Looking for the path of least resistance for One Health:

STEPPING UP THE FIGHT AGAINST ANTIMICROBIAL RESISTANCE (AMR)

EPHA Position Paper (2020 Update)
December 2020
About EPHA

EPHA is a change agent – Europe’s leading NGO alliance advocating for better health. We are a dynamic member-led organisation, made up of public health civil society, patient groups, health professionals, and disease groups working together to improve health and strengthen the voice of public health in Europe.
Introduction

This Position Paper updates and complements EPHA’s previous position released in May 2017\(^1\) prior to the publication of the European Commission’s One Health Action Plan against Antimicrobial Resistance (AMR)\(^2\). It explores the relevance and impact of the most important European, international and national developments that have taken place since then and discusses how they influence the advocacy work of EPHA and our partners. In addition, the paper reiterates key recommendations drawn from joint advocacy asks proposed in the framework of EPHA’s broader AMR work with members and partners.

Summary of EPHA’s recommendations

As part of this updated Position, EPHA proposes the following recommendations to complement those of the AMR Stakeholder Network\(^3\), in order to achieve least resistance for One Health:

(1) In the area of human health

- Ensure that antibiotic R&D is predicated on a common understanding that antibiotics are public and essential for public health, hence they must be accessible, affordable and available to all people
- Increase significantly the resources for the ECDC’s Antimicrobial Resistance and Healthcare Associated Infections (ARHAI) programme to allow the agency to deepen its activities related to surveillance, data analysis, risk assessment, guidance and awareness-raising
- Public education on reducing antibiotics use should be strengthened, including suggestions on the use of evidence-based integrative treatments

(2) As regards R&D and an antibiotics innovation model

- Set priorities and develop target product profiles (TPP) for new products through transparent and inclusive scientific consensus
- Support needs-driven innovation by providing public funding for end-to-end development of new antibiotics and support smaller, emerging biotech, SMEs and public-private partnerships while ensuring transparency throughout
- Ensure that public investments are driven by public health needs and that parties receiving biomedical research and innovation (R&I) funding agree on provisions to address the end product’s affordability, accessibility, availability and efficiency along all the R&I stages
- Strengthen public manufacturing capacity (together with a recommendation for the support of needs-driven innovation) to create a new, more diversified innovation ecosystem which does not rely exclusively on big pharmaceutical corporations

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1 https://epha.org/prevention-is-better-than-cure-europes-chance-to-act-on-amr-is-now/
2 For information about the One Health Action Plan and previous EU work, see: https://ec.europa.eu/health/antimicrobial-resistance/eu-action-on-antimicrobial-resistance_en
3 https://epha.org/amr-stakeholder-network/
• Introduce a ‘pay or play’ scheme for pharmaceutical companies to fund market entry rewards

• In addition to R&D to find new antibiotics, R&D should also be dedicated (and adequately financed) to identify methods that reduce or delay the use of antibiotics

(3) In the area of animal health

Efforts to reduce the threat of AMR linked to animal farming should remain focused on lessening antibiotics use. While suggestions are made that antibiotics should not be reduced for the sake of reduction, there is at present no other method to assess whether progress towards AMR risk reduction is being made. Besides, the potential co-benefits of low-antibiotics use and high animal welfare farming systems have to be taken into consideration. In the following period, efforts should focus on:

• Ensuring that the preventive use of antibiotics is curtailed in line with the Veterinary Medicines and Medicated Feed Regulations

• Promoting high animal welfare farming methods in line with the One Health approach

• Setting an ambitious list of medically important antimicrobials to be prohibited or restricted for use in animal agriculture, with due regard to animal welfare requirements

• Establishing an antibiotics use data collection system that gathers information on animal species, antibiotics family, farming system and type of use, e.g. group or individual treatment. This needs to be carried out in a way that does not impose a disproportionate burden on small-scale farmers

• Ensuring import standards for animal-derived products from third countries are equivalent to those in effect in the EU

