European Alliance for Responsible R&D and Affordable Medicines

Getting incentives right in the new EU pharmaceutical strategy

Executive Summary

This note outlines key recommendations of civil society organisations for the new EU pharmaceutical strategy. A key pillar for this new strategy is the balance between providing innovation incentives for new medicines and ensuring their accessibility, availability, and affordability.

The note looks at several EU pharmaceutical incentives (e.g., orphan drug legislation, Supplementary Certificates of Protection, market and data exclusivities and incentives for the development of new antibiotics). It also looks at current limitations to the use of compulsory licenses. For each of these areas, the note identifies current flaws and proposes improvements for the future.

In addition, the note provides the following general recommendations that civil society organisations believe should guide the new 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.
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.
4. Do not add new incentives without clear evidence, and transparent and inclusive discussions about their potential benefits for patients and society.
5. Remove unnecessary barriers to competition and address abuses of the system and unfair practices.
6. Bring coherence to the system by aligning R&D policies with access to affordable medicines policies.
7. Give serious consideration to alternative new models of organising, financing, and incentivising R&D for areas of unmet medical needs. This will help address the high and rising costs of medicines to treat diseases in these areas, as well as the persisting lack of development in some diseases of greatest unmet need.
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.

European Alliance for Responsible R&D and Affordable Medicines

About this note

This note is based on the experience and expertise of the European Alliance for Responsible R&D and Affordable Medicines' Members and presents key messages and recommendations for the new EU Pharmaceutical Strategy from the perspective of patients, consumers, healthcare professionals and public health organisations.

It has been endorsed by 13 organisations:

1. Consumer Association the Quality of Life (EKPIZO)
2. Access to Medicines Ireland
3. Global Health Advocates
4. Médecins du Monde France
5. Médecins du Monde Germany
6. NoGracias
7. SOMO-Centre for Research on Multinational Corporations
8. Asociación por un Acceso Justo al Medicamento, Spain
9. Prescrire
10. Pharmaceutical Accountability Foundation, Netherlands
11. Wemos foundation
12. Salud por Derecho
13. Médicos del Mundo España

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About the European Alliance for Responsible R&D and Affordable Medicines

The Alliance is a civil society coalition gathering consumer, patient and public health organisations calling for the creation of an R&D system that is driven by public health needs and delivers medicines that are universally accessible and affordable.

European Alliance for Responsible R&D and Affordable Medicines

Introduction

The new Pharmaceutical Strategy for Europe provides an ideal opportunity to address long standing issues for public health innovation and to redress the imbalance between innovation incentives and access to medicines. It is also an opportunity to learn from the COVID-19 pandemic. Through this note, the Alliance and its Members wish to give their contribution to this process.

Incentives within the new EU pharmaceutical strategy: striking the right balance

Intellectual property rights, including patents and other exclusive rights such as data and market exclusivities, exclusivities for drugs with orphan and paediatric designations, and supplementary certificates of protection (SPCs) aim to provide innovation incentives by rewarding successful innovations with a temporary monopoly. Exclusive rights are based on the assumption that the prospect of a temporary monopoly will encourage more innovation, but their downside is that they lead to high prices and limited production during the exclusivity period. Another downside is incentivising innovation in lucrative areas instead of areas with medical need (based on need or disease burden).

For medical innovations, where access "can be a matter of life and death, of wellbeing and illness"[1] maintaining a balance between the need to stimulate innovation and the need to guarantee access to affordable medicines is crucial[2]. This requires fine-tuning of the incentives system. Other innovation incentives, including public funding for medical technologies and prizes, also exist along with exclusivities. This adds a further layer of complexity that needs to be carefully considered.

What is wrong with the system?

Public health systems in high-income countries have been under increasing pressure due to the high prices of medicines. One primary cause for this are the market monopolies granted to pharmaceutical companies. These monopolies have been facilitated by expanded forms of intellectual property protections.

Over the past few decades, a plethora of new intellectual property incentives on top of patents have been created by the EU for pharmaceutical innovations. These new incentives have been justified under the purported need to compensate for delays in the regulatory approval of medicines (as in SPCs), or the need to create incentives in markets where "traditional" intellectual property rights do not work, either because the market is too small (as in the orphan/paediatrics legislation), or because it is not attractive enough for the private sector (as in the case of incentives for new antibiotics).

As a result, pharmaceutical incentives have been stacked on top of each other, creating multiple barriers and making the overall period of exclusivity longer. This, along with the emergence of abusive practices that take advantage of loops in the patent system (e.g. evergreening, secondary patenting) has increased barriers and delayed competition[3], ultimately leading to higher prices and lower production of critical medicines.

