Impending changes to European pharmaceutical regulations

Part II. The European Parliamentary Research Service in favour of a European Medicines Infrastructure

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 in advance: a consultation on its roadmap for its Pharmaceutical Strategy, followed by a consultation on the strategy itself; and a consultation on its roadmap for the revision of the legislation, followed by a consultation on the revision of the legislation itself (1-8).

The new legislative proposals are due to be published in 2023. They will be submitted to the European Parliament and Council for adoption (2).

In Part I, we published excerpts from the Commission's policy options 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 (9).

The present article reproduces extensive excerpts from a report published by the European Parliamentary Research Service, produced in connection with these consultations, which calls for the creation of a "European Medicines Infrastructure" (10). This report was commissioned by the Panel for the Future of Science and Technology (STOA), a group of Members of the European Parliament tasked with providing the European Parliament with information concerning the evaluation of science and technology policy (11). The report was authored by Italian and Czech academics (10).

Analysis of the limitations of the current research model, and proposal for a public infrastructure

The report analyses the strengths and weaknesses of the current pharmaceutical research and development (R&D) model in Europe. It then proposes a new approach to pharmaceutical policy, including the creation of a Europe-wide public R&D infrastructure.

"*In such a context of rethinking a European approach to pharmaceutical policy, the STOA Panel of the European Parliament has launched the present study to investigate the current model of pharmaceutical research and innovation system. The study explores the desirability and feasibility of setting up a large-scale European public infrastructure aimed at addressing long-term market and policy failures in the pharmaceutical sector throughout the whole drug life cycle (research, development, production and distribution)*" (10).

Six failures in the functioning and regulation of the pharmaceutical market

"*The study identifies six failures affecting the functioning and regulation of the pharmaceutical market, for which the current public policies and regulatory remedies are less than adequate, namely:*

Disconnection between corporate R&D choices and public health priorities. *While the industry has had and still has a brilliant track record of innovations, there is evidence that the productivity of its R&D has been shrinking, in terms of new medicines and their cost, particularly in certain areas. From a public health perspective, this raises concerns around the disconnection between corporate R&D priorities and the most urgent needs for human well-being. Governments have frequently considered subsidies to corporate R&D as a way to curb this disconnection. The policy is currently implemented generously by several governments through a number of grant schemes, with the US subsidies to industry for Covid-19 vaccines a notable example. However, beyond the current emergency, which has seen an unprecedented amount of government money transferred to the industry, there is evidence that this policy is not efficient and effective in the long term.*

Mismatch between open science in the public sector and patents protecting the investors. *The current business model of the pharmaceutical industry heavily relies on the 'legal monopoly' provided by filing a patent or family of patents. The traditional aim of patent legislation is to counterbalance the private incentives of legal monopoly with*

an obligation to publicly disclose information on inventions in the patent files. This disclosure in principle would create a positive externality, as the social value of a patent would be greater than its private value because third parties would benefit from such public information. However, this disclosure mechanism has limited scope because trade secrets remain de facto undisclosed, not to mention economic information on actual R&D and production costs. The protection granted by patents is even more disproportionate in consideration of the increasing diffusion of open science practices in fundamental research, largely funded by public money, providing free access to a wealth of scientific results to private companies. In the legislation or actual practice, there is no evidence of systematic policy frameworks to deal with the protection of the public interest when a combination of open science upstream, government subsidies to R&D, patents and market authorisation leads to unfavourable outcomes (such as unaffordable prices, scarcity of medicines in certain fields, uncompetitive corporate strategies).

Rents for financial investors in the pharmaceutical industry arising from government subsidies to R&D. *For each new authorised medicine, the R&D cost is generally directly and indirectly supported by a combination of public sector grants to biomedical research either upstream or directly to firms. Unfortunately, there is no systematic public scrutiny of the social cost and benefits of such a mechanism of subsidies, while it clearly implies rents ultimately captured in the abnormal shareholder value of pharmaceutical companies, as showed by international evidence. (...) Several governments try to curb excess profits in the pharmaceutical industry by implementing certain price controls. However, lacking reliable cost information for the regulators, this seems a scarcely effective instrument to contain the increasing price of new medicines.*

Oligopolistic market power on the supply side, and issues of access and affordability of medicines. *The pharmaceutical sector structure has a highly skewed distribution: an oligopolistic core with a fringe of companies acting in different submarkets or therapeutic areas. It effectively works as a set of legal or de facto monopolies on most medicines, with the unavoidable implications of market power: prices, particularly for new medicines, are associated with wide margins over opaque costs; frequent mergers and acquisitions lead to further market concentration; production choice and the value chain are optimised to extract rents for the top multinational corporations. This market structure contributes to high drug prices which, in turn, create affordability problems for patients and sustainability of healthcare systems. (...)*

Inadequate optimisation studies of medicines after market authorisation. *While companies have all the incentives to invest money in preparing clinical trials and other studies to support their applications for marketing authorisations, they have no incentive to perform comparative clinical trials and 'real life' studies after a drug has been authorised, especially if they include post-authorisation comparisons across medicines, including those of competitors. Regulators may try to convince companies to perform long-term studies, or they can commission such studies from third parties. The first approach may not be successful for lack of incentives. The second approach has been implemented, so far, only in a non-systematic and often voluntary manner by non-commercial entities.*

Information asymmetries in the public procurement of medicines. *While a considerable quota of the market for medicines, particularly in Europe, is ultimately with a government payer (hospitals, public health authorities, etc.), pharmaceutical companies have no interest in sharing information on the cost structure of R&D, or the production and distribution cost of medicines. Hence, most public authorities have limited data to ascertain whether their public procurement arrangements, including the long-term resilience of production capacity in a country, are efficient*" (10).

