

Antimicrobial Resistance (AMR)

EPHA Position Paper on the 2017
EU Action Plan on AMR
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european public health alliance



Table of Content

Executive Summary	1
Recommendations	2
Legislation	2
Guidance	3
Funding.....	4
Co-operation.....	5
1. Context.....	6
2. Policy recommendations for the EU Action Plan.....	7
2.1 AMR governance and resources.....	7
2.2 Better surveillance and common goal-setting.....	9
Recommendations	10
2.3 Prevention.....	13
2.4 Environmental policy dimension of AMR	16
2.5 Agriculture Policy	18
2.6 Refining existing Action Plan areas.....	19
2.7 Education and awareness-raising	21
3. Conclusion	23

Executive Summary

EPHA's Position Paper on the follow-up European Action Plan on Antimicrobial Resistance (AMR), expected to be released in June 2017, underlines the urgent need for making a strong and convincing case for increased EU action and responsibility on AMR, covering all domains of the One Health approach. If no action is taken soon to ensure that EU Member States' efforts to tackle AMR become better aligned and mutually reinforcing, the consequences for public health could be disastrous. The projected high numbers of deaths and disease-related complications that could arise from drug-resistant infections would threaten the sustainability of European health systems while also representing a major blow to the economy. At global level, the rise of AMR also poses a severe threat to achieving the Sustainable Development Goals and to universal access to healthcare.

A clear added value for stepping up EU action and providing more ample support, including funding for building up capacities at Member State level, is that everybody will gain from it: ordinary people, public authorities and budgets, healthcare settings, research, industry, and the economy. However, in order for Europe to shine as a global leader and best practice region, all Member States must have the political will - and access to dedicated resources and expertise - to improve their AMR situations given the continued discrepancies between and within the Member States.

Several Member States have tried and tested policies successfully, primarily in the human health and veterinary medicine sectors. They contain ambitious targets, supported by comprehensive data collection and surveillance systems, and other measures that have demonstrated rapid results in effectively reducing both AMR prevalence and excessive consumption of antimicrobials. It is important that these are explained and spread across Europe so that all Member States can develop similar models to improve their national AMR situations. Moreover, a sufficient range of regulatory tools are available at the EU level to fight AMR, including legislation, and it is important that these are activated and deployed in a strategic and coherent way.

Recognising the major public health threat that AMR presents to Europe and the rest of the world, as well as the complexities involved in devising an effective AMR safety net, EPHA's position:

- Emphasises the European added value and ensuring robust governance and accountability mechanisms for all actors involved in the fight against AMR; and
- Demonstrates the need for the EU's leadership role by taking a more holistic approach to AMR, making best use of the available EU legal competences and funding, and providing more targeted support for the implementation of national action plans so that best practices can be embraced across Europe.

Recommendations

Set ambitious, clear and realistic SMART headline targets at European level, requiring national commitments including for Overall reduction of AMR prevalence;

- a) Overall reduction in HCAI;
- b) Reduction of excessive consumption;
- c) Prescribing of antimicrobials in humans;
- d) Require Member States to set their own quantitative and relative reduction targets, and provide monitoring data, ensuring that all national contributions contribute to achieving the European headline targets.

Set 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).

Legislation

- Require mandatory routine collection and submission of national and local monitoring data at EU level, and establish appropriate indicators to measure progress.
- Require countries to establish their own cross-sectoral, national AMR platforms to design, oversee and implement national action plans, consulting and involving relevant stakeholders
- Enforce existing legislation on illegal practices related to non-pharmacy availability of antibiotics
- Propose a standardized system of antibiotic labelling and packaging to inform consumers of appropriate use, disposal, and risks associated with misuse
- Ensure transparency of global pharmaceutical production and supply chains, and include mandatory environmental risk assessments in Good Manufacturing Practice (GMP) rules
- Require Environmental Risk Assessment as a mandatory part of the marketing authorisation process for antimicrobials, and as a condition for public R&D funding
- Propose a complete ban of antibiotic residues in ground and surface water in the European Commission's Pharmaceuticals in the Environment strategy.