• Finding ways to address substances other than antimicrobials that may be used to compensate for poor animal husbandry practices

• Addressing standards in trade frameworks with third countries to reduce dependence on suppliers that abuse antimicrobials

(4) In the area of environmental health

• To tackle the lack of transparency in pharmaceutical production and supply chains

• To avoid having a sole focus on price in the procurement of pharmaceuticals

• To deal with the lack of comprehensive environmental criteria in legislation on and in procurement of medicinal products

• To reach a sustainable future in terms of health and environment, policymakers, private and public stakeholders should:


In all One Health areas

Recent AMR developments in the area of human health

(A) EPHA led

(1) ‘In the Red Zone – Antimicrobial Resistance: Lessons from Romania Report’6, commissioned by EPHA and published in March 2017, highlighted the urgent need for coordinated, well-resourced and effective EU policy action and programmes to tackle AMR. Romania made headlines in 2015 after a fire in a Bucharest nightclub exposed the fact that many of the burn victims were found to be resistant to antibiotics. Luckily, their condition was detected before they were dispersed across Europe for treatment. While Romania was selected as a case study country because of its excessive antibiotic use, prevalence of several strains of drug-resistant bacteria, coupled with an under-resourced health system, it is by no means an exception when it comes to inadequate funding for public health, health worker shortages, or lack of equipment and technology to safeguard patient safety. The report concluded that many EU Member States are facing similar challenges and risk tearing holes in Europe’s safety net.

(2) In 2019, EPHA conducted an in-depth study7 into the content and scope of National AMR Action Plans, which revealed important implementation gaps and big differences between the actions taken by EU and EEA countries. An event, “Invest and Protect”8 highlighted the continued need for financial and other resources (including qualified healthcare professionals) to develop and implement coordinated and strategic AMR action at a national level, promote prudent use of antibiotics and put in place effective antimicrobial stewardship programmes.

(a) Highlight and support the importance of the One Health approach as regards AMR, taking the example of environmental health
(b) Raise awareness about the role of the environment in the emergence of AMR
(c) Identify evidence-informed policy solutions at EU level to address environmental AMR

Recent AMR developments in the area of human health

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(3) Additionally, EPHA released a briefing on AMR indicators\(^9\), based on the need for more harmonised measures to align the monitoring efforts of Member States, enable benchmarking and highlight best practices. The ECDC, EMA and the European Food Safety Authority (EFSA) proposed a list of harmonised surveillance outcome indicators in the form of a Joint Scientific Opinion\(^10\). EPHA’s briefing argued that the approach could be strengthened by incorporating One Health elements, harmonising methodologies and establishing follow-up measures such as benchmarking and target setting.

(4) The AMR Stakeholder Network, established in 2017 and led by EPHA under the auspices of the European Commission’s Health Policy Platform, produced a Joint Statement and Call to Action\(^11\) in its first year.

**B) At a European level**

(1) The One Health Network of Experts has been meeting on an annual basis at a European level, although the impact of the dialogue initiated among the Member States has not yet been evaluated. The European Centre for Disease Prevention and Control (ECDC) and the European Medicines Agency (EMA) have both greatly increased their activities on AMR as a key priority, but the ECDC’s resources in particular have remained very limited, which has restricted its ability to provide comprehensive guidance and technical support to the Member States.

(2) The 2019 Council Conclusions of the Romanian EU Presidency confirmed 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”\(^12\).

(3) Following the European Parliament elections and institutional renewal process in 2019, the Mission Letter \(^13\) sent to European Health Commissioner Stella Kyriakides by the Commission President included the request to drive forward the full implementation of the EU Action Plan and to collaborate with international partners to advocate for a global agreement on the use of and access to antimicrobials.