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[1] Boulet P., Garrison C., Ellen't Hoen E. (2019). European Union Review of Pharmaceutical Incentives: Suggestions for Change. Available at: https://medicineslawandpolicy.org/wp-content/uploads/2019/06/MLP-European-Union-Review-of-Pharma-Incentives-Suggestions-for-Change.pdf

[2] Council conclusions on strengthening the balance in the pharmaceutical systems in the EU and its Member States [2016] C269/31, https://www.consilium.europa.eu/en/press/press-releases/2016/06/17/epsco-conclusions-balance-pharmaceutical-system/

[3] European Commission, Final Report in the Pharmaceutical Sector Inquiry (July 8, 2009), https://ec.europa.eu/competition/sectors/pharmaceuticals/inquiry/

In addition to exclusivities, pharmaceutical companies have had access to enormous amounts of public funding, an additional incentive that has traditionally played a crucial role for biomedical R&D. The most recent example of the unlimited combination of exclusivities and public funding to support medical technologies is in the development of COVID-19 vaccines[4].

Pharmaceutical incentives have been created without evidence that they are needed for the public interest, and with limited tools for governments to balance innovation incentives with public interest needs, or even obtain information about actual R&D costs of the pharmaceutical sector[5]. As a result, pharmaceutical profits have received increased protection, while EU citizens and payers are increasingly faced with limited access to affordable medicines[6]. As the EU maintains a leading role in many international fora, including the World Trade Organization, and as it aims to be "a global norm setter"[7], the consequences of its legislative and regulatory framework for pharmaceutical incentives affect other countries[8]. Many incentives, including SPCs, are actually binding for other countries as a consequence of free trade agreements (FTAs) --as well as binding for the EU itself (therefore limiting policy space). As a result, the EU pharmaceutical strategy provides an opportunity to redress these problems in the EU and beyond.

Opportunities within the new EU Pharmaceutical Strategy

One of the four pillars of the EU Pharmaceutical Strategy is ensuring access to affordable medicines for patients and addressing unmet medical needs. To achieve these goals, the EU must commit to supporting innovation based on people's needs and access to affordable health technologies. It will also need to improve transparency in the sector and ensure that public funding conditions are put in place to protect the public interest. Assessing and reviewing the current system provides an opportunity for the European Commission to restore a critical balance between public health needs, access, affordability and innovation, address some of the flaws of the IP and pharmaceutical systems, and place public health needs at the core of its strategy for the ultimate benefit of patients, citizens and health systems. It is high time to refine the Intellectual Property (IP) and pharmaceutical systems in order to ensure these crucial questions are approached properly.

As the EU embarks on a key revision of its pharmaceutical framework and takes stock of old and recently learned lessons, it should consider evidence on the impacts of exclusivities compared to other incentive mechanisms, such as public funding, prizes and others. Exclusivities, such as the ones covered

[4] Kiszewski, A. E., Cleary, E. G., Jackson, M. J., & Ledley, F. D. (2021). NIH funding for vaccine readiness before the COVID-19 pandemic. *Vaccine*, *39*(17), 2458-2466. Sampat, B. N., & Shadlen, K. C. (2021). The COVID-19 Innovation System. *Health Affairs*, *40*(3), 400-409. McMahon, A. (2021). Global equitable access to vaccines, medicines and diagnostics for COVID-19: The role of patents as private governance. *Journal of Medical Ethics*, *47*(3), 142-148.

[5] Secretary-General, U. N. Co-Chairs of the High-Level Panel (2016) The United Nations Secretary-General's High-Level Panel on Access to Medicines Report: Promoting Innovation and Access to Health Technologies. Perehudoff, K., Mara, K., & Hoen, E. T. (2021). *What is the evidence on legal measures to improve the transparency of markets for medicines, vaccines and other health products (World Health Assembly resolution WHA72. 8)?[Internet]*. WHO Regional Office for Europe.

[6] Boulet P., Garrison C., Ellen't Hoen E., 2019, op. cit. Ploumen, L., & Schippers, E. (2017). Better life through medicine—let's leave no one behind. *The Lancet*, *389*(10067), 339-341.

[7] European Commission, Communication from the Commission to the European Parliament, the Council, the European Economic and Social Committee and the Committee of the Regions, Making the most of the EU's innovative potential An intellectual property action plan to support the EU's recovery and resilience, COM/2020/760 final.

[8] Perehudoff, K., Durán, C., Demchenko, I., Mazzanti, V., Parwani, P., Suleman, F., & de Ruijter, A. (2021). Impact of the European Union on access to medicines in low-and middle-income countries: A scoping review. *The Lancet Regional Health-Europe*, *9*, 100219.

in this note, are rarely able to spur innovation in the most critically needed areas; conversely, they tend to stimulate investments in slightly different versions of existing medicines (me-too drugs)[9].

