EXECUTIVE SUMMARY

Workshop proceedings

ENVI Health Working Group

European Parliament

Antimicrobial resistance - New incentives to improve the accessibility and availability of antimicrobial medicinal products

ABSTRACT

These proceedings summarise the presentations and discussions before the European Parliament's Health Working Group's workshop on 'New incentives to improve the accessibility and availability of antimicrobial medicinal products', held on 26 October 2022. The five presentations touched, inter alia, upon the burden of AMR, the current research on development of antimicrobials, and incentive models.

Background

The workshop on 'Antimicrobial Resistance - New incentives to improve the accessibility and availability of antimicrobial medicinal products' was held on 26 October 2022 in Brussels for the Health Working Group of the European Parliament's Committee on the Environment, Public Health and Food Safety (ENVI).

The workshop convened leading experts in the field - from the World Health Organization, the medical profession, innovating SMEs, academic research in Public Health and civil society advocacy. The five speakers presented diverse perspectives on the current state of play of research and development of new antimicrobial medicinal products and availability of old products in Europe and shared their respective expertise and conclusions on concrete actions needed with the Members of the Health Working Group.

Aim

The workshop offered a comprehensive and multidisciplinary overview of the European and global situation on the research and discovery of antimicrobial medicinal products for human use and on the specific challenges faced by research on antimicrobials, as well as to present the current discussions on the way forward to stimulate research and development in this field, in the context of the upcoming revision of the European pharmaceutical legislation.

The present document is the executive summary of the workshop proceedings on *Antimicrobial resistance – New incentives to improve the accessibility and availability of antimicrobial medicinal products*. The full paper, which is available in english can be downloaded at: https://www.europarl.europa.eu/RegData/etudes/IDAN/2022/740069/IPOL_IDA(2022)740069_EN.pdf

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Main discussions

Current and projected burden of AMR

The speakers all confirmed the growing risk and concern represented by antimicrobial resistance (AMR) for populations and economies in Europe and globally. The co-chairs of the Health Working Group qualified AMR as a 'silent pandemic', and a possible 'COVID-19 2.0'.

The European Centre for Disease Prevention and Control and the World Health Organization's joint report on AMR for 2022 record 670 000 infections due to resistant bacteria and approximately 33 000 deaths per year in the EU/EEA region[1]. The death toll directly attributable to resistance was estimated to reach 1.27 million deaths worldwide in 2019. In addition, the global economic cost of AMR is significant, estimated to amount to USD PPP 3.5 billion per year on average between 2015 and 2050. The results of the OECD's research highlight that the cost of inaction is high compared to the human (large number of deaths avoided) and economic (higher return on investment) benefits of acting.

According to the medical community, it is crucial to have access to a wide pharmacopeia of narrow- and broad-spectrum antimicrobial medicinal products to best treat patients and to prevent the acceleration of resistance. The consequences of AMR are potentially far-reaching, and AMR negatively impacts the health outcomes of both patients treated for a critical infection inside or outside of a hospital, and patients undergoing routine surgeries for which antimicrobials are used as prophylaxis.

However, medical practitioners face issues of availability on 'old' (generic) antibiotics in the EU, due to a large extent to fragile globalised supply chains and to the deregistration of certain products by marketing authorisation holders. The consultations conducted in the context of EU-Joint Action on Antimicrobial Resistance and Healthcare-Associated Infections (EU JAMRAI) confirm that shortages of existing antibiotics are a serious problem, and that many countries report essential current antibiotics being withdrawn from their national markets. Furthermore, regarding newly approved antibacterials, a delay is observed between approval and commercial launch, as well as strong disparities in the availability of the products across EU Member States, including antibiotics considered essential in WHO's essential medicines list.

The number of recently approved antibacterial agents and of those currently in clinical and preclinical developments is considered insufficient by the WHO to address the emergence and spread of antimicrobial resistance infections, in particular considering the high failure rate in the development process.

Challenges of research and development on antimicrobials

The process for research and development of new antimicrobials is characterised by an increasing cost of development along the development phases of a product, combined with a decreasing number of candidates due to failures to show safety or clinical efficacy.

