Updated Note on Transferable Exclusivity Extension vouchers & Better Alternatives

November 2022

Medicines for Europe strongly supports the objective to fight antimicrobial resistance (AMR) and to develop medicines to address unmet medical needs, including in the field of orphan and paediatric medicines.

The European Commission has been considering introducing novel rewards to address unmet medical needs, including in the field of antibiotics, orphan and paediatric medicines. Among different options, the EC has been evaluating the introduction of transferable exclusivity extension vouchers, a system that does not exist anywhere else in the world.

As demonstrated in independent studies and stressed below, the introduction of transferable exclusivity extension vouchers in the EU would

- 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
- break the founding principle of the relationship between innovation and reward
- extend monopolies on more profitable products that would not otherwise qualify for that extension
- unduly delay access to generic and biosimilar medicines for patients.
- be unfair to those patient categories that would bear the financial burden for an innovation they do not use
- increase legal uncertainty & unnecessary litigation, including for users of SPC manufacturing waiver, which need predictability for their investment plans
- it would particularly hit biosimilar developers due to their very long development time and R&D costs

For these reasons, several countries around the world have adopted alternative novel incentives to stimulate the development of novel antibiotics and the development and production of generic antibiotics.

To tackle AMR and create a **market for reserve antibiotics**, a simple and efficient system could be introduced, including a ***(1)*** fast-track approval process for novel molecules and for the reintroduction of well-established molecules no longer licenced in Europe, coupled with ***(2)*** a EU fund to purchase the reserve molecules. With this model, the EU would ensure that physicians everywhere in Europe have access to reserve molecules at all times, which is certainly not guaranteed by the introduction of a transferable exclusivity extension

Background

In the context of the revision of the EU pharmaceutical legislation, the European Commission is considering the introduction of novel incentives for the development of novel antibiotics and potentially for medicines for rare diseases (*ie*. orphan medicines), in the form of transferable exclusivity extension vouchers (TEE). With a TEE, the developer of a novel antibiotic or an orphan medicine would be entitled to add a 1-year data exclusivity to one of the products in its portfolio or to sell such exclusivity to other companies that would use it for one of their products. This proposal is very controversial within the industry and among stakeholders. Better alternatives exist and have been introduced in other jurisdictions.

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The European Union Approach

For addressing unmet medical needs, including for antibiotics, medicines for children[1] and for rare diseases, the Commission is exploring different options[2] that would include transferable data exclusivity extensions. Such TEEs do NOT exist in any region of the world[3] and have been specifically rejected in the United States.[4] TEEs would lead to additional market protections applied to blockbuster products and would:

- ***i)*** dramatically increase healthcare systems expenditures, with significant risk of overcompensation
- ***ii)*** break the founding principle of the relationship between innovation and reward
- ***iii)*** extend monopolies on more profitable products that would not otherwise qualify for that extension
- ***iv)*** hinder timely access to market for generic and biosimilar medicines for the most expensive products
- ***v)*** be unfair to patient categories that would bear a financial burden for an innovation they do not use
- ***vi)*** increase legal uncertainty and unnecessary litigation, including for users of SPC manufacturing waiver, which need predictability for their investment plans
- ***vii)*** particularly hit biosimilar developers due to their very long development time and R&D costs

What independent studies say

A study by the Slovenian Presidency of the EU and the EU-JAMRAI, quoted in the EPSCO Conclusions on strengthening the European Health Union, includes transferable exclusivity vouchers among the "***discarded pull incentives***", since whereas they "*may be straightforward to implement, in the end,* ***the cost of these vouchers to healthcare systems is anticipated to far exceed the cost of revenue guarantees***"[5].

Another study, "Pull Incentives for Antibacterial Drug Development: An Analysis by the Transatlantic Task Force on Antimicrobial Resistance"[6], stressed that "***a tradable exclusivity voucher would be used to extend the exclusivity period of the most profitable drugs*** *in the market"*, with a high price "***in the range of billions of dollars***", concluding that "*they are an* ***inefficient mechanism for promoting innovation***", as it "*would be funded by the purchasers of the drug whose monopoly period is extended*", representing "***a disproportional level of subsidizing one area of healthcare at the expense of another***". It would have a "***negative impact on patient care, by delaying the generic entry (and therefore lower prices) of more widely used medications****. The* ***overall cost of this incentive, from both societal and healthcare perspective, may be too great****. Finally, tradable exclusivity vouchers do nothing to ensure appropriate use*."

This is also confirmed in another independent study, "Financing Pull Mechanisms for Antibiotic-Related Innovation: Opportunities for Europe", that calculates that Europe may have *"access to 1 new important antibiotic but at a price of USD 3.2 billion to national healthcare systems*", adding that a TEE "***does not guarantee that the market will have predictable access to the antibiotic*** *because it is a one-off transaction*".

All this was confirmed at an AMR Workshop held on 26 October 2022 at the Committee on Environment, Public Health and Food (ENVI) of the European Parliament.

What it would mean in practice

Taking as examples some of the EU most profitable blockbusters of recent years, an additional 1-year exclusivity on these products **would bring the following additional costs for EU healthcare systems**[7] (see fig).

