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Strengthening incentives for novel antimicrobials in the EU General Pharmaceutical Legislation

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Background

Given the growing threat of antimicrobial resistance (AMR) and the broken antimicrobial pipeline[1], Europe urgently needs to introduce predictable and meaningfully sized pull incentives to stimulate the research and development (R&D) of novel antimicrobials. Recognising this, the **European Commission put forward pull incentive provisions in its 2023 proposal for a Pharmaceutical Regulation. Chapter III introduced the Transferable Exclusivity Voucher (TEV), which has since been examined extensively by both the Council and Parliament**.[2] While both institutions have maintained the scheme, they have also introduced substantial modifications which risk weakening the effectiveness of the TEV.

Beyond the potential TEV, the EU has no centralised pull incentive for antimicrobials. **Existing initiatives are limited in scope and, at best, might improve uptake of existing antimicrobials but do not provide the predictable, long-term rewards required to bring novel antimicrobials to market.** For example, the 2025 EU4Health programme allocates negligible amounts to AMR incentives[3] and while national reimbursement schemes exist in a handful of Member States, these are either too small in budget, too limited in duration to provide a credible basis for sustained investment in R&D, or do not address key issues impacting the broken antimicrobial market. In addition, several of these schemes are not delinked from sales volumes, meaning they risk incentivising increased and potentially inappropriate use of existing antimicrobials, which is precisely the opposite of what stewardship requires. At the same time, they often fail to generate the level of revenues needed to change the economics of antimicrobial innovation.[4]

Other regions have demonstrated how a meaningful pull incentive can be introduced. For example, the UK's subscription model establishes contracts of up to £23.7 million per year per antimicrobial, awarded for an initial term of 3 years and extendable up to a maximum of 16 years or until market exclusivity ends.[5] The maximum value of a single contract is around £379 million. The scheme is designed as a long-term, predictable reward, spreading costs over time. By contrast, through the European Commission's proposal, a single TEV would provide a reward funded through the sale of a voucher offering one-year of additional exclusivity. The Commission's impact assessment estimates a single TEV could cost EU healthcare systems €294 million. Because this is shared across 27 Member States, the per-country burden would be a fraction of the UK's national commitment, with most Member States paying less than €10 million per voucher. Even if we take into account the UK reward being paid over time, rather than an upfront payment, the TEV represents a much smaller contribution by EU Member States. More recent estimates of the cost of the TEV suggests that the cost would be even lower (given the number of additional restrictions being imposed).[6]

The EU has the opportunity to build on these experiences and show leadership in the fight against AMR. While the **TEV proposed by the European Commission would still fall short of the scale of incentives needed to meaningfully replenish the antimicrobial pipeline** (for instance, when compared with the UK

[1] World Health Organization. (2024). Bacterial Priority Pathogens List, 2024.
[2] European Commission. (2023). Reform of the EU pharmaceutical legislation.
[3] In the 2025 EU4Health Work Programme, out of a total budget of €555 million, only €88.75 million is allocated to actions on antimicrobial resistance. These funds are spread across five programmes: €53 million for medical countermeasures (only partly AMR-related), €30 million in push funding for new antimicrobials, €3.5 million to WHO/GARDP activities, €2 million for an international evidence panel, and €0.25 million for monitoring implementation of EU AMR policies. In other words, the vast majority of EU4Health is directed elsewhere, and even the AMR envelope is focused on small-scale push measures and international coordination. None of this provides the kind of predictable, large-scale pull incentives needed to bring novel antimicrobials to market.
[4] Germany's recent reimbursement reforms illustrate this problem. By exempting certain antimicrobials from benefit assessments and reference pricing, the aim was to raise prices and improve market viability. However, analysis shows that this policy has had little impact on revenues, and that for Germany to deliver its "fair share" contribution to global pull incentives, prices for reserve antibiotics would need to increase by over 300% at current volumes.
[5] NHS England. (2024). Provision of antimicrobials to the NHS in England [and Scotland] [and Wales] [and Northern Ireland] via a subscription-based payment model.
[6] Wilsdon T. et al. (2025). A forward-looking assessment of the impact of introducing transferable exclusivity vouchers (TEV) in Europe. Charles River Associates.