The antibacterial drug discovery in Europe is dominated by small- and medium-sized enterprises, which are behind around 80% of drugs in development, including in clinical development. Larger pharmaceutical companies have left the field, which can be explained by the limited profitability compared to other medical fields and the limited forecast revenues on antibacterial medicinal products.

In recent years, improvements of the environment for research and development have been made in the EU and the preclinical pipeline is stronger than it has been in decades, in particular via the multiplication of 'push' incentives. The discovery of novel antimicrobial products remains, however, insufficient and 'pull' incentives could provide long-term / sustainable perspectives of financial return to those who invest in research and development.

The central challenge for policymakers is to determine which incentives are most appropriate to boost the

discovery of novel antimicrobials, and at which point of the R&D process the public intervention is the most impactful.

Recommendations

A consensus emerged in the discussions on the urgent need for Europe to take actions for its citizens, and on assuming a share of the global responsibility.

Furthermore, it is crucial to uncouple how much revenues a specific antibiotic will generate from the level of sales for this antibiotic. The **principle of delinking** the financial return for developers of antibiotics from the volume of antibiotics consumed received undisputed support among speakers. This should help conciliating the contradictory objectives of, one the one hand reducing the consumption (via antimicrobial stewardship policies), and one the other hand, incentives to produce new antimicrobial medicinal products with low sales and profitability prospects. In this context, two pull incentive instruments which could be implemented at EU level have been discussed during the workshop:

- **Transferable Exclusivity Extensions (TEEs)** which are tradable vouchers awarded to the innovator of a novel antimicrobial, meeting specifications that can then be used to extend the monopoly time period of any patented medicine. They can either be applied by the awardee to another medicinal product of its own portfolio or sold to another company.

This model is supported by the innovative pharmaceutical industry, including the BEAM Alliance, as a readily actionable mechanism to reward innovation, where the duration of the exclusivity can be tailored, and whose operation can be centralised at European level. The award of TEEs would be conditioned on the fulfilment of eligibility criteria, in particular the capacity of the product to address an unmet medical need and its innovative character. However, public health and civil society representatives at the workshop consider that the TEE model would lead to potential high cost for Member States, due to, *inter alia*, a prolongation of high prices of non-related medicines and the absence of a guarantee for the healthcare system regarding access to the products. The lack of legal precedent and significant opportunities for speculation were also considered as additional risk factors for this pull incentive.

As an alternative to TEEs, ReAct proposed gradually awarded rewards/prizes along milestone achievements in the development of antimicrobial products, to facilitate the pathway from preclinical to clinical stages, and to ensure sustainable access to a new medicinal product. Their recommendations included a stronger public leadership for public health needs-driven R&D with a non-profit (global/EU) coordination entity for antibacterial drug discovery and increased public oversight and control of end products (production, procurement, distribution and patient access).

- The **Annual Revenue Guarantee** is a predictable and increased revenue for producers of marketed antimicrobial pharmaceutical products with proven public health value, delinking revenues from sale volumes.

This model studied in the context of the EU-JAMRAI aims at securing revenues for producers of antimicrobial medicinal products, while ensuring stable access to important antibiotics for healthcare systems. It has been designed to work independently from national health processes (health technology assessment, pricing, and procurement). It is adaptable to ensure access to both old and new antibiotics. BEAM Alliance, however, considers that this model is difficult to implement in Europe and may lead to freeriding behaviours when implemented in a multi-country setting.

Beyond the discussion on the specific incentive models, WHO and ReAct Europe stressed the need for the adoption of a holistic and multilateral approach. ReAct supported an 'end-to-end approach' away from market-based rationales but requiring public authorities to coordinate and control the research and

development process in a public health needs-driven manner, including the provision of funding in a more sustainable way, as well as of mentorship, training and coordination in early research stages.

[1] European Centre for Disease Prevention and Control and World Health Organization's Regional Office for Europe, 'Antimicrobial resistance surveillance in Europe 2022, 2020 data'. Available at: https://www.ecdc.europa.eu/sites/default/files/documents/ECDC-WHO-AMR-report.pdf. Based on Cassini, A., *et al*, 'Attributable deaths and disability-adjusted life-years caused by infections with antibiotic-resistant bacteria in the EU and the European Economic Area in 2015: a population-level modelling analysis', Lancet Infect Dis 2019; 19: 56–66.

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