(4) Also in 2019-2020, the new European Commission drafted and published a number of other documents which influence the AMR policy debate:

- The EU Pharmaceutical Strategy\(^14\)
- The Farm to Fork Strategy\(^15\)
- The development of a European Health Data Space\(^16\) and Artificial Intelligence\(^17\) approach

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\(^9\) [https://epha.org/indicators-for-the-surveillance-of-amr-and-antimicrobial-consumption/](https://epha.org/indicators-for-the-surveillance-of-amr-and-antimicrobial-consumption/)


\(^14\) [https://ec.europa.eu/health/human-use/strategy_en](https://ec.europa.eu/health/human-use/strategy_en)


(5) In 2020, the MEPs fight AMR Interest Group was launched in the European Parliament. Their vision is ambitious and committed, and can play a crucial role in translating policy asks into political statements, which is particularly important given the complex and multi-layered (international, European, national, regional, local) problem posed by AMR, which requires close inter-sectoral collaboration to ensure that actions are aligned with One Health principles and create the necessary synergies between actors and geographic locations.

(C) At an international level

(1) A number of reports by the WHO, OECD and other stakeholders have flagged up some issues related to the effective implementation of One Health principles.

(2) The Health Paradox report by SwedWatch in Hyderabad, one of the global manufacturing centres for antibiotics, has shown health and environment are directly intertwined with human rights, which establishes an important direct link with the Strategy on Pharmaceuticals in the Environment, finally released by the European Commission in early 2019 after a delay of several years.

(3) In a show of global coordination, G20 leaders, after discussing future priorities of the group, decided to include AMR as a key priority in the G20 Riyadh Declaration.

(D) The effects of the COVID-19 pandemic

The 2020 pandemic has clearly demonstrated the crushing effects cross-border health crises can exert on Europe’s – and global – health systems. While understandably the policy focus was at the outset very much on the immediate crisis caused by the coronavirus, it soon became clear that the potential consequences of a combined outbreak of AMR-related bacterial infections would have been devastating. On the one hand, COVID-19 temporarily displaced AMR on the health threat hierarchy; on the other, it also 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.

In late May 2020, the EC released its draft EU4Health Programme, written in direct response to the pandemic and the wake-up call the COVID-19 crisis presented to EU and national policymakers, highlighting that no country is resilient enough on its own when it comes to severe global threats to health. Importantly, AMR features among the specific objectives of the draft EU4Health Programme, by aiming to “foster and support the prudent and efficient use of medicines, and in particular of antimicrobials, and more environmentally friendly production and disposal of medicines and medical devices”.

18 https://epha.org/amr-interest-group/
19 https://www.who.int/publications/i/item/monitoring-and-evaluation-of-the-global-action-plan-on-antimicrobial-resistance (as an example)
22 https://www.g20riyadhsummit.org/pressroom/g20-riyadh-summit-leaders-declaration/
24 https://ec.europa.eu/health/funding/eu4health_en
Recent developments in agricultural policy and animal health

Four developments at an EU level will have important repercussions for addressing the threat of AMR linked to animal farming:

(1) The Veterinary Medicines and Medicated Feed Regulations, which will apply from 2022, will ban all purely preventative group treatments and restrict all antibiotic treatments, including group treatments, to non-routine use. As part of these Regulations, a list of medically important antimicrobials to be prohibited or restricted for use in animal agriculture will be established. Likewise, a system of data collection on antibiotics use across species will be phased in.

(2) The adoption of the EU Farm to Fork (F2F) Strategy in May 2020 sets a target to reduce the sales of antimicrobials for farmed animals and in aquaculture by 50% by 2030, with 2017 as the baseline year. Data from the latest European Surveillance of Veterinary Antimicrobial Consumption (ESVAC) report shows a reduction in antibiotics sales by 34% between 2011 and 2018\(^25\). While a positive development, vast differences in the intensity of use remain between countries - ranging from 2.9mg/PCU to 466.3mg/PCU. This suggests a similarly vast potential for improvement, and that the F2F target is definitely (and maybe relatively easily) within reach.

