also concerned that the proposed list is limited to products for which coordinated action is needed. Rather, we believe that a **Union List of Critical Medicinal Products** should be prioritised while avoiding national lists which create duplication and confusion, undermining the unity of the regulatory system.

Shortage prevention plans

(Regulation, Article 117, The shortage prevention plan)

The requirement to develop shortage prevention plans (SPP) should be based on a risk-based approach to determine which medicines should be covered by a SPP. This approach would avoid unnecessary duplications and administrative burdens associated with the preparation of SPPs and submissions, without compromising public health. This risk-based approach would also facilitate

targeted prevention and mitigation actions by manufacturers and regulatory authorities, while also considering the practical limitations and feasibility of preparing shortage prevention plans for all licensed medicines. A shortage Prevention Plan should therefore be limited to critical medicines, and especially for those that have no alternatives available on the market, rather than attempting to cover all licensed medicines in the EU (currently there are 500.000 licensed medicines in the EU).

Electronic product information to mitigate and prevent medicine shortages

(Directive - Chapter VI, Product Information and labelling, Article 63, General principles on package leaflet

Medicines for Europe welcomes the introduction of the digital leaflet (electronic product information-ePI) and is looking forward to continuing working with the relevant national regulatory authorities for its fast implementation in the European Union in a patient-centric approach.

Improve the security of the medicines supply. Building on the Covid-19 lessons learned and on the timely support of the Ukrainian population from EU manufacturers, the replacement of the paper leaflet by ePI will undoubtedly facilitate the reallocation of products without time-consuming and expensive repackaging and prevent and mitigate shortages.
The removal of the paper leaflet removes language barriers so that medicines could be easily moved across Member States to relieve local shortages in a timely manner while ensuring patients have access to the product information. This measure is particularly relevant because, according to a Commission study, on average a shortage affects 1 Member State[22].

Patients and healthcare professionals will be instantly updated with the most up-to-date information on the correct use of medicines. By including the digital leaflet in the regulatory dossier[23] the product information will be updated in real-time and in compliance with regulatory requirements. This will be relevant for:

- Healthcare professionals who will receive in real-time any information (new indication, side effects, etc) that will support and improve their daily activity while reducing medication errors.
- Patients affected by chronic diseases would be supported by digital solutions (such as multimedia, video, dictionary, and search tools) that will support the understanding and engagement of their health and management of their medications.

Patients will not be left behind. For patients who are confident using digital tools, ePI can play a role in improving health literacy, notably by giving patients easier access to information, for example for

[22] December 2021 EC study on shortages root causes, figure 10, page 37.
[23] Substance, product, organisation and referential (SPOR) master data, reference to EMA website

those who struggle to read the small characters of paper leaflets (bigger font sizes or digital solutions such as multimedia, video, dictionary, search tools) or patients who currently do not receive leaflets for products administered by healthcare professionals (such as vaccines).[24]
At the same time, patients who are not confident using digital tools have the right to receive a paper copy, therefore we are looking forward to working with authorities and relevant stakeholders to find the best solution to ensure access to product information.

Support the Green Deal objectives by reducing paper waste. The Green Deal emphasises the potential of digital transformation as a key enabler for reaching its objectives. In Europe in 2021, 14 billion packs were distributed to hospital and 13 billion packs to retail, a fast introduction of the digital leaflet would massively reduce paper waste. For hospital products notably, the paper leaflet is routinely discarded as soon as the pack is opened without being read or given to the patient.

MEDICINES FOR EUROPE RECOMMENDATIONS

1. **Increase visibility of supply chain and leverage existing data sources by using the EMVS serialisation system**

To increase the visibility and transparency of the supply chain, a single interoperable shortage reporting system accessible should be used, leveraging existing sources of data included as the data stored in the interoperable network of national repositories being set up in the context of the European Medicines Verification System (EMVS), introduced by the Falsified Medicines Directive (2011/62).

2. **Fast and harmonised implementation of electronic product information by 2030**

The introduction electronic product information should happen in the fastest and most harmonised way possible to increase the availability of medicines, especially in smaller markets. Based on the learnings of hospital pilots, the obligation to provide a paper leaflet for products not intended to be delivered directly to the patient should therefore already be removed

3. **Adopt a single EU-wide list of critical medicines and use a risk-based approach for targeted prevention and mitigation actions**

A single Union List of Critical Medicinal Products should be created, avoiding national lists which creates duplication and confusion. This list should be the basis of prevention measures such as Shortages Prevention Plans should be developed based on a risk-based approach to consider the unfeasibility of preparing shortages prevention plans for all medicines, without compromising public health.