- Require and support site inspections of pharmaceutical factories based outside of the European region to be carried out by European medical agencies to ensure compliance with GMP rules
- Ban the routine preventive mass medication of groups of animals with antibiotics via feed or water
- Ban the use of critically important antibiotics for preventative use and group treatments
- Set binding limits for antimicrobial use in meat and dairy producing animals
- Prohibit veterinarians from selling antibiotics to remove the economic incentive to prescribe antimicrobial therapies to livestock.
- Insist that the European ban on growth promotion in agriculture must be upheld
- Extend the standards and restrictions of antimicrobial use outlined in Council Regulation (EC) No 834/2007¹ and Commission Regulation (EC) No 889/2008² to apply to non-organic farming as well as organic farming.

Guidance

- Set ambitious, clear and realistic SMART headline targets at European level, including for reducing antibiotic use and prescribing on farms
- Include an ex-ante impact assessment and mandate a mid-term review and ex-post impact evaluation of the new AMR plan
- Improve data collection on disease- and treatment-specific costs arising from AMR
- Oblige prescribers, pharmacists and other health professionals to inform patients (and agricultural users) about rational use and available alternatives to antibiotics
- Create harmonised quality standards in EU-wide curricula for health professionals in the area of AMR, which highlights the risks related to inappropriate prescribing, dosage, use, and disposal

¹ European Council (2007). *Council Regulation (EC) No 834/2007*. Available at: <http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:L:2007:189:0001:0023:EN:PDF>

² European Commission (2008). *Commission Regulation (EC) No 889/2008*. Available at: <http://eur-lex.europa.eu/eli/reg/2008/889/oj>

- Support health professionals with positive incentives to encourage all prescribers to become advocates of prudent use and practise the “as little as possible, as much as necessary” axiom.
- Establish multidisciplinary common antimicrobial stewardship programmes, facilitated by the EU throughout Europe, both on- and offline to encourage joint ownership of the problem.

Develop and support educational interventions, following the example of the e-Bug platform so that all members of society can be reached

Funding

- Expand the role and funding of the ECDC, particularly the ARHAI programme.
- Support the follow-up Action Plan and ensure it is accompanied by implementation funds, ensuring that countries are also aware of existing funds to combat AMRDirect a greater proportion of public funding to universities, research centres, and initiative such as the Drugs for Neglected Diseases initiative (DNDi)
- Provide funding for – and encourage companies to invest in - diagnostic tools, including rapid diagnostic tests
- Support more research, including from the disciplines of social science and behavioural psychology, into the various reasons for irrational and unnecessary consumption and prescribing,
- Support research to better understand how people and animals can be enabled to lead healthy lives, whilst minimising the use of antimicrobial drugs
- Support research into the various transmission dynamics of AMR via the environment
- Undertake an ex-post evaluation of the overall results of public expenditure for projects coordinated by the Joint Programming Initiative on AMR and IMI as part of the follow-up EU Action Plan on AMR.
- Develop de-linkage pharmaceutical incentive models (price/sales volumes) to deliver new types of antimicrobial treatments.
- Increase funding to promote the European Antibiotics Awareness Day (EAAD) action throughout the year on drug-resistant infections, their consequences and how to prevent them from spreading further.

Co-operation

- Establish the One Health-AMR Network to serve as the principal forum for advancing coordinated European policy action on AMR and facilitate the drafting of national action plans, requiring it to assess the commitments proposed in each national action plan
- Within the European Commission and Member States, bind in expertise and resources from beyond the health policy sector
- Promote increased vaccination in agriculture and aquaculture and scale up best practices via the One Health AMR Network
- Introduce electronic decision support systems and boost laboratory capacities in the subscribing on antibiotics, enabling safety issues and overuse and abuse of antibiotics to be highlighted
- Work with the pharmaceutical industry and suppliers to ensure they commit and contribute to the fight against unlicensed / illegal OTC and Internet sales of antibiotics
- Support farmers in the transition from intensive to sustainable animal husbandry practices, as intensive farming is exacerbating the AMR problem
- Facilitate dialogue between Chief Veterinary Officers, veterinarians, farmers and the animal health industry, to inspire responsible use of antimicrobials
- Safeguard that international trade agreements between the EU and third countries support the goals of the WHO Global Action Plan and the follow-up EU Acton Plan
- Use international health diplomacy as a lever to make sure that the results of high-level negotiations (G20/ G7, UNGA, WHO, etc.) must be taken into account in trade agreements