Another major component of the Strategy is the commitment that “products of animal origin imported into the EU will have to comply with strict requirements on the use of antibiotics in line with the recently agreed veterinary medicinal products Regulation”\(^26\). This has direct implications for trade policy and implies putting import modalities in place that exceed requirements that imported products should not be produced using antibiotics as growth promoters only.

Moreover, one action under the Strategy is to review the Feed Additives Regulation\(^27\). This may provide an opportunity to address the use of substances not currently classified as antimicrobials, like ionophores and other coccidiostats, which may be used in animal agriculture in high quantities for preventative use. These substances could be used in a way to compensate for poor animal husbandry conditions, may contribute to pharmaceutical pollution in the environment and could be associated with horizontal transfer of resistance, thereby potentially undermining the spirit of the Veterinary Medicines and Medicated Feed Regulations.

(3) The EU Biodiversity Strategy\(^28\) will require at least 25% of the EU’s agricultural land to be be organically farmed by 2030. Complementary/integrative medicine (CAM/CIM) can make a valuable contribution to reducing the use of antibiotics in this regard, which has also been recognised by the EU Organic Farming Regulation (EU) 2018/848 that explicitly calls for the preferred use of homeopathy and phytotherapy before conventional medicines, including antibiotics, are used\(^29\).

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(4) The impending adoption of the post-2020 Common Agricultural Policy (CAP) reform, which is, at the time of writing, in trilogue negotiations between the EU Council, Parliament and Commission. The CAP, responsible for over one third of the EU budget, will be critical in either enabling, or hampering, the transition towards animal farming systems that are consistent with antibiotics use reduction. In its analysis on the alignment between the CAP and the EU Green Deal (including the F2F Strategy), the Commission has pointed out the need to strengthen the CAP legal framework on antibiotics use.

In the current state of the proposal, a new specific CAP objective will be introduced on ‘food and health’, covering, among other things, farm antibiotics use. Member States will have to include antibiotics use reduction strategies in their national CAP Strategic Plans, with more focused farm advisory services. However, achievements in this area do not have to be reported in terms of ‘real’ impact (i.e. reduced antibiotics use), but in terms of numbers of animals covered by antibiotics use reduction projects.

Where should we go from here?

Much of the work undertaken by EPHA since 2017 has underlined the need for more ubiquitous AMR resources and the findings of our study on National Action Plans support this stance. Since 2017, a number of EU Member States have still not developed and/or implemented a proper AMR Action Plan stating that a lack of financial resources and know-how is a barrier.

With the publication of the European Commission’s Pharmaceutical Strategy and the inclusion of AMR as a specific objective in the EU4Health Programme proposal, the issue of industry incentives for the development of new antibiotics is a particularly important topic right now.

EPHA has noted the launch of a new AMR Action Fund, an initiative of the International Federation of Pharmaceutical Manufacturers & Associations (IFPMA) as a good, but far from ambitious enough commitment from the private sector to take AMR seriously. The partnership includes more than 20 leading biopharmaceutical companies committed to creating two to four new antibiotics by 2030.

Funding and technical support to accelerate antibiotic development will also be provided by philanthropies, development banks, and multilateral organisations. Nearly US$1 billion has already been raised to support clinical research of new antibiotics that are addressing the most resistant bacteria and life-threatening infections. It will be particularly important for these new antibiotics to be truly innovative if the declared objective of meeting urgent public health needs is to be attained.

32  https://amractionfund.com/
Industry has long maintained that antibiotic pipelines have run dry due to lack of funding available for the later stages of antibiotic R&D, which arguably presents a major hurdle for enabling patient access. At the same time, the industry is requesting that policymakers put in place “market-based reforms, including reimbursement reform and new pull incentives”.

As EPHA recognises, AMR is a platform which allows the industry to talk about incentives in a positive light. All too often, the call for “more incentives” is coupled with higher prices for new antibiotics, more unconditional public funding and market-based exclusivities. Clearly, there are competing visions for creating more sustainable antibiotic pipelines, driven by different value sets. Therefore, it will be important to ensure that the development of urgently needed public goods is embedded in a more ethical and transparent R&D regime that does not allow for a replication of current business models.