[24] Replacing vaccine paper package inserts: a multi-country questionnaire study on the acceptability of an electronic replacement in different target groups.

2.3 Efficient regulatory system that delivers on medicine availability

The regulatory framework for Marketing Authorisations (MAs) is a critical initial step for both timely patient access to medicines and the sustainable development of the industry to meet future patient needs. The revision of the pharmaceutical legislation shall remove current barriers and create a modern, fit-for-purpose regulatory framework for continued access to future off-patent medicines.

The legislative proposal introduces several provisions to optimise regulatory operations for both authorities and industry:

- Introducing a broader and future-proofed definition of generic medicines, allowing an openness to more sources of evidence than bioequivalence studies.
- Shortening the MA (Marketing Authorisation) procedure from 210 to 180 days.
- Abolishing the sunset clause and MA renewal as unnecessary administrative process, without any value for patients' access.
- Improving a Repeat Use Procedures (RUP, enabling quicker reactions to patients' needs and efficient solutions to mitigate a shortage.
- Modernising the variations system with the digital maintenance of marketing authorisations and reporting changes directly into databases.
- Building on existing knowledge without duplication of the Risk Management Plan (RMP) and Environmental Risk Assessment (ERA) for generic and biosimilar medicines by relying on originator data.
- introducing a single assessment and certification procedure for the Active Substance Master File (ASMF), not repeatedly and redundantly assessing the same documentation for an active substance . **Adjustment is still needed for the ownership of the 'active substance master file'. The ASMF Holder should be the legal entity that has the ultimate responsibility for the Active Substance Master File, not necessarily the manufacturer**.

In addition to the positive developments above, there **are areas for improvement to fully deliver on pharmaceutical legislation objectives:**

1. A too restrictive scope of the Marketing Authorisation (MA) procedures.
2. Reducing the need for duplicate Marketing Authorisations Applications in the Centralised Procedure which create confusion for patients.

3. The possibility for Member States to opt-in to generic decentralised application procedures shall not lead to extensive obligations on the MAH and the process of opting-in by a MS shall be efficient for authorities and industry (Opting -in Member States to recognise, for public health reasons, the outcome of the MA procedure within 5 days after the procedure has been closed, upon agreement with the applicant, instead of proposed process which would cause unnecessary administrative burden and delay in MA procedure.
4. Restricting the Mutual recognition application within a year from the granting of that marketing authorisation.

1. **Too restrictive scope of the Marketing Authorisation (MA) procedures. The proposal is restrictive on the pathways for authorising generic, hybrid and fixed dose combination of known molecules' medicines applications.**

Generic, hybrid and fixed dose combination of known molecules' applications need access both the Centralised (CP) and the Decentralised DCP (national) to ensure the widest possible access to medicines for patients in Europe. Procedures to offer EU patients wider access to medicines (by using the CP) ; but at the same time allowing smaller/ regional companies to provide access and competition to medicines in those markets where they are commercially active (by access to the DCP and without being forced to use the quite costly centralised procedure). Restricting access to these procedures could reduce access for many smaller markets or certain regions with low access to medicines. Consequently, the access of generic medicines applications to the Centralised Procedure should be made clear in the proposal (although it is possible under the current framework) as this is important for EU-wide access. In contrast, for hybrid applications (when full conditions of a generic application cannot be met due to some additional bridging studies to be provided), the proposal restricts this to the Centralised procedure when it should be possible to use either the CP or the DCP (national) process.

The legal basis and requirements for the MA application of combination products containing known active substances needs to be adjusted. For medicinal products containing two or more active substances previously used in the composition of authorised medicinal products, the results of relevant pre-clinical tests or relevant clinical trials or bibliographic references relating to that combination should be provided. This however, is not necessary for molecules where *already known and available* data and references relating to each individual active substance are available as this would be a redundant repetition of data requirements.

2. Duplicate Marketing Authorisation Applications in the Centralised Procedure.

The revised legislation should address the negative impact of "use" patents on generic and biosimilar medicines as this clearly undermines the uptake of generic/ biosimilar medicines and creates unnecessary confusion for patients.