subscription model), **strengthened appropriately, the TEV could become Europe's first dedicated pull incentive and send a clear signal of political commitment to antimicrobial innovation**. EFPIA's position is that the **TEV should be strengthened, rather than diluted further.** In parallel, **complementary measures, either EU-wide or at the Member State level, should also be implemented** to ensure that any shortfall of the TEV is filled through other instruments.

Several provisions currently under discussion risk rendering TEV ineffective in practice. These include:

- **Eligibility criteria** restricted to narrowly defined public health value (Commission proposal, tightened further by Council).
- A **mandatory application of the TEV in the 5th year of the buyer product's regulatory data protection** (Commission proposal, amended by Council).
- A **revenue cap of €490 million in annual sales** on the buyer product (Council proposal).
- A **requirement to file first in the EU or within 90 days of another jurisdiction** (Council proposal).
- **Modulation of TEV duration**, reducing the voucher from 12 to 9 or 6 months depending on pathogen priority (Parliament proposal).

The rationale behind some of these restrictions is to contain potential costs for Member State healthcare systems. Research shows that under a hypothetical framework including the 5th year RDP restriction and the €490 million sales cap, the estimated cost of a TEV would fall to around €162 million, approximately 45% lower than the Commission's original estimate of €294 million.[7] **This is problematic, as the Commission's proposal was already insufficient to deliver Europe's fair share[8] of global antimicrobial incentives, and further reductions undermine the TEV's effectiveness as a meaningful pull mechanism.** It is also important to note that the cost to healthcare systems is not equivalent to the benefit received by the antimicrobial's developer. The "cost" reflects one additional year of branded sales before generic entry, while the developer's actual reward is determined through competitive bidding. **For the mechanism to function efficiently, a broad pool of eligible buyers is essential.** If the pool is too narrow, competition weakens, which drives down the price paid from the TEV buyer to the developer (i.e., the value of the TEV). In this context, measures designed to limit payer exposure will indeed lower the cost for payers, but in practice **they create inefficiencies meaning more of the reward is captured by the TEV buyer, rather than the antimicrobial developer.** This outcome risks defeating the primary purpose of the TEV to provide an appropriately sized incentive for investment in antimicrobial R&D.

These provisions **compound other Chapter III conditionalities on access, supply, transparency and global access planning** that, while well-intentioned, risk becoming impractical if not adapted to the realities of the broader access landscape and to companies' operations.

Furthermore, the **broader Pharmaceutical Legislation already contains general provisions on access and supply that apply to all products**, and these obligations would come on top of the current Chapter III requirements. **It also remains unclear how the Critical Medicines Act would interact with this framework**. If novel antimicrobials were to be classified as vulnerable critical medicines, this could trigger yet another layer of obligations, further intensifying the cumulative burden.

The question is whether co-legislators intend to design an instrument that can genuinely work, or one so constrained by cost-containment logic that it becomes unfit for purpose. The following recommendations set out how EFPIA believes the TEV can be improved to ensure it delivers real impact.

[7] Wilsdon T. et al. (2025). A forward-looking assessment of the impact of introducing transferable exclusivity vouchers (TEV) in Europe. Charles River Associates.

[8] According to the literature, an effective global pull incentive would need to reach EUR 4 billion in order to effectively impact R&D investment decisions. The EU's "fair share" of this global amount would be 34%, i.e., EUR 1.3bn per antimicrobial.

