Deputy Permanent Representative of
the Kingdom of the Netherlands
to the European Union

Brussels, 30 November 2022

Dear Commissioner Kyriakides,

I have the honour to enclose herewith a non-paper on behalf of Mr Ernst Kuipers, Minister of Health, Welfare and Sport of the Kingdom of the Netherlands, dated 30 November 2022, concerning novel stimuli for the development and keeping on the market of antimicrobials.

This non-paper is based on an initiative from the Netherlands, and is supported by Austria, Belgium, Finland, France, Hungary, Ireland, Latvia, Lithuania, Luxembourg, Poland, Portugal, Slovakia, and Slovenia.

Yours sincerely,

Michael Stibbe
Ambassador

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Non-paper

– Novel stimuli for the development and keeping on the market of antimicrobials –

Based on an initiative from the Netherlands, and is supported by Austria, Belgium, Finland, France, Hungary, Ireland, Latvia, Lithuania, Luxembourg, Poland, Portugal, Slovakia, and Slovenia

Summary

- **The current system of incentives has failed** to stimulate the development and keeping on the market of (novel) antimicrobials to tackle the emerging global crisis of antimicrobial resistance.

- **New types of incentives** are therefore needed to address both market failure and availability of antimicrobial products across the EU.

- The Commission consideration to introduce as reward **transferable exclusivity vouchers for novel antimicrobial products** is however **not supported** for several reasons.

- They are an **indirect, non-transparent form of financing**, that do not always directly benefit those companies that actually contribute to bringing new products to the market, that stifle innovation and block generic competition and, thereby, availability and accessibility to patients, and that lead to unpredictable but likely high costs to national health systems.

- Instead, **direct financial incentives are needed**, that are not necessarily legislative in nature and are ideally facilitated through HERA, that are developed in European collaboration and allow Member States to tailor towards their individual needs, and that contribute to making new medicines available across the EU and for a meaningful period of time.

- Possibilities whose feasibility deserve exploring are **market entry rewards**, **a guaranteed minimum turnover per Member State** and **milestone R&D payments**.

- In addition, the revision of the EU pharmaceutical legislation should incorporate **measures for prudent and standardised use**, such as personalised and evidence-based treatment, the classification of all antibiotics as prescription-only, and harmonisation of product information.

- The revision should also look at ways to **reduce the administrative burden** associated with the lifecycle of medicines in order to stimulate innovation and the staying on the market of older products.

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The need for novel stimuli and business models to address antimicrobial resistance

The current pharmaceutical legislation performed well in ensuring that only medicines that are safe, effective and of high quality enter the Union's market. It further stimulated research and development (R&D) in areas where previously few medicines were available. However, **this incentive system has proven to be not specific enough to steer innovation towards the highest patients' needs**.

This is illustrated by the emerging global public health crisis of antimicrobial resistance (AMR) with high public health, social and economic costs. The current system of incentives and rewards has failed to stimulate the development of novel antimicrobials that sufficiently address AMR. The pharmaceutical framework has further not been successful in ensuring that older antimicrobial products remain available on the European market.

The current framework mainly incentivises development of products in areas where sales volumes and profits are high or where low sales volumes can be compensated by high prices, such as for orphan indications. However, good stewardship practices, which are crucial to limit development of antimicrobial resistance, result in limited use (e.g. by avoiding unnecessary prescription) and short treatment courses. In addition, low sales volumes and revenue are common, as novel products are either reserved as last resort treatment or are not prescribed because cheaper generics are available for the same treatment indication, regardless of whether they provide improved treatment. As a result, the current system of incentives does not enable companies to recover their investment costs for R&D, nor does it enable them to cover their expenses to keep (novel) products on the market. New types of (pull) incentives or rewards and business models are therefore needed to address market failure and stimulate development and innovation in the area of antimicrobials.

It is our opinion that **novel incentives or rewards should:** be developed in **European collaboration** to ensure a clear unified policy; **directly incentivise** the development of novel antimicrobials with a clear cost structure; **contribute to making new medicines accessible and available** throughout the European block, and; when relevant **decouple revenue from sales** to ensure stewardship. In addition, new incentives should aim to incorporate strategic goals for production and supply within Europe.

