Impending changes to European pharmaceutical regulations

Part I. Civil society's analysis of the Commission's proposals: major changes ahead, improvements needed

In 2020, the European Commission announced its new "Pharmaceutical Strategy for Europe" for the coming years (1). One aspect of this strategy involves a major revision of the European Union's (EU) general pharmaceutical legislation, and its legislation on rare diseases and paediatric drugs (2).

In order to prepare these documents and initiatives, the Commission organised several public consultations beforehand, concerning: its roadmap on its Pharmaceutical Strategy; the strategy itself; its roadmap on the revision of the legislation; and the revision of the legislation itself (1-8).

The new legislation is due to be published in 2023. It will be presented to the European Parliament and Council for approval (2).

This article consists of excerpts from the Commission's proposals, as well as excerpts from contributions submitted to the Commission's public consultations by Prescrire and a European alliance of civil society organisations, in which Prescrire participated.

In a future issue, we will publish excerpts from a report produced for the European Parliament, in connection with these consultations, which calls for the creation of a "European Medicines Infrastructure" (9).

Roadmap for the Pharmaceutical Strategy for Europe: drug shortages, pricing and innovation (mid-2020)

The European Commission held a consultation on its proposed "Pharmaceutical Strategy for Europe" between June and September 2020 (1).

The Commission's objectives stated in its roadmap. "*Medicines play an important role in assuring diagnosis, treatment and prevention of diseases. We as citizens across the EU expect to benefit from equal access to safe, innovative and affordable therapies because our health often depends on them. If treatments are not available due to shortages or because we simply cannot afford them, our health can be compromised. The Commission intends to design a plan that will address the current issues of access, availability and affordability of medicines, while still promoting sustainable innovation and support EU industry to remain an innovator and world leader. It also aims to strengthen the current system and help it respond to public health threats such as the coronavirus pandemic, without compromising patient safety*" (1).

Prescrire's response to the consultation on the roadmap: more transparency and robust evidence for evaluations and decisions. Prescrire responded to this consultation in July 2020. Our contribution set out our priorities for the Pharmaceutical Strategy:

– Higher regulatory standards for marketing authorisation of new drugs based on robust evidence and obligatory randomised comparative trials;

– The revision of the incentives and rewards provided by the current legislation on orphan drugs and paediatric medicines should put a stop to the abuses of these provisions over the past years;

– Improved patient safety, including improvements to drugs already on the market, in particular through better packaging and better product information, clearly stating the quality of the data underpinning the authorisation;

– Greater efforts to prevent drug shortages, ensuring the diversification of supply chains and clarifying the pharmaceutical industry's legal obligations;

– Greater independence of the European Medicines Agency (EMA) and European institutions' decision-making processes from the influence of the pharmaceutical industry, and eliminating the risk of regulatory capture, through which the decisions of public bodies are made in favour of commercial interests.

Prescrire considers that transparency, evidence-based policy development and access to clinical data are priorities that benefit patients and the public in general. These points should be reflected in Europe's future Pharmaceutical Strategy (3).

The Pharmaceutical Strategy adopted by the European Commission, following its roadmap (late 2020)

The European Commission adopted its Pharmaceutical Strategy for Europe in November 2020, which reprised the broad lines of its roadmap (2).

The four-pillared strategy, as seen by the Commission. "*Adopted on 25 November 2020, the Pharmaceutical Strategy for Europe aims at creating*

a future proof regulatory framework and at supporting industry in promoting research and technologies that actually reach patients in order to fulfil their therapeutic needs while addressing market failures. It will also take into account the weaknesses exposed by the coronavirus pandemic and take appropriate actions to strengthen the system.

It will be based on 4 pillars, which include legislative and non-legislative action:

– Ensuring access to affordable medicines for patients, and addressing unmet medical needs (in the areas of antimicrobial resistance and rare diseases, for example);

– Supporting competitiveness, innovation and sustainability of the EU's pharmaceutical industry and the development of high quality, safe, effective and greener medicines;

– Enhancing crisis preparedness and response mechanisms, diversified and secure supply chains, address medicines shortages;

– Ensuring a strong EU voice in the world, by promoting a high level of quality, efficacy and safety standards" (2).