The COVID-19 crisis showed the potential for accelerating R&D through public funding, stimulating global independent and coordinated research (e.g. the WHO solidarity clinical trial), and using joint EU procurement to improve the public leverage of agreements, and therefore, access to life-saving treatments. Yet, the crisis also showed that with the absence of strong access commitments, companies can freely increase prices in the middle of a health crisis, and so innovation is not sufficient to guarantee access to affordable medical tools[10].

As the EU develops its new Pharmaceutical Strategy, it will also need to reflect on its impact on global access to affordable medicines, which has been amplified by the inclusion of its own EU terms in trade agreements. There is a concrete risk that over emphasis on pharmaceutical incentives within the EU could harm global access to medicines, especially as a global R&D framework still needs to be developed[11]. Opportunities to redress this are offered by the new EU Pharmaceutical Strategy and other ongoing initiatives, such as a proposed global treaty on pandemics, and the creation of the new European Health Emergency preparedness and Response Authority (EU HERA).

General recommendations: the Alliance's vision for a well-balanced EU Pharmaceutical Strategy

While this concept note develops further recommendations addressing several EU pharmaceutical incentives, 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[12] 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: there should be provisions to waive the orphan, market, data, and other exclusivities where a compulsory license has been granted for a patent on public health grounds. In light of the lessons learned during the COVID-19 pandemic, a voluntary mechanism is not sufficient, and a binding provision is needed.

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[9] See Mazzucato, Mariana. How taxpayers Prop Up Big Pharma, and how to cap that. Los Angeles Times. October 27th, 2015, https://www.latimes.com/opinion/op-ed/la-oe-1027-mazzucato-big-pharma-prices-20151027-story.html, arguing that:
"Roughly 75% of so-called new molecular entities with priority rating (the most innovative drugs) trace their existence to NIH funding, while companies spend more on "me too" drugs (slight variations of existing ones)."

[10] Moon, S., Agarwal, S., Becker, A., & Ruiz, A. A. (2021). Embedding global access in development of future pandemic vaccines.

[11] Secretary-General, U. N. Co-Chairs of the High-Level Panel (2016), op. cit, proposing a binding R&D Convention. Moon, S. (2014). WHO's role in the global health system: what can be learned from global R&D debates?. *public health*, *128*(2), 167-172.

[12] World Health Assembly, Improving the transparency of markets for medicines, vaccines and other health products, Seventy-second World Health Assembly, Agenda item 11.7, A72/A/CONF./2 Rev.1. 2019, https://apps.who.int/gb/ebwha/pdf_files/WHA72/A72_ACONF2Rev1-en.pdf

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[13]. On the contrary, extending market exclusivities to any other medical products only allows more profits for the companies at the expense of the patients that will ultimately have to pay more for a longer period. As demonstrated above, the introduction of incentives without clear evidence and assessment about their potential benefits, such as the orphan drug exclusivity or the SPCs, have been harmful and difficult to amend or reverse.
5. **Remove unnecessary barriers to competition and address abuses of the system and unfair practices.** Increasing the duration, scope and number of different market monopolies has not so far served the public interest. At the same time, this trend has led to substantial problems in terms of lack and delayed access to affordable medicines as well as threats to the sustainability of national healthcare systems[14]. 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. Efforts should be made to reduce the inappropriate use and abuse of incentives, including practices that impair competition.
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. This would place the EU as a responsible investor and a global leader to address unmet health needs around the world. As demonstrated by COVID-19 and other challenges like AMR, most health needs are of a global nature. The EU could improve the coherence of its R&D and access policies by:
    - Ensuring transparency and accountability of R&D agreements across the EU
    - Insert specific access provisions linked to public funding
    - Support collaborative R&D efforts at a global level
    - Adopt a global and long-term publicly driven agenda on its EU HERA
7. **Give serious consideration to alternative new models of organising, financing, and incentivising R&D for areas of unmet medical needs.** This will help address the high and rising costs of medicines to treat diseases in these areas, as well as the persisting lack of development in some diseases of greatest unmet need. 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.** It is key that the legislation not only provides rewards and incentives, but also obligations: transparency on R&D costs, fair & affordable prices, marketing in all Member States, access to clinical data and clinical trial results.
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.** They should have access to the results of clinical trials and patient-level data, including unpublished data from failed trials, to enable high-quality assessments. Specific incentives could be envisaged for very small companies or not-for-profit research institutes and academia, marketing a small number of medicinal products to support sustainable manufacturing and production.

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[13] Outterson, K., & McDonnell, A. (2016). Funding antibiotic innovation with vouchers: recommendations on how to strengthen a flawed incentive policy. *Health Affairs*, *35*(5), 784-790, https://www.healthaffairs.org/doi/pdf/10.1377/hlthaff.2015.1139

[14] Fonteijn C, Akker I, Sauter W. Reconciling competition and IP law: the case of patented pharmaceuticals and dominance abuse. ACM working paper. [Online]. 2018 [cited 2021 Apr 22]. Available from: https://www.acm.nl/sites/default/files/documents/2018-03/acm-working-paper-reconciling-competition-and-ip-law-2018-03-07.pdf

10. Prioritize and support the needs of public health and patients when making changes to the current legislative framework.