[1] If to stimulate new orphan medicines around 20-30 TEEs were expected to be granted per year, this would mean that almost all of the new chemical entities approved per year in Europe (30-50) would obtain a data exclusivity extension.
[2] Ibid
[3] *Incentivising the development of new antibacterial treatments Progress - Report by the Global AMR R&D Hub & WHO,* p.16.
[4] TEEs were proposed in the REVAMP Act and rejected by the US Congress.
[5] *Improving Access to Essential Antibiotics*, by the Slovenian Presidency of the EU and the EU Joint Action on Antimicrobial Resistance and Healthcare-Associated Infections (EU-JAMRAI), available here.
[6] *Clinical Infectious Diseases*, Volume 65, Issue 8, 15 October 2017, Pages 1378–1382, https://doi.org/10.1093/cid/cix526. The study concludes that the best solutions would be market entry rewards, like delinkages or new pricing models.
[7] Considering available data for 2018. MIDAS Quarterly Audit from Q2/2018 to Q1/2021

The Adopted Alternatives

Based on in-depth analyses, a number of countries have adopted different measures to support antibiotic innovation, some of them **explicitly dismissing the idea of transferable exclusivity extensions**. These measures should duly analysed by the European Commission.

US approach

- Transferable vouchers exist in the US **only in the form of a transferable priority review voucher**[8], which could be used exclusively to accelerate the FDA review process. It does NOT provide regulatory nor IP exclusivity extensions[9].
- The 2022 PASTEUR Act foresee a 10-year subscription system for qualifying medicines identified by the Department of Health and Human Services, delinking payment from volume with specific government contracts.

UK approach

- The UK incentivises the development of novel antibiotics through **different AMR funds**, **public-private product development partnership** programmes aimed to **prioritise public health needs over profit and a subscription-type payment model**[10].
- In 2019, it launched a subscription payment plan for developing novel antimicrobials, with a 10-year plan that is already producing positive results[11].

Swedish approach

- Sweden launched a similar **successful subscription model even if specifically aimed at stimulating access to existing antibiotics,** with positive results[12].

German approach

- Germany introduced in 2017 a system of **reimbursement exemptions and higher prices for targeted antibiotics, also backing development and production of generic antibiotics**.

[8] Under the FD&C Act, section 529.
[9] United States FDA guidance for industry on "Rare Pediatric Disease Priority Review Vouchers".
[10] *Tackling antimicrobial resistance 2019–2024 - The UK's five-year national action plan*, 24 January 2019.
[11] *How the 'NHS model' to tackle antimicrobial resistance (AMR) can set a global standard*, 18 December 2020.
[12] *Incentivising the development of new antibacterial treatments Progress Report by the Global AMR R&D Hub & WHO*

An Alternative Proposal for the EU

To tackle AMR, the EU assessed it would need novel antibiotics and access to a wide range of anti-infective molecule options to treat patients (both on and off-patent). To create a market for reserve antibiotic molecules (both on and off-patent), a simple and efficient system could be introduced. This could include a ***(1)*** fast-track approval process for novel molecules and for the reintroduction of well-established molecules no longer licenced in Europe, coupled with ***(2)*** a EU fund to purchase the reserve molecules.

In concrete, the EU could purchase a pro-rata of the reserve molecules for each Member State (to be stored for that purpose in each Member State) and a stock of additional reserve to be held by the EU centrally in case of a demand surge anywhere in the EU. This would be economically efficient as originator and generic manufacturers would not have to engage in marketing these molecules and would have a guaranteed market for the whole of Europe. The Commission could be advised on the selection and purchase of reserve molecules by a Member State committee to ensure the appropriate use of public funds - with democratic oversight by the European Parliament and Court of Auditors - and a fair return on investment for research and development and for manufacturing of these molecules. The volume effect of the EU would make the market more attractive than the current fragmented system.

With this model, the EU would ensure that physicians everywhere in Europe have access to reserve molecules at all times, which is certainly not guaranteed by the introduction of a transferable exclusivity extension just as the Supplementary Protection Certificate offers no guarantee of access across Europe.

Conclusion

Medicines for Europe strongly supports the objective to fight antimicrobial resistance (AMR) and to develop medicines to address unmet medical needs, including in the field of orphan and paediatric medicines.

As demonstrated in independent studies and stressed above, the introduction of transferable exclusivity extension vouchers in the EU would

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For these reasons, several countries around the world have adopted alternative novel incentives to stimulate the development of novel antibiotics and the development and production of generic antibiotics.

To tackle AMR and create a market for reserve antibiotics, a simple and efficient system could be introduced, including a ***(1)*** fast-track approval process for novel molecules and for the reintroduction of well-established molecules no longer licenced in Europe, coupled with ***(2)*** a EU fund to purchase the reserve molecules. With this model, the EU would ensure that physicians everywhere in Europe have access to reserve molecules at all times, which is certainly not guaranteed by the introduction of a transferable exclusivity extension.

Therefore, it is of utmost importance that the European Commission would consciously evaluate the actual impact of the introduction of transferable exclusivity vouchers or the extension of IP/regulatory exclusivities, and would rather consider the more efficient alternative options proposed in this paper.