The issues, according to the Commission. "*People across the EU expect to benefit from equal access to safe, modern and affordable therapies. Medicines play an important role in this regard, as they offer therapeutic options for diagnosis, treatment and prevention of diseases. Europe's pharmaceutical sector is a major contributor to the EU economy in terms of creation of highly skilled jobs and investment in innovation.*

Digitalisation and innovation in the use of real world data open new possibilities in how medicines are developed and used. However, innovative therapies do not reach all patients across Europe at the same speed and patients might not have access to medicines they need due to shortages. The unprecedented coronavirus pandemic further demonstrated how important it is to have a crisis-resistant system and ensure availability of medicines under all circumstances.

At the same time, Europe's population is ageing and the EU faces a rising burden of diseases and emerging health threats such as COVID-19. Moreover, health systems and patients have difficulty bearing the cost of medicines. The EU is also becoming increasingly dependent on non-EU countries for importing medicines and their active ingredients; and issues such as antimicrobial resistance and environmental sustainability of medicines is also a concern.

The strategy, through its objectives described above, is a policy instrument that aims to tackle these important challenges and adapt the EU pharmaceuticals system in the years to come" (2).

A European alliance of civil society organisations responds to the new Pharmaceutical Strategy with a set of proposals (2021)

The European Alliance for Responsible Research and Development (R&D) and Affordable Medicines published a set of recommendations in December 2021, endorsed by Prescrire and 12 other European organisations (4).

"*Civil society organisations believe that the following general recommendations should guide an efficient and balanced EU Pharmaceutical Strategy.*

1. ***Ensure that access and affordability of safe and effective pharmaceuticals are addressed in all aspects of the EU pharmaceutical strategy***.
2. ***Ensure transparency for R&D costs and in all steps of the process.*** *The strategy should be aligned with the 2019 World Health Organization resolution on transparency. A requirement should be introduced at the stage of market approval for companies to disclose their R&D and manufacturing costs, as well as the public funding contributions received, and other key information regarding the regulatory dossiers containing clinical trial data, active pharmaceutical ingredient sources, number and status of patents and patent applications and information about their supply chains.*
3. ***Remove incentives that impede access to affordable medicines and consider the harmful effects of incentives that act as barriers for the use of flexibilities to ensure access to medicines.*** *Existing and new incentives should not be an obstacle for the use of flexibilities such as compulsory licensing (…). In light of the lessons learned during the COVID-19 pandemic, a voluntary mechanism is not sufficient, and a binding provision is needed.*
4. ***Do not add new incentives without clear evidence, and transparent and inclusive discussions about their potential benefits for patients and society.*** *For instance, new incentives to stimulate the development of new antibiotics through transferable exclusivity vouchers do not seem to be supported by evidence that they could address the complexities and vulnerabilities of the R&D context for new antibiotics.* (…)
5. ***Remove unnecessary barriers to competition and address abuses of the system and unfair practices.*** (…) *Competition law and policy should be actively used to correct abuses of the system and unfair practice, while generic competition should be promoted for off-patent drugs for rare diseases.* (…)

6. ***Bring coherence to the system by aligning R&D policies with access to affordable medicines policies.*** *The EU is an important public funder of R&D at global and EU level, and a major buyer of medicinal products. It should hence seek to align its R&D policies with its ambitions to foster access to affordable medicines.* (...)
7. ***Give serious consideration to alternative new models of organising, financing, and incentivising R&D for areas of unmet medical needs.*** (...) *This can include the promotion of early-stage research by academic and public institutions, later stage development approaches tested in the neglected diseases field, advanced market commitments and subsidies for non-for-profit manufacturers.*
8. ***When public funding is used to support R&D, targeted obligations in the form of conditionalities and transparency should be used to guarantee public return on public investment.*** (...)
9. ***The role of non-profit parties such as academia and research institutes should be enhanced and supported to cover disease areas with low commercial interest.*** (...)
10. ***Prioritize and support the needs of public health and patients when making changes to the current legislative framework***" (4).