Reaching a global agreement on AMR is a key priority for the European Commission in this area, but this clearly depends on being able to establish an advanced level of coordination and establish common ambitions with international partner organisations (WHO, FAO, OIE, OECD, UN agencies, etc.) and, crucially, with high-level political fora such as the G20 and G7 groups.

In addition, bilateral dialogues with non-EU countries and the Trans-Atlantic Task Force for Antimicrobial Resistance (TATFAR) will also be needed. As a leader in the fight against AMR, the EU is well placed to propose concrete tools, practices and mechanisms for improved global governance and collaboration on AMR and to build up political will among diverse partners. Further alignment of objectives and joint actions with WHO could be most powerful in this regard.

Another step toward strengthening the global health governance structure, has been introduced by the establishment of the One Health Global Leaders Group on Antimicrobial Resistance. In a letter to the Tripartite Collaboration on AMR dated 15 June 2020, the UNSG approved the Terms of Reference and the Group is set to move forward.

Recommendation 10 of the 72nd World Health Assembly (WHA) on AMR (2019) called for the submission of consolidated biennial reports on progress achieved in implementing the resolutions from this round of the Assembly and that of the 68th Assembly in 2015. Going forwards, the 74th, 76th, and 78th WHA, through the Executive Board, will incorporate this work into existing antimicrobial reporting in order to allow Member States to review and evaluate effort made.

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34 https://epha.org/the-top-4-issues-in-medicines-policy-for-2020/
35 https://www.cdc.gov/drugresistance/tatfar/index.html
36 https://www.who.int/news-room/articles-detail/one-health-global-leaders-group-on-antimicrobial-resistance
37 https://www.who.int/foodsafety/areas_work/antimicrobial-resistance/tripartite/en/
The Interagency Coordination Group (IACG) on AMR 2019 final report, “No time to wait: securing the future from drug-resistant infections”\(^3\) calls, inter alia, for the “development of new antimicrobials, diagnostics, vaccines, waste management tools, and safe and effective alternatives to antimicrobials across the One Health spectrum.” However, several voices at an international level have highlighted serious obstacles to the effective implementation of AMR National Action Plans (NAPs)\(^4\).

New initiatives are emerging to provide data and quantitative analysis on AMR to European Union officials, as well as the international community, such as the AMR Benchmark Index, presented in its second edition\(^5\) by the Access to Medicines Foundation at the World Economic Forum in 2020.

The COVID-19 crisis has also renewed attention to the systemic interactions\(^6\) and interdependence between human, ecological and animal health described by the One Health principle. While already referred to in the EU One Health Action Plan, it can be expected that this line of thought, which further elevates the importance of animal health and welfare, will become increasingly prominent in approaching food systems sustainability.

However, there are significant concerns that the current CAP model is not fit to drive a real transition in animal farming practices towards more sustainable systems, including in terms of antibiotics use. The question whether the CAP, as it is taking shape today, is likely to be the instrument to drive a sustainable transition across the EU, as opposed to a few more forward-looking countries only, has been answered negatively by a wide range of civil society organisations. These, including EPHA, have called on the Commission to withdraw the current CAP proposal and start with a new reform, which is more clearly based on the EU Green Deal and F2F Strategy targets and objectives.

The main driver of EU farm policy should change from ‘producing food’ to developing ‘healthy farming’. Farms need to become dynamically healthy rather than just being part of the food industry. Instead of trying to reduce the use of antibiotics in farming, a kind of farming that has very little need for the use of antibiotics (and pesticides) should be promoted by learning from examples where this already happens. Such farming is likely to also be good for the environment, animal welfare, produce more nutritious food and be the kind of farming the EU population prefers. The argument for the need to produce sufficient food has to be more carefully examined. For instance: more nutritious food can reduce food consumption, better farm to fork management can reduce waste.