Detailed recommendations

TEV component	Policymaker rationale	Unintended consequence	EFPIA recommendation
Eligibility Criteria (restricted to antimicrobials that meet narrow criteria demonstrating significant public health value)	• The European Commission proposed a narrow TEV eligibility through stricter criteria that would allow only a small subset of antimicrobials to be deemed "priority antimicrobials" and therefore eligible to receive the TEV. These were maintained by the Parliament but narrowed further by the Council. This requires that products must address multi-drug resistant organisms and serious or life-threatening infections. This is an addition to the EC proposal which requires that products have preclinical and clinical data demonstrating significant clinical benefit in terms of AMR, and have additional characteristics such as representing a new class of antimicrobials. • This approach aims to ensure the TEV is reserved only for antimicrobials that are expected to have a significant public health impact.	• The current criteria are likely too restrictive and risk excluding antimicrobials that, while not meeting the narrow threshold, still offer meaningful clinical and public health value, such as those improving existing treatments, or addressing resistant strains in specific geographies. • This reduces the number of products eligible for the TEV, and overlooks the incremental innovation often required in AMR. **Supporting evidence** ➢ The focus on severity ignores the reality that many initially non-severe infections (such as urinary tract infections) can progress into severe illness, particularly in vulnerable populations such as the elderly, resulting in longer hospital stays, greater complications and higher mortality rates.[9] ➢ Furthermore, there are significant challenges in conducting trials in patients with life-threatening infections due to the urgency of care, high mortality rates and associated	• Expand eligibility to include antimicrobials that meet broader public health criteria. For example, allow inclusion of priority products identified by the WHO Priority Pathogens list, such as those treating resistant infections (including non-severe), and consider other factors including transmission potential and preventability. This would be consistent with the revised German Reserve Antibiotic criteria,[12] which clarified that severity of infection is no longer the central determinant. Instead, the main aspect for classification is proven efficacy against relevant multidrug-resistant pathogens with simultaneously limited alternative, clinically equivalent therapy options (fulfilment of an unmet medical need). Reserve status is also justified if efficacy is shown against pathogens on the national non-exhaustive list, since such infections—even if not initially severe—can lead to complications and permanent damage. •

[9] Hsiao, C. Y., Chen, T. H., Lee, Y. C., Hsiao, M. C., Hung, P. H., & Wang, M. C. (2020). Risk factors for uroseptic shock in hospitalized patients aged over 80 years with urinary tract infection. *Annals of translational medicine*, *8*(7), 477.

[12] Robert Koch-Institut (RKI) & Bundesinstitut für Arzneimittel und Medizinprodukte (BfArM) (2025). Freistellung von Reserveantibiotika von der Nutzenbewertung nach § 35a SGB V – Nicht abschließende Liste multiresistenter bakterieller Krankheitserreger und Kriterien zur Einstufung eines Antibiotikums als Reserveantibiotikum. Stand 04.08.2025.

		ethical constraints (e.g. trial randomization). A recent trial for severe carbapenem-resistant infections was only able to recruit 39 patients out of 2000 that were screened due to these challenges.[10] It is inherently difficult for new antibiotics to launch with evidence of effectiveness against severe infections. ➢ A retrospective analysis of antibiotics approved by the EMA and FDA between 2012-2022, found that less than 40% would meet the initial criteria of addressing multi-drug resistance and a serious or life-threatening infection. This number would be further reduced when applying the strict threshold of significant clinical benefit and meeting additional criteria such as representing a new class of antibiotics; as such only a small number of products are expected to ultimately meet the TEV eligibility criteria.[11]	• A broader approach would allow more products to deliver public health benefit. Concerns that this would lead to too many eligible products or incentivize development of the "wrong type" of antimicrobials are not supported by the current R&D pipeline which remains extremely thin with an "insufficient" number in clinical development as of 2024 and many of these are unlikely to reach approval.[13] Even if eligibility were broadened, the number of products realistically qualifying for a TEV incentive would remain very limited. • Furthermore, by tying eligibility to scientific and public health criteria, such as the above WHO criteria, this would ensure that only products with meaningful public health impact are rewarded.
Requirement that TEV be applied during 5th year of buyer product's RDP	• The restriction to limit the use of the TEV to the 5th year of regulatory data protection (RDP), introduced by the Council, is another	• Along with the revenue cap, the restriction on RDP use greatly limits the pool of potential buyer products, with the risk that very few	• Allow the TEV to be applied within a broader timeframe e.g. use in RDP years 3–5. • This would continue to address concerns

[10] Gargate, N., Laws, M., & Rahman, K. M. (2025). Current economic and regulatory challenges in developing antibiotics for Gram-negative bacteria. *npj Antimicrobials and Resistance*, *3*(1), 50.