EU Pharmaceutical incentives

1. Orphan/paediatrics legislation

Orphan medicinal product (orphan drug) incentives aim to promote the development of drugs to treat rare diseases. Because these diseases affect a small number of patients, it is believed that such a small market will not give sufficient incentives for the pharmaceutical sector to invest in the development of new medicines.

Based on this, the EU set up a system of incentives, which include "push" incentives that aim to reduce the cost and uncertainty of the development of orphan drugs and "pull" incentives that increase the probability that once developed, the products will be profitable[15]. Incentives include regulatory assistance, waivers of fees related to pre and post marketing authorisation activities for orphan drugs, a market exclusivity of 10 years (which can be extended to 2 more years in the case of a paediatric indication, and other "push" incentives such as aid for research for small and medium sized companies[16].

Box 1: the flaws of orphan drug legislation within the EU

- The orphan legislation has led to unequal availability, delayed access, and often unaffordable treatments for patients in the EU Member States[17].
- The development of orphan drugs has become a very attractive business[18]. In 2018, orphan drugs accounted for 22 out of 99 new medicines or indications assessed by Prescrire[19]. However, only a few of the newly developed drugs brought actual benefits for society: out of 22 assessments, 11 drugs or new indications were rated as an advance, but in most cases this was considered only a minimal advance, and at least 1 new orphan drug (obeticholic acid -Ocaliva°- used in primary biliary cholangitis) was considered more dangerous than useful.
- Some orphan drugs benefit from subsequent marketing authorisation in several indications. In 2018, lenalidomide (Revlimid°) was authorised in a third indication as an orphan drug for patients with multiple myeloma, after being granted orphan drug status for certain types of myelodysplastic syndrome and lymphoma. In 2015, lenalidomide was the ninth highest selling drug in the world, with global sales of 5.8 billion US dollars. This raises the question of whether the orphan drug status is granted too generously, which could lead to an "abuse" of the orphan drug incentives[20]. An illustrative case is the primary bile acid chenodeoxycholic acid (CDCA), which had been used to treat gallstones since 1976 at a price of €0,28 per capsule. In 2017, Leadiant Biosciences, a pharmaceutical firm, acquired the rights to sell CDCA a marketing authorisation to commercialise CDCA as an orphan medicinal product to treat cerebrotendinous xanthomatosis (CTX), a rare genetic disease blocking the ability to produce enough quantities of CDCA. As a result, and even though CDCA had previously been used off-label to treat CTX, Leadiant increased the product's price from €0,28 to €140 per capsule -a 500-fold increase in price without much or any R&D expenditures made possible by the 10-years market exclusivity provided by EU orphan legislation.
- Too many R&D initiatives focus on some cancers or niche-buster products while there is insufficient development in areas of the greatest needs for patients - the main justification for setting up orphan drug

[15] Boulet P., Garrison C., Ellen't Hoen E. (2019), op. cit., p. 40.
[16] https://ec.europa.eu/health/human-use/orphan-medicines_en
[17] Prescrire Editorial Staff "Orphan drug status: abuse of incentives" Prescrire Int 2016; 25 (171): 138.
[18] Marselis D., Hordijk L. (2020). From Blockbuster to "Nichebuster": How a Flawed Legislation Helped Create a New Profit Model for the Drug Industry. *BMJ* 370, m2983. 10.1136/bmj.m2983
[19] Prescrire «L'année 2018 du médicament, en bref» Rev Prescrire ; 2019 ; 39 (424) p. 142-144.
[20] Bannenberg, W. J., & t Hoen, E. F. M. (2020). Orphan drugs and drug pirates. Nederlands Tijdschrift Voor Geneeskunde, 164.

exclusivities in the first place[21]. As a result, there has been an increased "orphanisation" of common disorders and endless research of subgroups or very specific indications where a product might be helpful[22].