\(^3\) https://www.who.int/antimicrobial-resistance/interagency-coordination-group/final-report/en/

\(^4\) https://www.southcentre.int/policy-brief-53-september-2018/


\(^6\) https://www.pnas.org/content/pnas/110/21/8399.full.pdf

\(^7\) https://www.nature.com/articles/s41586-020-2562-8.epdf
Policy recommendations

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, and the majority of recommendations brought forward by EPHA remain valid.

This includes the points made in EPHA’s 2017 Position Paper, which advocated for a comprehensive One Health Action Plan and addressed seven different areas: AMR governance and resources; better surveillance and common goal-setting; prevention; environmental policy; agriculture; refining Action Plan elements; and education and awareness-raising. In combination, our recommendations could be grouped under the headings of Legislation, Guidance, Funding and Cooperation.

Among the primary asks was our request to “Set ambitious, clear and realistic SMART headline targets at European level”, requiring national commitments on:

- reducing AMR prevalence
- lowering health care associated infections (HCAIs)
- preventing excessive consumption of antimicrobials
- decreasing prescriptions of antimicrobials to humans
- requiring Member States to set their quantitative and relative reduction targets
- providing monitoring data, to ensure that all national contributions contribute to achieving the European headline targets

In addition, we recommend the setting of a European headline target for reducing antibiotic use and prescribing on farms, coupled with specific targets for different types of animals (e.g. per unit of meat output). While steps have been made in this direction in a number of Member States, overall target-setting remains insufficient and it is hoped that the renewed interest in AMR in relation to COVID-19 might encourage further action in this direction.

The integrative medical approach has potential to contribute to tackling AMR. For example, some studies suggest it could lower antibiotic prescription rates when patients present with a cough\textsuperscript{44,45}; and that integrative medicinal products could offer an alternative to antibiotics as a first line of treatment, though more research is needed. In addition, the environmental impact is negligible.

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Recently, the consensus Roadmap, produced in 2019 by the growing and diverse AMR Stakeholder Network, called for the implementation of five chief strategies to tackle AMR by supporting the implementation of the EU and national action plans:

1. Set targets and performance indicators
2. Help countries mobilise resources for better implementation of national AMR policies
3. Close the existing collaboration gap between civil society and EU policymakers
4. Put prevention at the heart of AMR policymaking
5. Tackle the environmental dimension of AMR in the framework of the European Green Deal

These strategies are also closely linked to the aims and Work Programme of the MEP Interest Group in the European Parliament whose secretariat is jointly hosted by EPHA and our partners Health Care Without Harm Europe. The Interest Group, currently composed of 18 AMR champions, presents a concrete opportunity to scale up messages at a political level and push for progress at an EU and national level.

As mentioned above, the new EU4Health Programme views AMR as a specific objective in the context of national health system strengthening and for scaling up resilience in the face of future cross-border health threats. In times of COVID-19, it will be even more important to address AMR in the most timely and comprehensive manner possible. While the world is shocked to learn that nearly a million people have died worldwide from the coronavirus, AMR has for years accounted for more than 700,000 deaths globally and yet this is rarely talked about and not part of public consciousness.

Conclusion

While AMR continues to occupy a prominent position on the EU health policy agenda, especially in times of COVID-19, it is crucial that it is not viewed and tackled as an isolated health threat; the fight against AMR must go hand-in-hand with Europe’s renewed drive to join forces, to protect public health for all and act in solidarity. Just as nobody could have foreseen the rapid spreading of the coronavirus and the immense economic and social scars it has caused, AMR could have a devastating impact on health systems, especially should a spike in drug-resistant infections occur in parallel with future pandemics or communicable disease outbreaks. The post-COVID recovery offers a unique opportunity to align health and economic recovery with efforts to reduce AMR and environmental sustainability and should be embraced by the EC and our international partners.