Proposed revision of Europe's pharmaceutical legislation: Prescrire's responses to the public consultations (2021)

The European Commission continued implementing its Pharmaceutical Strategy for Europe by organising two public consultations in 2021 on its planned revision of Europe's pharmaceutical legislation, which reprised the broad lines of its strategy (5,6).

Public consultations on the roadmap and on the proposed revision. In April 2021, Prescrire raised the following points in its response to the Commission's public consultation on the roadmap for its revision of Europe's general pharmaceutical legislation:

– On the fundamental need to maintain high standards of rigorous evaluation, we reminded the Commission of the need for robust evidence before marketing authorisations are granted, based on double-blind randomised comparative clinical trials;

– Accelerated assessment procedures are legitimate when there is a real unmet health need. However, because they increase the uncertainty regarding the clinical value and safety of the drug in question, accelerated assessment procedures should only be used in exceptional cases, in serious situations for which no appropriate treatment exists, so as to avoid unnecessarily exposing patients to avoidable harm;

– Accelerated procedures require that evidence be gathered after marketing authorisation has been granted. Failure to respect post-marketing commitments and requirements should not be tolerated.

– On the matter of security of supply, Prescrire stressed the need to clearly inform and remind marketing authorisation holders of their legal obligations, the need for minimum stock levels, diversification of supply chains and potential alternative production sites, as well as transparency over production sites and production capacity (5).

Prescrire responded to the consultation on the revision of European legislation in December 2021, reprising the demands expressed on the Commission's roadmap (7).

Revision of the legislation on orphan drugs and paediatric medicines. The Pharmaceutical Strategy for Europe also includes a revision of the regulations relating to paediatric drugs and orphan drugs (1). Prescrire responded to the consultations on these issues.

The planned revision is based on the observation that the incentives in place have not been effective in stimulating R&D in areas of unmet medical need, nor at ensuring access to drugs in all member states.

In our response in July 2021, Prescrire argued that the system of incentives and rewards to encourage R&D in orphan and paediatric drugs should be adjusted to concentrate on unmet medical needs for which no specific treatments exist. One option would be to combine the two criteria of rarity and unprofitability: the disease must be rare and the return on investment to develop the product must be low.

The system of incentives and rewards should also include obligations, such as transparency over R&D costs, access to clinical data, and fair and affordable drug prices.

In the case of paediatric drugs, Prescrire stressed the importance of developing dose strengths and formulations adapted to the needs of children (8).

In a future issue, we will publish excerpts from a report produced for the European Parliament, in connection with the consultations surrounding the Pharmaceutical Strategy for Europe, which calls for the creation of a "European Medicines Infrastructure".

► Translated from *Rev Prescrire* October 2022
Volume 42 N° 468 • Pages 784-787

Selected references from Prescrire's literature search

1- European Commission "Pharmaceuticals – safe and affordable medicines (new EU strategy)". ec.europa.eu accessed 2 February 2022: 2 pages.
2- European Commission "Pharmaceutical strategy for Europe". ec.europa.eu accessed 2 February 2022: 4 pages.
3- Prescrire "Prescrire response to the pharmaceutical strategy roadmap" 7 July 2020: 4 pages.
4- European Alliance for Responsible R&D and Affordable Medicines "Getting incentives right in the new EU pharmaceutical strategy" 21 December 2021: 14 pages.
5- Prescrire "Prescrire response to European Commission public consultation on the roadmap/inception impact assessment on the evaluation and revision of the general pharmaceutical legislation" 27 April 2021: 5 pages.
6- European Commission "Towards a reform of EU's pharmaceutical legislation" Brussels 28 September 2021: 2 pages.
7- Prescrire "Prescrire response to the open public consultation on the revision of the general pharmaceutical legislation" 15 December 2021: 26 pages.
8- Prescrire "Final response - Open Public Consultation on the revision of EU rules on medicines for children and rare diseases" 12 July 2021: 14 pages.
9- European Parliament Research Service "European pharmaceutical research and development. Could public infrastructure overcome market failure?" December 2021: 129 pages.