Transferable exclusivity voucher

The European Commission recognised in their Pharmaceutical Strategy for Europe the issue of AMR as a prime example of unmet medical need and examines, as part of the revision of the pharmaceutical legislation, novel incentives to address AMR. Under consideration is a transferable regulatory data protection voucher which would allow the developer of a novel antimicrobial product to benefit from an additional period of data protection on another product in their portfolio. They could also choose to sell the voucher to another company.

Although we believe novel incentives or rewards are indeed necessary to tackle AMR, **we do not support the introduction of transferable exclusivity vouchers**. Whilst possibly effective to a certain degree, the instrument does not fulfil the criteria we outlined above.

Transferable vouchers **do not directly incentivise the development of novel antimicrobials, nor do they ensure that products are accessible and available throughout the EU for an agreed upon time period**. In addition, vouchers will benefit, upon transfer, the developer of medicines for other (more profitable) indications. The deployment of an exclusivity voucher for profitable products that do not need further incentives will both **stifle innovation** from competitors and delay the introduction of generics and biosimilars of those very profitable products, thus **affecting both availability and affordability** of medicines in those therapeutic areas. Equally, it negatively impacts generic companies, as their business plan is now subject to a degree of uncertainty beyond their control. **Vouchers are an indirect and non-transparent form of financing**; costs incurred by national healthcare systems in the EU are unclear and unpredictable. Importantly, limited clarification is currently given on what achievement actually merits a voucher.

If introduced, it is to be expected that active trade in transferable vouchers between separate legal entities will ensue. This complicates an objective and quantified assessment of the impact of said vouchers. The only certainty is that **costs for national health systems will be high**.

So what is needed?

To address the issue of AMR, we urge the European Commission to consider actions and measures that are not necessarily legislative in nature. These actions and measures are ideally **facilitated through HERA** as it has a role in combating AMR in line with the goals set in the Pharmaceutical Strategy for Europe. HERA can create a viable ecosystem for R&D of novel products. In addition, new business models are required that may promote decoupling revenue from sales to ensure appropriate stewardship. This also applies to already authorised products that are not or no longer in use, as in the (near) future a situation may occur that requires the use of these antimicrobials.

Several options could be considered. The first would be **direct financial incentives**, such as the introduction of **market entry rewards** for companies that bring the product to the market. This is in line with our stance on directly financing the development of antimicrobials themselves. Another option might be a **guarantee for minimum turnover per Member State**, regardless of volumes actually prescribed. This gives companies prospect for bringing their product to and keeping it on the market whilst promoting stewardship. A third option would be to invest in **R&D incentives**, for instance by means of milestone payments. This could be shaped in the way of contract research where HERA stimulates research into pre-specified product / indication combinations via public tenders.

Market entry rewards, guarantees for minimum turnover and milestone payments are direct forms of financing by means of pre-determined amounts for a specific antimicrobial product that are **paid towards a company that actually contributes** to its market launch or to the necessary R&D. Furthermore, Member States can **tailor the turnover guarantee to national needs**.

Furthermore, **reducing the regulatory and administrative burden** associated with the lifecycle of a medicinal product, whilst preserving guarantees for their high quality, safety and efficacy, will contribute to innovation and the staying on the market of older products. Antimicrobials may qualify for faster approval schemes and extended protection periods.

While investment in and appropriate incentives for new antimicrobials are needed, if new treatments are not used prudently, AMR is not addressed sustainably. **Priority should be given to reducing unnecessary use** by changing the regulatory framework so that it promotes **personalised and evidence-based treatment** (use of point-of-care diagnostic tests) where and when possible. In addition, all antibiotics should be classified as **prescription-only** across the EU. Finally, **harmonisation of the product information, conditions for use and national treatment guidelines** for antimicrobial products could aid in reducing differences in the prevalence of infectious diseases and antimicrobial resistance in the EU.

As a final note, several suggestions to incentivise innovation and access and to stimulate antimicrobial stewardship have already been made at the EU level, notably in the Joint Action on Antimicrobial Resistance and Healthcare-Associated Infection (JAMRAI), and some of those have been piloted (e.g. the guaranteed minimum annual sales in Sweden).

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This non-paper is without prejudice to national positions voiced or submitted by individual Member States.