24 March 2022

European Public Health Alliance's response

to the European Commission's call for evidence on AMR

Introduction

European Public Health Alliance (EPHA) welcomes the opportunity to comment on the European Commission's call for evidence on antimicrobial resistance (AMR). We support the idea of setting concrete objectives and activities to strengthen Member States' actions against AMR. Meanwhile, we do see a role for the European Union to complement, coordinate and support national level actions.

The development and spread of multidrug resistance have far-reaching and potentially life-threatening consequences for humans, animals, plants, and the environment, and jeopardises the achievement of the Sustainable Development Goals (SDGs). So far, the activities of the European Commission and its agencies led to some progress, but there is little evidence that the health burden of AMR has been reduced. The COVID-19 pandemic has served as a reminder that too little action has been accomplished across Europe and that the collective effort to combat AMR needs to be stepped up in a timely fashion. Even before the pandemic, a Chatham House report released in 2019 noted that too little progress had been made regarding the implementation of steps proposed in the globally acclaimed AMR Review led by Jim O'Neill[1].

This response will focus on three areas that requires the particular attention and support where the EU can positively influence in the fight against AMR, namely: (1) the development of new antimicrobials, (2) preventative measures, and (3) National Action Plans.

1. The development of new antimicrobials

In its 2017 EU One Health Action Plan on AMR, the European Commission had tasked itself with supporting research into the development of new economic models to support the development of new antimicrobials. Meantime, the major pharmaceutical companies decided to withdraw from the markets of certain Member States antimicrobial treatments that continue to work[2], and it has been 34 years since the last class of antibiotics was discovered. Moreover, most antibiotics in the clinical pipeline do not match the greatest needs, for instance in reference to the list of WHO priority pathogens. Since then, all antibiotics are modifications of existing classes, which poses a risk of faster development of resistance[3].

[1] https://www.cidrap.umn.edu/news-perspective/2019/10/uk-report-cites-lack-progress-amr-review-steps
[2] European Court of Auditors, Addressing antimicrobial resistance: progress in the animal sector, but this health threat remains a challenge for the EU, 2019
[3] European Alliance for Responsible R&D and Affordable Medicines, Getting incentives right in the new EU pharmaceutical strategy, 2022

It is becoming clear that minor improvements in the current model for the development of new and effective antibiotics will not suffice[4]. The proposed recommendations for the Council Conclusions represent a timely opportunity to set effective and efficient priorities, to prevent the current AMR challenge from growing into an unstoppable crisis. It is clearly the time for the public authorities to comprehensively evaluate the support given to AMR R&D, and to develop a strategy to address existing market failures affecting the development of new antibiotics.

Recommendations:

1.1 Development and placing on the market of new and effective antibiotics

The crisis in the development of new antibiotics is complex, due to the nature and challenges in the basic science, but one of the critical failures is that the current incentive system, which relies on patents and other intellectual property rights, is not fit for purpose. Consequently, the private pharmaceutical sector does not have sufficient incentives to invest in the development of new antibiotics, especially new classes of antibiotics[5]. Without adequate private investment, the EU and its Member States must increase their public expenditure, notably through "push" funding. Beyond funding, the public authorities should ensure that their priority-setting and overall stewardship meet European and global health needs[6].

- **End to end approach –** the EU and its Member State need to adopt a holistic approach and provide more public R&D funding for new antibiotics to public, private and not-for-profit developers. Smart public R&D funding can help to de-risk the development of novel antibiotics. However, public funding cannot become a blind investment without conditions. The public should demand that developers supported with public funding ensure the affordability, availability, and accessibility of any final product. When significant public funds are in place, public institutions should retain control of the output to assure access and affordability of the antibiotics developed[7].
- **New approach –** a paradigm shift is needed to address rising AMR and the antibiotic market failure. Against this background, the role of the public sector is gaining importance. National authorities and the EU institutions should coordinate joint efforts to develop new antibiotics. Various policy instruments should be considered that go beyond the push/pull (supply/demand) dichotomy of incentives. The medical innovation literature focuses most on addressing market failures to spur R&D, with less attention given to supporting innovation systems or societal challenges. This neglects a role of public policy coordination in innovation. A model of delinkage of the costs of R&D from sales revenues should be encouraged and implemented widely. This can be done, for example, through incentives, such as milestone prizes, that have funding conditionalities as well as public buyouts of compounds. Positive experiences with delinked models have been already applied in the field of neglected diseases. Products Development Partnerships (PDPs) represent one of the models that has successfully de-risked R&D investments and built affordability and access into the business model[8].

[4] European Alliance for Responsible R&D and Affordable Medicines, Getting incentives right in the new EU pharmaceutical strategy, 2022
[5] https://epha.org/wp-content/uploads/2021/11/position-paper-on-pharma-strategy-23-nov-19.pdf
[6] https://epha.org/wp-content/uploads/2020/12/epha-amr-position-paper-updated-2020.pdf
[7] ReAct, Action on Antibiotic Resistance, 2021
[8] European Alliance for Responsible R&D and Affordable Medicines, Getting incentives right in the new EU pharmaceutical strategy, 2022

- **Approach to avoid -** 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
- **Coordination –** the new approaches need to give a clear impetus to developers to focus their R&D efforts and investments on the areas of high unmet needs and priorities as set out by the WHO's priority Pathogen List. The EU and its Member States should coordinate effective and efficient R&D efforts that respond to global unmet health needs.