Recommendations for Orphan/pediatrics legislation

- **Develop a clear definition of unmet medical needs based on transparent and objective criteria.** This definition should include incidence, survival rates, existing alternative treatments, mortality, and severity of disease.
- **Correct legal loopholes/ issues that create uncertainty or impair competition.** This is the case with art. 8(2) of Regulation 141/2000, which requires further clarity for the definitions of 'sufficient ' and 'excessive' profitability and those of 'sufficient' and 'insufficient' return on investment (ROI). In addition, the lack of a definite limit on market exclusivity impairs the ability of generic manufacturers to produce these products after the originally intended market exclusivity expires, which restricts access and availability and may have an impact on pricing[23].
- **Remove the prevalence route to orphan designation.** Instead of this, adopt the return on investment (ROI) route for all applications for orphan designation, with supporting evidence to justify the incentives being made available. Transparency of R&D costs should be ensured to justify this pathway.
- **Consider the introduction of a clause enabling the withdrawal of an orphan designation when a medicinal product is sufficiently profitable irrespective of whether the prevalence or ROI route was used.** The revision of art.8(3) must avoid "evergreening" and the extension of market exclusivity beyond ten years as their impact on availability and affordability of the orphan medicine results in unaffordable and therefore inaccessible medicines. Currently, the availability of orphan medicines varies in Member States across the EU due to price. This inequitable access is unacceptable and has proven immensely harmful to the pan -European goal of availability and accessibility of medicinal products.
- **A mechanism similar to the 'withdrawal clause' from the early drafts of the Regulation should be re-introduced to the present Art. 8 (2).** The re-introduction of such a mechanism should provide a meaningful break on the behaviour of some pharmaceutical firms operating in the orphan disease field in those cases where orphan exclusivity extends beyond the life of their other intellectual property rights and where there are other firms able and willing to compete.
- **Ensure that the collection and storage of data within the remit of public authorities is duly enforced and published.** A European portal implementing obligations from the EU's Clinical Trial Regulation, which will come into force on 31 January 2022 and will provide access to all on-going and finalised clinical trials should include the results (whether positive or negative) on orphan drugs and paediatric medicines[24]. Whenever possible, the conduct of comparative randomized clinical trials (RCTs) should be required.
- **For paediatric medicines, incentives and rewards should only be allocated to medicines marketed with an adapted pharmaceutical form and packaging suitable for paediatric use. For clinical practice, the focus alone on the unmet medical need is not enough.** Paediatric medicines need to be offered in a safe and suitable form for this population[25].

2. Supplementary Protection Certificates (SPCs)

Supplementary Protection Certificates are *sui generis* rights that serve as an extension of up-to-5 years protection to some patents on pharmaceutical products. SPCs form part of a group of mechanisms to restore or extend the patent term for pharmaceutical patents.

[21] European Commission (2020b). Evaluation of the Orphan and Paediatric Regulation. Available at: https://ec.europa.eu/health/sites/health/files/files/committee/ev_20200312_791_en.pdf

[22] https://www.prescrire.org/Docu/DOCSEUROPE/20190425_PrescrireResponseConsultationOrphanDrugs.pdf

[23] See Teva Pharma BV V European Medicines Agency. (2016) C-138/15P.

[24] https://www.transparimed.org/single-post/european-medicines-regulators-set-to-tackle-missing-clinical-trial-results

[25] https://www.prescrire.org/fr/3/31/61047/0/NewsDetails.aspx

SPCs were introduced in the EU under Regulation 1768/92/EEC (now Regulation 469/2009/EC, amended). Their justification is to compensate for the period under which the patent could not be exploited because the pharmaceutical product had not received regulatory approval. As pharmaceutical products are subject to regulatory approval, patent holders cannot exploit their patents until regulatory approval is obtained, which often happens after the patent is granted. By extending the exclusivity period, SPCs prolong pharmaceutical monopolies and prevent generics from entering the market.

Box 2: the flaws of EU SPCs

- After more than 20 years of implementation it is not clear whether SPCs are justified[26]. This is also due to the fact that obtaining an SPC is not conditioned to an assessment of the revenue or profit that a pharmaceutical company has obtained for a product. Therefore, it is possible that a highly profitable product will still be awarded an SPC, which hardly justifies the award of this exclusivity and can instead promote opportunistic behaviour from pharmaceutical companies.
- There is evidence of the negative impact of SPCs on timely access to affordable medicines. Based on an analysis of three medicines for hepatitis C and cancer treatments, Médecins Sans Frontières highlighted the social cost of the introduction of SPCs, including in terms of delaying competition and maintaining high medicines prices in European countries[27].

Recommendations for SPCs

- **Subject SPCs to higher standards.** The possibility of granting an SPC should be conditioned to several factors, including the ability of the requesting party to show that R&D costs are higher than the profit obtained during the normal patent protection period on top of prejudices due to administrative or bureaucratic delays in the regulatory approval of medicines[28].
- **Promote transparency in R&D costs.** Because SPCs would only be justified upon evidence that the patent term is insufficient to cover R&D investments, data on profits should be submitted by pharmaceutical companies on a periodic basis, or at least before the expiration of the basic patent.
- **Promote transparency regarding the basic patent applied** with its corresponding dates in the different Member States, so there is no possibility for companies to apply the most favourable option for each case.
- **Facilitate the involvement of third parties to challenge SPCs.** Third parties might hold useful information, including on whether an SPC should not be granted or whether profits have been sufficient to cover R&D costs. The provision of information by third parties to either pre-empt an SPC or revoke it after it is granted, should be encouraged.
- **Ensure that SPCs do not block the use of IP flexibilities.** While IP flexibilities under the TRIPS Agreement have been deemed pivotal for the advancement of public interest and development goals, in practice, instruments such as SPCs have hindered the use of flexibilities such as compulsory licenses or the Bolar exemption. SPCs should not stop the use of these flexibilities and the possibility of introducing exceptions or waivers for Member States should be introduced[29].