EPHA Position Paper on the 2017 EU Action Plan on AMR

1. Context

With the increased emergence and rapid global spread of multi-drug resistant pathogens, Antimicrobial Resistance (AMR) is rapidly becoming the largest public health threat in Europe and worldwide. If left unchecked, a dramatic rise in fatalities will follow, with up to 10 million deaths every year by 2050. The detrimental impact of AMR on the sustainability of health systems, agriculture, and the economy will be vast and unprecedented. The European Commission must therefore act swiftly and firmly to make Europe a best practice region and lead the global fight against AMR.

EPHA's Briefing on the Evaluation of the AMR Action Plan 2011-2016 points out a number of elements that were under-represented by the European Commission in its first Action Plan, such as the impact of pharmaceutical pollution. EPHA's briefing also calls for an update of the evidence base for the impact and cost of AMR in order to underline the importance of the Action Plan and recognise the real scale and urgency of the problem. The Commission's Evaluation uses outdated figures, e.g. stating that annual AMR-related deaths in Europe amount to 25,000 people (although actual numbers are now much higher) while also using old estimates for the associated healthcare costs and productivity losses. Moreover, it disregards the trends revealed in the surveillance data produced by the European Centre for Disease Prevention and Control (ECDC) on consumption of antibiotics, as well as the prevalence of AMR and healthcare associated infections (HCAI). This data exposes a widening gap between countries, with AMR becoming significantly worse in some Member States. With multi-drug, resistant infections on the rise, and the reduced effectiveness of last-line antibiotics such as colistin and carbapenems threatening patient safety and healthcare systems, ECDC's data provides ample evidence for the urgent need to ensure that Europe's safety net is not dismantled by inaction in certain countries or regions. It is essential that the failures of the previous Action Plan are corrected by the new plan.

The outcome of the Evaluation presented a vital opportunity for the European Commission to make a forceful and convincing case for strengthened action at EU level, including dedicated funding and new legislation. It is crucial that the 2017 action plan builds upon the steps already taken and outlines clear, concrete and ambitious strategies to curb the threat of AMR. Disconcertingly, AMR is not mentioned in the Commission's 2017 Work Programme, where it should feature as a stand-alone policy priority and as a provision to be mainstreamed into other policy areas.

The fire that broke out in a Bucharest nightclub in 2015 exemplifies the need for comprehensive European action. The incident resulted in the hospitalisation of many

patients, many of whom died as a result of hospital-acquired (multi-)drug resistant infections. The limited capacity of Romanian hospitals to treat and accommodate the victims led to patients being transferred to clinics in other countries, thereby exporting resistant bacteria across Europe. Such events fundamentally challenge the EU's capacity to protect public health and the security of its citizens. AMR can strike with such unpredictable vigour that all countries must put forth their best efforts, both individually and in partnership, to avoid the worst-case scenario. Without such effort, countries like Romania, which already struggle to care for high numbers of multi-drug resistant TB patients, could provide an entry point for a cross-border public health emergency.

Following the release of a Roadmap in October 2016, the Commission is expected to present its follow-up EU Action Plan on AMR in June 2017. This position paper outlines important elements that the follow-up Action Plan should incorporate or address more forcefully than its precursor.