2. Preventative measures against AMR

Prevention is essential in the lasting fight against AMR, yet it seems that most recommendations and measures do not adequately consider this aspect. In addition to the point made above, R&D should *also* be dedicated (and adequately financed) to identifying methods that reduce or delay the use of antibiotics, not just the development of new ones[9].

Effective AMR prevention measures in *practice* are also critical, and whilst there has been significant progress at the EU level in addressing antimicrobial stewardship in animal farming, an ongoing concern is the inappropriate antimicrobial use in human health. Indeed, 50% of antimicrobials used in human health may be inappropriate[10]. The coronavirus pandemic has demonstrated this problem, with concerns of overuse of antibiotics in hospital patients with COVID-19 infections and widespread mis-use by the public, seemingly due to a lack of information or understanding respectively when faced with a novel disease[11]. Mis- and overuse of antimicrobials are a major cause of AMR and therefore must be addressed as a matter of urgency.

Recommendations:

2.1 Support research into the development and assessment of interventions that prevent the development and spread of AMR

As mentioned above, delinking the cost of investment in R&D on AMR from the price and volume of sales can facilitate equitable and affordable access. This is also applicable for the R&D of alternative tools to antibiotics including vaccines and diagnostic tests (the importance and relevance of this aspect has already been highlighted by the agreement in the Political Declaration of the high-level meeting of the UN General Assembly[12]).

2.2 Provision of educational resources

More should be done towards ensuring patient and public access to accurate and reliable information on the uses and effects of antimicrobials, as well as ensuring timely dissemination of clinical pharmaceutical guidelines for novel diseases, to support prescribers. Improving understanding will help prevent antimicrobials, particularly antibiotics, being mis- or overused, especially in any potential future health crises.

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[9] https://epha.org/wp-content/uploads/2020/12/epha-amr-position-paper-updated-2020.pdf
[10] https://www.oecd.org/health/health-systems/AMR-Policy-Insights-November2016.pdf
[11] https://epha.org/wp-content/uploads/2021/11/covidvsamr-2021-epha.pdf
[12] https://digitallibrary.un.org/record/842813?ln=en

Health professionals are a key group on the fight against AMR, both in terms of directly influencing the consumption of antibiotics they prescribe and provide, and in terms of stimulating behavioral change in consumption patterns for the public, by raising awareness and bridging information asymmetry. Given the critical role of health professionals, there is a clear need for stewardship programmes that bring together all health professionals ensuring interprofessional training and collaboration[13].

3. Development and implementation of National Action Plans

While arguably, political attention in the Member States has significantly increased since the release of the European Commission's One Health Action Plan, the AMR threat itself has not diminished[14]. The 2019 Council Conclusions of the Romanian EU Presidency noted that more support is required for less affluent countries to develop and implement National Action Plans (NAPs) and included a call to the European Commission to "continue to support Member States in the implementation of multi-sectoral NAPs and national strategies on AMR and increase the dedicated funding"[15]. However, the EU-JAMARI's analysis showed that not all countries have a NAP in place – or still under development, lacking political endorsement or funding – even though all states committed to doing so by 2017[16]. Where they are in place, not all reflect a One Health approach – environmental health being the most understated – to tackle AMR and address AMR in different fields separately.

Of relevance, the EU scientific agencies, whilst having increased their work on AMR surveillance including annual data monitoring reports, their resources – particularly the ECDC's – have remained very limited, which has restricted their abilities to provide comprehensive guidance and technical support to the Member States[17].

Recommendations:

3.1 Support the development and implementation of NAPs, to encapsulate all areas of 'One Health'

Continue to provide help for the development/implementation of NAPs, including the provision of more comprehensive resources that cover all aspects of 'One Health' to inform, educate, guide, and support Member States in their individual NAP development; and ensure (dedicated) funding – especially for the less affluent – countries, to ensure successful implementation of NAPs.

- **Improving environmental health awareness** - policymakers should highlight and support the importance of the One Health approach as regards AMR, taking the example of environmental health; raise awareness about the role of the environment in the emergence of AMR and identify evidence-informed policy solutions at EU level to address environmental AMR[18].

[13] https://epha.org/wp-content/uploads/2021/12/position-paper-on-pharma-strategy-20.pdf
[14] https://epha.org/wp-content/uploads/2022/01/amr-roadmap-22.pdf
[15] https://data.consilium.europa.eu/doc/document/ST-9765-2019-INIT/en/pdf
[16] https://eu-jamrai.eu/wp-content/uploads/2020/07/EUjamrai_Results_Mapping_National_Action-Plans_WP5.1_2018.pdf
[17] https://epha.org/wp-content/uploads/2020/12/epha-amr-position-paper-updated-2020.pdf
[18] https://epha.org/wp-content/uploads/2020/12/epha-amr-position-paper-updated-2020.pdf