[26] See Thyra de Jongh and others, 'Effects of Supplementary Protection Mechanisms for Pharmaceutical Products' Final Report (Technopolis Group, May 2018) 54, finding that SPCs offer an adequate compensation to patent holders for the effective loss of patent term but they didn't have SPCs a clear impact as a pharmaceutical incentive.

[27] Hu, Y., Eynikel, D., Boulet, P., & Krikorian, G. (2020). Supplementary protection certificates and their impact on access to medicines in Europe: case studies of sofosbuvir, trastuzumab and imatinib. *Journal of pharmaceutical policy and practice*, *13*(1), 1-12.

[28] Health Action International, Consultation Response, European Commission Intellectual Property Action Plan, https://haiweb.org/wp-content/uploads/2020/07/HAI-Wemos-contribution-to-EU-IP-Roadmap-consultation.pdf

[29] ibid.

3. Market and data exclusivities

According to the Regulation ((EC) No 726/2004), medicinal products which have been authorised shall benefit from an eight-year period of data protection and a ten-year period of marketing protection. During the first period, known as "data exclusivity", the marketing-authorisation holder benefits from the exclusive rights to the results of preclinical tests and clinical trials on the medicine. As a result, a generic company cannot rely on or refer to this data when registering a generic product, even if the medicine is needed for compelling public health reasons, emergencies, or when a compulsory or government use license has been issued during this period. Such data also on preclinical tests and clinical trials cannot be produced again, not only due to the economic costs, but also due to ethical reasons. The EU pharmaceuticals legislation has no exception to this rule[30]. During the two additional years of "market exclusivity", a generic company can prepare and apply for marketing approval but cannot market the product.

The EU legislation on medicinal products interferes with the effective use of compulsory licensing by Member States because it prohibits registration of generic equivalents, regardless of patent protection. It can therefore block generic manufacturers from gaining marketing approval even if the patent has expired or the original pharmaceutical product does not qualify for patent protection. It also renders useless other TRIPS flexibilities such as patent oppositions.

A strategy with more stringent and/or longer market monopolies has not served the public interest. On the contrary, it has proven to undermine the fiscal sustainability of national health care systems and to delay access to more affordable generics and biosimilars.

Box 3: The flaws of data and market exclusivities

- The underlying assumption of data and market exclusivities is that they will encourage innovation. As these exclusivities co-exist with other IP rights and exclusivities, evidence about their effects is not clear. EU and US reports did not find evidence on the impact of these exclusivities and the extent to which they were able to achieve their objectives[31].
- In 2016 the government of Romania explored the possibility of issuing a compulsory license for hepatitis C treatment sofosbuvir (priced at around 50000 for a 12-week treatment in Europe against around 400$ for a complete treatment with a generic equivalent in Egypt). Due to a data exclusivity which is due to expire in 2022, it was not possible to issue a compulsory license.

Recommendations for market/data exclusivities

- **Replace the data exclusivity system with a compensatory system.** A compensatory system can acknowledge the effective investments in the generation of data without providing rights to exclude others from the use of such data. This would address some of the flaws created by data and market exclusivities, encouraging competition while rewarding the efforts on the production of data.
- **Include a waiver on data/marketing exclusivity protections in cases of public health need, and for compulsory or government use licenses.** Currently, these exclusivities give the producer of the original clinical data related to the medicine additional legal protections and prevent a generic manufacturer registering/marketing a generic product by relying on the same data for a period of 8-10 years. This can be a significant barrier to the practical use of compulsory licensing in the EU, and needs urgent reconsideration.
- **As market and data exclusivities are justified on the need to protect or reward innovators for their R&D investments, more clarity about the entity behind these investments, vis-a-**

[30] FM't Hoen, E., Boulet, P., & Baker, B. K. (2017). Data exclusivity exceptions and compulsory licensing to promote generic medicines in the European Union: A proposal for greater coherence in European pharmaceutical legislation. *Journal of pharmaceutical policy and practice*, *10*(1), 1-9, https://joppp.biomedcentral.com/articles/10.1186/s40545-017-0107-9.

[31] Thyra de Jongh and others, 'Effects of Supplementary Protection Mechanisms for Pharmaceutical Products' Final Report (Technopolis Group, May 2018). U.S. Federal Trade Commission, 'Emerging Health Care Issues: Follow-on Biologic Drug Competition' (FTC, June 2009).

vis other contributions such as public funding, is crucial. It is noteworthy that data should not be produced again due to ethical reasons.