[11] CRA analysis of drugs approved as identified in "García-Castro, M., Sarabia, F., Díaz-Morilla, A., & López-Romero, J. M. (2023). Approved antibacterial drugs in the last 10 years: From the bench to the clinic. *Exploration of Drug Science*, *1*(3), 180-209."; the 22 antibiotics included in the analysis were *Bedaquiline, Bezlotoxumab, Cefiderocol, Ceftazidime-avibactam, Ceftolozane-tazobactam, Dalbavancin, Delafloxacin, Eravacycline, Imipenem-cilastatin-relebactam, Lefamulin, Meropenem-vaborbactam, Obiltoxaximab, Omadacycline, Oritavancin, Ozenoxacin, Plazomicin, Pretomanid, Rifamycin, Sarecycline, Secnidazole, Tedizolid, and Vonoprazan*

[13] World Health Organization. (2024). 2023 Antibacterial agents in clinical and preclinical development: an overview and analysis

	attempt to reduce the risk of overcompensation and potential costs to Member State healthcare systems.	products will actually be eligible for the TEV. With few products, competition amongst buyers will be weak or nonexistent, reducing the TEVs market value and the intended incentive. • As such, the TEV's value is contingent on there being a buyer product "at the right time", which developers cannot reliably predict during long R&D timelines. **Supporting evidence** ➢ In CRA's forward looking analysis, the application of RDP during the buyer's 5th year reduces the pool of potential buyer products for the TEV by ~25%.[14]	regarding overcompensation while providing greater predictability to both buyers and developers.
Revenue Cap on Buyer Product (€490M annual sales ceiling)	• The cap was introduced by the Council to ensure that higher selling products are not able to benefit from the TEV. • It aims to mitigate the perceived risk of overcompensation of the TEV to Member State healthcare systems, by preventing the TEV from being applied to higher-selling products.	• The introduction of the revenue cap, despite revenue already being reduced due to the RDP restriction, further risks negatively impacting the effectiveness and intended function of the TEV. While the objective may be to limit potential over-compensation, this approach will reduce the pool of eligible buyers. • Fewer eligible purchasers will result in reduced demand and undermine the market value of the TEV, further reducing its attractiveness to developers and the incentive to invest in antimicrobial R&D.	• To ensure that the effectiveness of the TEV is maintained the cap should be removed altogether.

[14] Wilsdon T. et al. (2025). A forward-looking assessment of the impact of introducing transferable exclusivity vouchers (TEV) in Europe. Charles River Associates.

		Supporting evidence ➢ CRA's analysis shows that the revenue cap has no impact on reducing the number of higher selling drugs that would be eligible for the TEV (these were already made ineligible due to the requirement of RDP application) and it only serves to further decrease the number of potential buyers for the TEV and negatively impact its potential value.[15]	
EMA Submission Requirement (application must be submitted to EMA first or within 90 days of the first submission outside the EU)	• The Council included this provision to ensure that the public health benefits stemming from the availability of any priority antimicrobial rewarded through the TEV are available within the EU, to EU patients as soon as possible.	• The "first file" clause risks undermining the purpose of the TEV by introducing an artificial and unnecessary restriction on developers. • Medicines are submitted for regulatory approval in different regions at different times due to various factors including evidence requirements, procedural timelines, and disease epidemiology. • This clause ignores those realities and may result in otherwise eligible antimicrobials, delaying or not launching in the EU, denying European patients' timely access to vital medicines. **Supporting evidence** ➢ A review of EMA & FDA approved antibiotics between 2012-2022 found that only 5/22 antibiotics were submitted to the EMA before, or within 90 days of FDA	• Allow developers to retain TEV eligibility provided that submission to the EMA occurs within a broader and more practical window (e.g.,no later than 2 years from the first regulatory submission outside of the EU). • This would continue to preserve EU access objectives within a reasonable timeframe without risking non-launch in the EU.