The requirement to duplicate generic/biosimilar packaging and brand names multiple times due to "use" patents (often linked to evergreening strategies to delay competition) of the originator is a waste of resources and time for industry and medicine agencies. It also creates confusion for patients as the marketing names of the medicines must be changed. The legislation should stop requiring generic and biosimilar medicine manufacturers to multiply duplicates for "use" patents over which they have no control. The legislation could easily adapt labelling to the "use" patent landscape across EU MSs (a set of patient leaflets to be used in Member States depending on the use patent landscape under the umbrella of one CP Marketing Authorisation). In addition, the legislative proposal removed the existing option to vary the term of the marketing authorisation (thus, to keep an existing name of a generic/ biosimilar medicine already familiar to patients) and to add information for which the corresponding patent(s) or supplementary protection certificate(s) has(ve) expired. If the proposal of a set of patient leaflets reflecting use patent landscape under one CP Marketing Authorisation is not accepted, the option of varying the existing MA should be reintroduced to avoid confusion for patients.

For public health reasons, safety related information claimed by a patent and included, in sections 4(c) to 4(i) of Annex V of the summary of product characteristics and in the package leaflet of the reference product, should not be considered a patent infringement (or used as evidence of infringement). The information in the SMPC cited under Articles 9 till 12 is necessary for the safe use of the medicinal product and, therefore, should not be considered a patent infringement.

3. The possibility for Member States to opt-in to generic decentralised application procedures

The possibility for Member States to opt-in to generic decentralised application procedures triggers certain questions regarding the obligations of MAHs who may have no commercial activities in those member states. We recognise the opportunity to facilitate availability in smaller national markets provided there are no regulatory delays, additional costs/burdens (fees, reporting, supply obligations, etc.) pertaining to those markets, and no direct market obligations (commercial establishment, registration for pricing and reimbursement lists or to procurement registries and procedures). The Directive should explicitly state that MAHs (Marketing Authorisation Holders) will have no additional national obligations (i.e. no obligation to remain in pricing and reimbursement lists, to participate in procurements and to contribute to clawback taxes that force the generic medicine industry to subsidise the originator industry). This approach is fair because the generic industry will not receive

any incentives to supply more national markets. In contrast, the originator industry will be provided 2 years of data protection/monopoly to launch in these markets which is a massive incentive.

It is also important to ensure that the process of opting-in by a MS remains manageable for authorities and industry (obligation to inform **all** MSs Authorities about **thousands of** on-going procedures). For example, allowing the opt-in within 30 days of the submission of the application, which is longer than foreseen validation period and when the procedure should have already started, would cause unnecessary delay and disruption of the process (especially in view of shortening procedure time from 210 to 180 days). A practical solution to achieve the same objective would be for the competent authority of a Member State to **recognise for public health reasons the outcome of the MA procedure within 5 days after the procedure has been closed, upon agreement with the applicant** and the competent authority of the reference Member State for the authorization procedure. The applicant could then provide the competent authorities of those Member States entering the procedure with the application without undue delay.

4. **Regulatory Procedures not fully supporting the objective of improving access by restricting the Mutual recognition application to within a year from the granting of that marketing authorization**

While the new proposal prevents mutual recognition application submitted within the granting of that MA, the repeat use procedures should not be prevented within the first year, as in practice, it is often necessary to initiate a repeat use procedure within the first year for several reasons:

- IP considerations: There may be circumstances where a particular country, such as Portugal, cannot be included in the first round of authorisation due to IP evergreening restrictions. As a result, a repeat use procedure is necessary within the first year to include the country in question.
- Marketing authorisation transfer: When a marketing authorisation is transferred from one company to another, the acquiring company may have a different commercial structure or operational requirements. This scenario often requires a repeat use procedure within the first year to align the marketing authorisation with the new company's specific circumstances.
- Additional marketing authorisations: Sometimes, an additional marketing authorisation may be needed due to supply constraints from the original authorisation source. In such cases, a repeat use procedure within the first year becomes essential to secure an alternative authorisation to address the supply constraint effectively.
- Changes in commercial situations: The commercial landscape is dynamic, and circumstances may arise where the original commercial plan needs adjustments. For instance, market conditions may change, necessitating a repeat use procedure within the first year to accommodate the new commercial situation effectively.

2. Make medicines available via a robust and digital supply chain and an efficient regulatory system

MEDICINE S FOR EUROPE RECOMMENDATIONS

1. **Ensure flexibility through the scope of the Marketing Authorisation (MA) procedures**

Offer flexibility in marketing authorisation applications by ensuring the possibility for generic, hybrid and fixed dose combination of known molecules' marketing authorisation applications to choose between the centralised procedure and the decentralised procedure. This flexibility enables broader availability of medicines through the option of the centralised procedure while avoiding imposing the burden of the higher costs of the centralised procedure for smaller companies for whom the national routes might be more appropriate.