2. Policy recommendations for the EU Action Plan

2.1 AMR governance and resources

European action on AMR is a cornerstone of global efforts to mitigate the problem. European governments and academic institutions have a longstanding record of leadership in identifying the scale and urgency of AMR as a global threat to public health. Several EU Member States have developed world-leading expertise in how to effectively tackle AMR prevalence, HCAI and over-consumption of antimicrobial drugs. As a supranational entity working in close partnership with all relevant AMR stakeholders, and equipped with numerous legal competences and funding tools, the EU is best placed to bring about change in a timely manner by requiring uptake of effective, tried and tested policies and strategies in every Member State. The EU also has important leverage with other countries and global regions as a standard setter and trading partner, as well as diplomatic clout in international fora (as seen in UN climate change negotiations). Given Europe's leading role on AMR, stepping up EU action is vital to advance the progress of international organisations such as the United Nations, or the World Health Organization (WHO) or forums such as G20 / G7.

A crisis on the scale of AMR requires EU support for European countries and other actors, coupled with enhanced surveillance data and guidance. Thanks to some EU Member States being at the vanguard of policy action to tackle AMR, there is a very clear European evidence base for judging which policies and measures are effective. The focus now needs to lie on implementation rather than discussion.

Regarding AMR governance and resources, the follow-up Action Plan should include the proposals below:

Recommendations

- 1. Expand the role and funding of the ECDC.** Equipped with a unique scientific knowledge base, the ECDC is well placed to assume a greater policy and advocacy role. Given the need for a horizontal approach to AMR, more joint work between ECDC, the European Medicines Agency (EMA) and the European Food Safety Authority (EFSA) would also be helpful to increase the understanding of how human health, animal health and the food chain are connected in the framework of AMR.³
- 2. Within the European Commission and Member States, bind in expertise and resources from beyond the health policy sector,** including the EU External Action Service (international health diplomacy and international agreements), trade, environment, agriculture, industrial and market policies, taxation and customs, etc. For example, the EEAS should lead EU coordinated inputs to the WHO developments of a Global Development and Stewardship Framework as initiated by the UN High Level Declaration of Heads of State and Government on AMR of September 2016.
- 3. Establish the One Health-AMR Network to serve as the principal forum for advancing coordinated European policy action on AMR and facilitate the drafting of national action plans.** The Network can streamline this process by facilitating the sharing and comparing of European, national and regional initiatives and targets and gather evidence on why certain approaches work in certain settings. It should establish a repository of transferable policies and good practices, and support target setting (and enforcement) at national level, and determine what elements must be in place to attain them.
- 4. Support the follow-up Action Plan and ensure it is accompanied by implementation funds:** a European AMR Fund should be created, which could be replenished in various ways (e.g. taxation, “pay or play” schemes as proposed by the UK Review on AMR⁴). The Fund should support national and regional health systems that lack the necessary operational infrastructure, technology, and skilled health workforce to adapt best practices to their circumstances. Many countries are also unaware of existing EU funds to combat AMR, spread across different programmes, which could be drawn upon for implementing national

³ ECDC, EFSA, EMA (2015). *ECDC/EFSA/EMA first joint report on the integrated analysis of the consumption of antimicrobial agents and occurrence of antimicrobial resistance in bacteria from humans and food-producing animals*. Available at: http://www.ema.europa.eu/docs/en_GB/document_library/Report/2015/01/WC500181485.pdf

⁴ Review on Antimicrobial Resistance (2016), op. cit., p.3

action plans. Clear EU guidance and simplification is needed on how to access these resources.

- 5. Include an ex-ante impact assessment and mandate a mid-term review and ex-post impact evaluation** in order to clearly assess the follow-up AMR Plan's effectiveness. The new Plan must particularly address the failings of the 2011-2016 Action Plan. To support this, a better evaluation methodology needs to be established.

To effectively reduce the threat of AMR, action taken in Europe must also contribute to a greater global strategy. **Policy alignment with the EU's neighbouring countries in the WHO European Region** must therefore be sought to close the AMR safety net and avoid aggravating health inequalities between blocks of countries. The European Union should demonstrate leadership at the global level and ensure that access to antibiotics is improved where necessary. Encouraging ownership of the AMR agenda in all nations, not only high-income countries, is necessary to achieve lasting, structural change⁵. Persistent shortages of antimicrobials⁶ and counterfeit medicines demand further attention. The EU must promote solidarity within and beyond its borders, with AMR policies regarding antibiotics as a public good.