[15] Wilsdon T. et al. (2025). A forward-looking assessment of the impact of introducing transferable exclusivity vouchers (TEV) in Europe. Charles River Associates.

		submission. Several reasons have been attributed to delays/withdrawals in EMA submissions (vs. the FDA), including the requirement for additional evidence studies and challenges commercializing products in the EU.[16] ➢ This demonstrates that a significant number of antibiotics would likely be ineligible for the TEV under this restriction, unnecessarily risking both patient access and innovation efforts.[17]	
Modulation of TEV Duration Based on Pathogen Priority (12 months for 'critical', 9 months for 'high', 6 months for 'medium' pathogens)	• Introduced by the European Parliament, the clause links the length of the TEV reward to the public health priority of the pathogen targeted. The aim is to align the incentive's size (duration) with societal need. • This also seeks to avoid over-rewarding lower priority antimicrobials and to ensure that investment is targeted towards the most urgent AMR threats.	• Given the current landscape of antimicrobial R&D, few pipeline candidates are likely to meet the stringent criteria required for the "critical" category. • Most new products will likely fall into the "high" or "medium" category due to scientific, technical, or epidemiological factors. As a result, many of these products, despite addressing real-world resistance challenges, would receive a reduced incentive, lowering the TEV's value and undermining the TEV's objective to support a sustainable innovation ecosystem. • To offset the reduction in the TEV's value (and align with the EU's required fair share),	• There is already significant concern regarding the value of the TEV falling short of the EU's required fair share, i.e. as designed. • Given that the 12-month extension is already insufficient to incentivize R&D investment at the scale required to replenish the broken pipeline, the modulation component which would likely result in most products receiving less than 12 months, should be removed from the TEV framework.

[16] AMR Solutions. (2020). New antibiotics are not being registered or sold in Europe in a timely manner

[17] CRA analysis of drugs approved as identified in "García-Castro, M., Sarabia, F., Díaz-Morilla, A., & López-Romero, J. M. (2023). Approved antibacterial drugs in the last 10 years: From the bench to the clinic. *Exploration of Drug Science*, *1*(3), 180-209."

		Member States will need to supplement the TEV with complementary measures such as pricing, reimbursement, or procurement mechanisms (e.g. a revenue guarantee model). This will need to involve an assessment of the value of the antimicrobial, however, many Member States' HTA and pricing frameworks do not appropriately account for the value of antimicrobials (such as their societal and public health benefits). Without the capability to integrate these broader value considerations into assessments, the overall package of incentives is likely to remain insufficient to stimulate investment in antimicrobial R&D. ➢ **Supporting evidence:** In the 2024 WHO Priority Pathogen List, it was stated that there were "very few or no' products in development for the "critical" category; this is before even considering the low probability of success in clinical development which further limits the chances of any product reaching the market and benefiting from the 12-month extension.[18] ➢ Prior to the proposed amendments which negatively reduce the value of the TEV, the Commission estimated the value of a TEV providing a 12-month	

[18] WHO Priority Pathogens List 2024

		extension to be €413 million. This is already significantly below the EU's fair share which is estimated to be EUR 1.3bn.[19] Any reduction to the 12-month extension would further lower the value of the TEV, and increase the gap to the required EU fair share.	

[19] According to the literature, an effective global pull incentive would need to reach EUR 4 billion in order to effectively impact R&D investment decisions. The EU's "fair share" of this global amount would be 34%, i.e., EUR 1.3bn per antimicrobial.

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