4. Patents and limits to compulsory licensing

Compulsory licensing (CL) is an important public health safeguard to ensure access to essential medicines. By issuing a compulsory license, a government allows third parties to produce a patented product without the consent of the patent owner. This legal instrument can be used to meet public health needs when access to necessary pharmaceuticals must be guaranteed. Unfortunately, there are legal obstacles that can hinder the effective and rapid use of this mechanism in public health emergencies, including in the EU.

Box 4: The flaws of limitations to compulsory licenses

- Global rules have often been misinterpreted. Compulsory licensing is a flexibility allowed by the global patent system under certain requirements. Under the TRIPS Agreement, and as reaffirmed by the Doha Declaration -which is also binding on EU countries- compulsory licenses can be issued under different circumstances as determined by each country. This may include emergencies, other situations of urgency, for public non-commercial purposes, and to remedy anti-competition behaviour. Countries are therefore free to use compulsory licensing for a variety of reasons and not only during emergencies. The argument that compulsory licensing should be used only as a measure of "last resort" is an inaccurate and misleading interpretation of the TRIPS Agreement.
- To effectively use compulsory licensing as a flexibility in the patent system, countries need to implement rules in their national legislation. The EC acknowledges the need to improve effective use of compulsory licensing, but it does not specify concrete actions to ensure national laws on compulsory licensing are improved to better protect public health needs.
- The EU legislation on medicinal products interferes with the effective use of compulsory licensing by Member States because it prohibits registration of generic equivalents for a defined period by the regulator (the EMA), regardless of patent protection[32]. Therefore, EU countries cannot register a generic product during the data/market exclusivity period, even when the medicine is needed for compelling public health reasons, emergencies, or when a compulsory or government use license has been issued on a medicine patent and the EU pharmaceuticals legislation has no exception to this rule.

Recommendations for patents and compulsory licensing

- Remove obstacles to the use of CL, including exceptions for data and market exclusivities as well as for SPCs.
- Refrain from exporting EU IP rules, including on data exclusivity, in bilateral trade agreements with other countries. This amplifies barriers to the effective use of compulsory licensing globally[33].

5. Incentives for new antibiotics

Effective antibiotics are a cornerstone of health systems -they are crucial to treat life threatening conditions, prevent infections in patients at risk, and support the performance of surgeries and transplants. However, it is estimated that around 750 000 people die each year due to antimicrobial resistance (AMR) in what has been described as a silent pandemic of drug-resistant infections[34]. Antibiotic market failure is acknowledged globally and within the EU as one contributing factor to

[32] FM't Hoen, E., Boulet, P., & Baker, B. K. (2017). Data exclusivity exceptions and compulsory licensing to promote generic medicines in the European Union: A proposal for greater coherence in European pharmaceutical legislation. *Journal of pharmaceutical policy and practice*, *10*(1), 1-9, https://joppp.biomedcentral.com/articles/10.1186/s40545-017-0107-9

[33] https://msfaccess.org/analysis-eu-position-compulsory-licensing-and-trips-waiver-covid-19-pandemic

[34] Aagaard Helle, Malpani Rohit, Zorzet Anna, ReAct report "Ensuring sustainable access to effective antibiotics for everyone, everywhere – How to address the global crisis in antibiotic Research and Development", https://www.reactgroup.org/wp-content/uploads/2021/09/ReAct-Report-Ensuring-sustainable-access-to-effective-antibiotics-for-everyone-everywhere-How-to-address-the-global-crisis-in-antibiotic-Research-and-Development-March-2021.pdf

AMR. Access to affordable and effective antibiotics is a key component of care, and can also be critical to address secondary bacterial infections during viral pandemics, although evidence is mixed for the use of antibiotics during the COVID-19 response.[35]

Box 5. the antibiotic market failure

- It has now been 34 years since a new class of antibiotics was discovered. In April 2021, the WHO warned again in its "Antibacterial Pipeline Report" that the drug-development pipeline was inadequate and insufficient to address rising drug resistance[36]. Of the 43 antibiotics in the clinical pipeline, only 26 are active against the WHO priority pathogens.[37] The antibiotics under development do not necessarily match the most crucial needs and do not reach vulnerable populations, especially children and neonates, that are at greatest risk. Moreover, how new antibiotics will be made available and accessible in all countries without misuse and overuse, is a key issue.
- While several factors contribute to the crisis in antibiotic R&D, for example the complex underlying science, one critical failure is that the current incentive system, which relies on patent and other IP based incentives to encourage the private sector to develop new drugs, is not fit for purpose. Thus, there is inadequate or no commercial interest of the private (pharmaceutical) sector in investing in the development of new antibiotics and especially new classes of antibiotics. Therefore, without adequate private investment, there must be increased EU public spending, especially through push funding, to address AMR is urgent as a strategy for preparedness and should be treated as spending on essential infrastructure.[38]