Transparency is a prerequisite when it comes to maximising civil society's and other stakeholders' ability to effectively contribute to the fight against AMR and support the EU. **The Commission should therefore publicise the composition and meeting minutes of the inter-service group on AMR**, so that the work of other stakeholders can benefit from their insights.

Finally, it is reasonable that a public health crisis of such magnitude as AMR be framed as a health security issue, e.g. via the Health Security Committee.

2.2 Better surveillance and common goal-setting

AMR control can be seen as a journey: some countries may have further to travel, but all can take steps towards common goals.⁷

The availability of comprehensive, harmonised and comparable data at European, national and local level is crucial in averting a looming public health crisis. Due to the inherent cross-border nature of AMR, the EU has an indispensable

⁵ Wellcome Trust (2016). *Evidence for action on antimicrobial resistance*, p. 4. Available at: <https://wellcome.ac.uk/sites/default/files/evidence-for-action-on-antimicrobial-resistance-wellcome-sep16.pdf>

⁶ European Association of Hospital Pharmacists (2014). *Medicines shortages in European hospitals – The evidence and case for action*. Retrieved from: <http://www.eahp.eu/practice-and-policy/medicines-shortages>

⁷ Wellcome Trust (2016), op.cit.

role to play in ensuring that effective surveillance data are produced, compiled and analysed, to determine the root causes of the spread of AMR and HCAI, as well as excessive antimicrobial consumption and prescribing.

Recommendations

- 1. Set ambitious, clear and realistic SMART headline targets at European level**, requiring national commitments including for Overall reduction of AMR prevalence;
 - a) Overall reduction in HCAI;
 - b) Reduction of excessive consumption;
 - c) Prescribing of antimicrobials in humans;
 - d) Require Member States to set their own quantitative and relative reduction targets, and provide monitoring data, ensuring that all national contributions contribute to achieving the European headline targets.
- 2. Set 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).
- 3. Require mandatory routine collection and submission of national and local monitoring data at EU level** in order to define and achieve European and national targets and goals. Data must be sufficiently harmonised and comprehensive so that instructive comparisons can be drawn between countries and regions to better understand consumption and AMR prevalence trends.
- 4. Establish appropriate indicators** so that progress can be measured in a meaningful way. As per the Commission's evaluation report, a majority of European countries have established indicators for the assessment of their national action plans, in the hospital and ambulatory care sectors, with fewer countries having implemented indicators for nursing homes and other long-term care facilities⁸. In order to make best use of national data, such indicators must be established at European level.
- 5. Require countries to establish their own cross-sectoral, national AMR platforms to** design, oversee and implement national action plans, gathering actors in all relevant policy areas, including the public and private sectors, as well as civil society. They could designate "AMR champions" (clinical leads, for example from the office of the Chief Medical Officer) and expedite the

⁸ European Commission (2016). *Prudent use of antimicrobial agents in human medicine: third report on implementation of the Council recommendation*. Available at: http://ec.europa.eu/dgs/health_food-safety/amr/docs/amr_projects_3rd-report-councilrecprudent.pdf

implementation of national and EU targets and good practices. **Improve data collection on disease- and treatment-specific costs arising from AMR** to gain a better understanding of its actual impacts, both general and sector-specific, in terms of disease burden and economic costs. This applies, for example, to projected impacts for chemotherapy, infectious disease control (including tuberculosis), and HCAI. Noting that the estimated 25,000 deaths and associated AMR costs across the EU from the previous Action Plan is an underestimate and needs to be updated to make the case for coordinated policy action.