A public infrastructure to overcome market failures

"*Such market and policy failures suggest exploring a policy approach based on a more direct public intervention (as it was successfully experienced for space policy and other science-based sectors): the creation of a pan-European R&D infrastructure and delivery organisation for medicines in certain critical areas. It should be based on frontier biomedical science, with an overarching public-health mission and a long-term vision and funding. More specifically, such European Medicines Infrastructure should:*
– have the sole mission of fulfilling European citizens' interest in being offered under all circumstances safe, effective, innovative and affordable medicines in R&D areas affected by market failures and other issues of concern;
– have a comprehensive, forward-looking, long-term strategy and dedicated leadership and governance supported by the consensus of scientific communities and health authorities;
– own the results of the R&D projects it undertakes, either fully or in specific cases with public-private partnerships, and manage its intellectual property rights and any other ownership rights on innovations exclusively in the public interest;
– be largely open to collaborations, in partnership with third-party research centres at national or European level and with pharmaceutical companies, even outside the EU when needed, based on clear, transparent contractual arrangements".

Main missions of the public medicines infrastructure. "*The main missions for the European Medicines Infrastructure may include:*
– Building a portfolio of innovative pharmaceutical R&D projects in selected pharmaceutical areas and related biomedical fields over a period of thirty years

(2050) in the spirit of looking at the needs of the next generation of European citizens. In the most ambitious option, such projects should address therapeutic areas: (i) not sufficiently addressed by the private sector; or (ii) where the private sector charges exorbitant prices; or (iii) where there are shortages or supply is not secure.

– Carrying out clinical studies relating to drugs already authorised such as: (i) comparative safety and effectiveness trials of existing drugs; (ii) long-term safety studies; and (iii) studies for drug repurposing.

– Monitoring the supply of raw materials or components for drugs, often imported from outside the EU. Based on the results of the monitoring, it should also take action, when needed, to address bottlenecks in the supply, and promote projects aimed at improving the security of supply for Europe, in collaboration with other EU institutions".

Four policy options for the public medicines infrastructure. "*The study suggests four policy options* (…):

Policy option 1. *Beyond such baseline, the first option, the most constrained one, involves the creation of a European Medicines Infrastructure for pharmaceutical R&D in the public interest, based on its own agenda specifically in the highest priority field: R&D on vaccines and medicines for infectious/transmissible diseases and arrangements for their delivery. The new organisation will have its own governance (with both top-level scientific and managerial skills), its own budget, and would essentially work through R&D contracts with selected third parties. Such contracts are not to be seen as grants or subsidies to such third parties, but as public procurement arrangements, with the intellectual ownership rights of any discoveries and the delivery mechanisms of new medicines under the ultimate responsibility of the new European public infrastructure. A core, but relatively limited, in-house R&D capacity (staff and laboratories) would be necessary for certain tasks.*

Policy option 2. *The second option is similar to the previous one but with a wider mission. Under this option, the infrastructure scope would include other fields where both the public and private sectors are under-investing, such as, again, vaccines and medicines for infectious diseases, but also for example medicines related to neurogenerative conditions, rare diseases, some types of cancer and genetic conditions. (…) As in the previous option, the new organisation will have its own governance (with both scientific and managerial skills), budget, contractual arrangements with external suppliers and partners, and a core but relatively limited in-house laboratory and staff capacity. It will mainly work with a range of procurement contracts with third parties around the horizontal missions.*

Policy option 3. *The third option concerns the creation of a large-scale, mission-oriented, European Medicines Infrastructure with an exclusive focus on infectious diseases, but – differently from the previous two options – such a new organisation, while also working through contracts with third parties, would have its own hired scientific staff and world-class dedicated laboratories to manage most of its research in-house. It would cover most of the cycle from basic research to delivery of new medicines, with appropriate contractual arrangements with third parties, as in the above options, but would have greater R&D autonomy and delivery mechanisms.*

Policy option 4. *The fourth option is the most ambitious one in terms of scope and delivery mechanisms. It is similar to the previous one, as it concerns the creation of a large-scale, mission-oriented European R&D infrastructure. It would have, however (similarly to Option 2), a wider R&D agenda, i.e. not constrained to infectious diseases, as compared to the previous option. This option would manage its own scientific staff and laboratories, and create the most important public R&D infrastructure in the world, at a scale comparable with the intramural research programme of the US federal government sponsored National Institutes for Health, and going beyond it in terms of ownership and delivery mechanisms of innovative medicines and related technologies. It would firmly place Europe as the top global player in the field of R&D for medicines, with direct benefits for patients and public health systems, early career researchers, and also with potential benefits for the European pharmaceutical industry in terms of possible partnership on specific projects*" (10).

Future articles will address the announced revisions of the EU's general pharmaceutical legislation and legislation on rare diseases and paediatric drugs.

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