2. **Address the negative impact of use patents and duplicate MA applications**

Remove the requirement for generic and biosimilar manufacturers to duplicate packaging and brand names for use patents, by instead adapting labelling to the use patent landscape, and reintroduce the option to vary the term of the marketing authorisation to add information once the corresponding patents or SPCs have expired.

3. **Offer a pragmatic approach to the opt-in mechanism**

While the opt-in proposal can facilitate availability in smaller national markets, it should be shaped pragmatically to ensure fairness by avoiding imposing additional regulatory delays, costs, burdens, or market obligations on the MAH (Marketing Authorisation Holder). Instead of opting in the procedure, the competent authority should have the opportunity to recognise the outcome of the procedure which would ensure it causes no delay

4. **Avoid unnecessary barriers to availability of medicines which would result from the restriction of the mutual recognition application within a year from granting the marketing authorisation**

Allow repeat use procedures including within the first year of granting of the marketing authorisation.

5. **Ownership of the 'active substance master file (ASMF) certificate'**

Adjustment is needed for the ownership of the 'active substance master file'. The ASMF Holder should be the legal entity that has the ultimate responsibility for the Active Substance Master File, not necessarily the manufacturer.

2.4 Environmental footprint

Our sector is engaged in efforts to reduce pharmaceutical residues in the environment with the Eco-Pharmaco-Stewardship initiative (EPS) through a science-based approach covering the full lifecycle of a medicine. These commitments include the development and implementation for strict standards for the management of manufacturing effluents for antimicrobials (AMR Industry Alliance) and other products, as well as awareness-raising campaigns on the proper disposal of unused medicines (Meds Disposal).

Medicines for Europe encourages a pragmatic approach to the environmental risk assessment (ERA), which makes the most efficient use of time and resources of both industry and regulators and has the goal to minimise environmental impact while respecting the EU proportionality principle. Medicines for Europe is fully supportive of the Commission proposal to continue to allow generic and biosimilar companies to reference the data of the originator thus avoiding repetition of unnecessary studies and delays in access to medicines.

In addition, Medicines for Europe supports Commission's efforts to tackle antimicrobial resistance through the development of a further detailed ERA for these medicines, as well as through the development of an antimicrobial stewardship plan and the use of an awareness card to inform patients on the appropriate use and disposal of antimicrobials.

MEDICINES FOR EUROPE RECOMMENDATIONS

- The environmental assessment should be based on the perceived risk associated with the release of the product into the environment rather than on its hazard element.
- For medicinal products referred to in Articles 9 to 14, the applicant may refer to ERA studies conducted for the reference medicinal product when preparing the ERA or studies of any other medicinal product containing the same active substance(s).
- For medicinal products authorised before 30 October 2005 that have not been subject to any ERA ("legacy products"), there should be a clearer focus on high risk (for the environment) medicines to avoid overwhelming the regulatory network with submissions. This must be done with environmental risk as the priority keeping in mind the limited resources of national medicines agencies and joint assessment should be encouraged.
- For active substances, where no ERA is yet available, missing ERA data should not be grounds for refusal of marketing authorisation. The applicant should follow the programme to conduct joint studies for the ERA (if applicable) to minimise unnecessary duplication of data and use of animals as a part of the post-MA commitments (instead of rejection).
- In the assessment of environmental risk for the legacy products, EMA should play a leading role as opposed to other EU agencies which do not deal with medicines.

3.

Affordable innovation that addresses patient needs

3. Affordable innovation that addresses patient needs

3.1 Repurposing (Value Added Medicines)

(Directive Chapter VII, Data protection for repurposed medicinal products, Article 84)

The revision of the pharmaceutical legislation should address patient needs and the accessibility and affordability of medicines. This is especially important as **out of 7000 diseases with a known molecular basis, only around 500 have approved treatments[25], which leaves an enormous gap in the system**. Moreover, many existing treatments could be improved to reduce the risk of adverse events or to help patients comply with their treatment. Value added medicines, which are obtained by repurposing off-patent molecules can serve as an accessible, affordable type of innovation to address unmet health needs, relieve burden on health systems and lead to better quality of life for patients[26].