Recommendations

- The EU Strategy should consider the entire end-to-end chain of actors, investments and regulatory issues in order to introduce new antibiotics effectively and sustainably while ensuring accessibility and affordability for all people, including in low-and-middle-income countries, and for vulnerable populations such as children. Only in this way will the right antibiotics be developed and be accessible and affordable for those in need.
- Apply an end-to-end approach to antibiotic R&D and provide push funding (public R&D funding for new antibiotics) to public, private and not-for-profit actors. Such push funding decreases the cost and risk of novel antibiotic research and development. These should be accompanied by appropriate obligations for all developers to ensure affordability, availability, and accessibility of any end product. When significant public funds are in place, public institutions should retain control of the output (for instance, via golden share) to assure access and affordability of the antibiotics developed.
- The development of new antibiotics requires new approaches. Minimal modifications of the existing model for pharmaceutical funding R&D will not suffice: in addition to push funding, there should be pull incentives that delink or separate the cost of R&D from sales revenue (both prices and sales volumes), that encourage the development of relevant antibiotics, and ensure the affordability and rational use of antibiotics. This can be done, for example, through pull incentives, such as milestone prizes, that have funding conditionalities as well as public buyouts of compounds[39]. Positive experiences with delinked models have been applied in the field of neglected diseases[40].

[35] Global Antibiotic Research and Development Partnership (GARDP), Learning from COVID-19 to tackle antibiotic resistance, November 2020, https://gardp.org/uploads/2020/11/GARDP-Learning-COVID19-Tackle-AMR-En.pdf

[36] https://www.who.int/news/item/15-04-2021-global-shortage-of-innovative-antibiotics-fuels-emergence-and-spread-of-drug-resistance

[37] Aagaard et al., 2021, op. cit.

[38] Access to Medicines Ireland, Revision of General Pharmaceutical Legislation under the EU Pharmaceutical Strategy.

[39] Improving transparency and access to affordable, quality, and sustainable medicines in Europe, Joint position paper on the Pharmaceutical Strategy for Europe, July 2020, https://medicinesalliance.eu/wp-content/uploads/2020/07/Joint-position-pharma-strat_200713.pdf

[40] See Aagaard et al., 2021, citing the experiences of a patent-free novel antimalarial combination therapy (ASAQ) and a vaccine against Meningitis A by the product development consortium MenAfriVac. See also ASAQ and Pécoul B, Sevcsik A-M, Amuasi J, Diap G, Kiechel JR. The Story of ASAQ: the first antimalarial product

- A delinked financial model could be set up with public funding and include collaborations with not-for-profit entities, such as the Global Antibiotic Research and Development Partnership (GARDP), that are developing novel or repurposed antibiotics.[41]
- Incentives should not expand or extend monopolies for antibiotics or for other products or require unaffordable prices for antibiotics or other health products as a means of paying for the development of novel antibiotics. Therefore, transferable exclusivity vouchers, and similar incentives that seek to extend monopolies, should be avoided. Such measures and incentives lead to higher prices for health products, and rather than addressing the dearth of antibiotics would further cement a model which for the last 34 years has not been able to bring forward a new class of antibiotic drugs[42]. They validate a model for which the accumulated evidence indicates that incentives based on monopolies are not appropriate to stimulate the development of new antibiotics[43].

development partnership success. Health Partnerships Review, Global Forum for Health Research, Geneva, May 2008 : 77-83 103.

[41] Nielsen TB et al. 2019. Sustainable Discovery and Development of Antibiotics — Is a Nonprofit Approach the Future? New Eng J Med 381:503- 505. DOI: 10.1056/NEJMp1905589.

[42] Outterson, K., & McDonnell, A. (2016). Funding antibiotic innovation with vouchers: recommendations on how to strengthen a flawed incentive policy. *Health Affairs*, *35*(5), 784-790, showing that the experience from the US shows that antibiotic voucher proposals may lead to significant inefficiencies and inequalities, and that while it has been suggested that vouchers would need to be carefully tailored to avoid these problems, this system has also been considered as non-suitable and wasteful for countries with national social insurance systems, which is the case for many European countries (as it only defers the costs supported by patients).

[43] Aagaard Helle, Malpani Rohit, Zorzet Anna, ReAct report "Ensuring sustainable access to effective antibiotics for everyone, everywhere – How to address the global crisis in antibiotic Research and Development", https://www.reactgroup.org/wp-content/uploads/2021/09/ReAct-Report-Ensuring-sustainable-access-to-effective-antibiotics-for-everyone-everywhere-How-to-address-the-global-crisis-in-antibiotic-Research-and-Development-March-2021.pdf

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