Value added medicines developed through different repurposing strategies make a difference in the daily life of patients and contribute to the sustainability of health systems and healthcare systems:

1. REPOSITIONING: FINDING NEW INDICATIONS TO ADDRESS UNMET MEDICAL NEED

A great example is **dexamethasone**, an affordable steroid normally used to treat inflammatory conditions (such as allergic disorders and skin conditions) and severe autoimmune diseases (ulcerative colitis, arthritis, lupus, psoriasis, and breathing disorders), was where it **repositioned for Covid-19 treatment, reduced deaths by 1/3 in hospitalised Covid-19 patients receiving mechanical ventilation in ICU (Intensive Care Unit)**[27].

[25] Online Mendelian Inheritance in Man, Morbid Anatomy of the Human Genome
[26] Medicines for Europe White Paper: Creating a European Ecosystem for safe, timely and affordable patient-centric innovation

[27] Source RECOVERY TRIAL.

2. REFORMULATION: EXPANDING PATIENT ACCESS TO TREATMENT AND REDUCING BURDEN ON HEALTH SYSTEMS

Repurposed medicines obtained through reformulation of existing molecules can bring care closer to patients, while removing pressure off health systems, through changes to new routes of administration or pharmaceutical forms such as sublingual films or pre-filled syringes, which can be used in a **home setting. This has a great relevance for oncological patients who will not be obliged to go to the hospital**, as was recommended during Covid-19.

Reformulation is also particularly important to expand treatment to **paediatric populations**, for example, a reformulated liquid form of midazolam (normally used before having minor surgery and treatment of seizures), has been used to treat close to 7 million seizures in children with epilepsy in the past 5 years[28].

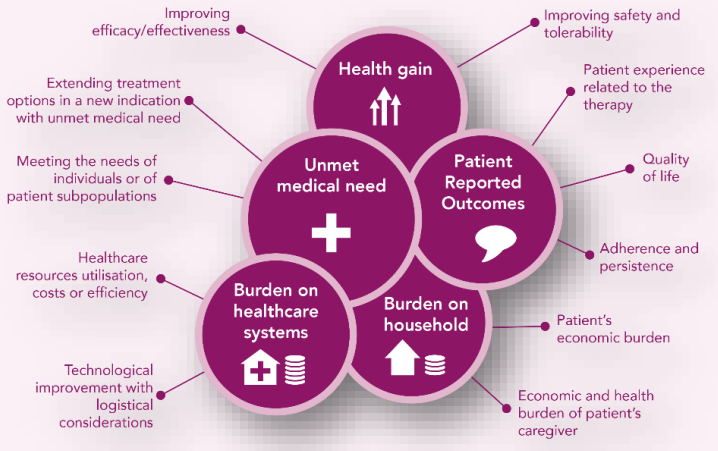
3. COMPLEX COMBINATIONS: CREATING BETTER HEALTH OUTCOMES THORUGH PATIENT CENTERED CARE

In chronic respiratory diseases, where 1 in 2 patients struggles with adhering to treatment, combining a medicine with a delivery device which had an audiovisual reminder, led to a 20% increase in adherence. Combining medicines with innovative digital health solutions can also support the patient-HCP relationship, though, for example, monitoring in a remote care setting, and create better health outcomes by leveraging technological progress[29].

[28] IQVIA MIDAS Database

[29] Source: Principal trial Inhaled corticosteroids to be investigated as a possible treatment for Covid-19 in national PRINCIPLE Trial — PRINCIPLE Trial

MEDICINES FOR EUROPE RECOMMENDATIONS



The Commission recognises the importance of repurposed value added medicines as a source of affordable innovation and their value for patients, their caregivers, and the healthcare systems with a non-cumulative 4-year data protection period set out in Article 84 of Directive 2023/0131. This is an excellent basis for supporting the development of alternative affordable sources of innovation brought by value added medicines.

The legislation should:

- Clarify the article to **include all changes brought through repurposing, including changes in methods or routes of administration, posology, or pharmaceutical form if they bring a significant benefit to patients**.
- Align to the concept of significant benefit in the orphan legislation which recognises patient centred benefits, such as improvements in quality of life, adherence, or burden on the patient.
- Future-proof the legislation by referring to non-clinical and clinical evidence, as many repurposing projects have their origins in the real world.
- Ensure that the **Article is not misused for evergreening practices**, by also excluding products which have benefitted from market protection and making the link to the concept of a global marketing authorisation in Article 84(1) point b.

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