- 6. Increase significantly the resources for the ECDC’s ARHAI programme** (AMR and HAI) to allow the Agency to deepen its activities related to surveillance, data analysis, risk assessment, guidance and awareness-raising. In particular, the ARHAI country visits could serve to test the implementation of national action plans from a One Health perspective, resulting in publicly available reports that could offer countries an overview of where the problems lie, how they compare to other countries, as well as concrete advice on how to achieve improvements at national and regional level.
- 7. Require the One Health-AMR Network to assess the commitments proposed in each national Action Plan**, and check against overall Europe-wide reduction targets, to see whether actions committed to will be sufficient and effective.

At a basic level, common goal-setting means ensuring that best practices, such as those presented in the AMR Next document⁹ of the Dutch Council Presidency, are disseminated across Europe, to encourage their widespread take-up. Greater knowledge of how successful policies and best practices have been implemented, including evidence of their positive contributions, would offer policymakers concrete choices and leave them with no justifiable excuse to disregard solutions that have been proven to work elsewhere.

National targets have proved effective:

Country	National AMR Action Plans / strategies: Healthcare targets & achievements	National AMR Action Plans / strategies: Animal health targets & achievements
Netherlands ¹⁰	<ul style="list-style-type: none"> • 50% reduction of avoidable HCAI in 5 years 	<ul style="list-style-type: none"> • Banned routine preventative use of antibiotics in animals

⁹Dutch Council Presidency (2016). *AMR next*. Retrieved from: <https://www.eu2016.nl/documenten/publicaties/2016/02/10/amr-next>

¹⁰ Schippers, Van Rijn, Dijkma, Mansveld (2015), *Letter to parliament about the approach to antibiotic resistance*. Available on ECDC website at: <http://ecdc.europa.eu/en/healthtopics/Healthcare->

	<ul style="list-style-type: none"> • 50%+ reduction in the use of incorrectly prescribed antibiotics across the entire healthcare chain • Reduction in the emergence & spread of multi-resistant bacteria in healthcare becomes visible • Infections and deaths due to antibiotic resistance will remain at the current level or decrease • Possibilities for effective treatment of patients with infections with resistant bacteria will not reduce any further 	<ul style="list-style-type: none"> • Achieved large reductions in farm antibiotics use • Cut farm use of critically important antibiotics in main food-animal species by over 90% in three years, contributing to a fall of livestock-associated MRSA in people • 70% reduction target (2012)
Sweden¹¹	<ul style="list-style-type: none"> • Achieved over 40% decrease of antibiotics prescription since mid-1990s 	<ul style="list-style-type: none"> • Achieved lowest use of antibiotics in EU: 60% decrease since mid-1980s • Routine use of antibiotics banned since 1980s
Denmark¹²	<ul style="list-style-type: none"> • The Antibiotic Council, made up of elected officials from the public health and food authorities works to reduce AMR and antimicrobial use in animal and human medicine. 	<ul style="list-style-type: none"> • Since 1990, achieved biggest reduction of farm antibiotic use in Europe • Targeted initiatives (e.g., “Yellow card”) resulted in 22% reduction of antibiotics use in pigs, five years before the target year • MRSA Action Plan goal: 15% reduction of antibiotics use in pigs (2015-2018)

[associated_infections/guidance-infection-prevention-control/Pages/antimicrobial-resistance-strategies-action-plans.aspx](http://ecdc.europa.eu/en/healthtopics/Healthcare-associated_infections/guidance-infection-prevention-control/Pages/antimicrobial-resistance-strategies-action-plans.aspx)

¹¹ Ministry of Health and Social Affairs (2016). *Swedish Strategy to combat Antibiotic Resistance*. Available on ECDC website at http://ecdc.europa.eu/en/healthtopics/Healthcare-associated_infections/guidance-infection-prevention-control/Pages/antimicrobial-resistance-strategies-action-plans.aspx

¹² Indenrigs- og Sundhedsministeriet (2010). *Fælles antibiotika- og resistenshandlingsplan*. Available on ECDC website http://ecdc.europa.eu/en/healthtopics/Healthcare-associated_infections/guidance-infection-prevention-control/Pages/antimicrobial-resistance-strategies-action-plans.aspx

<p>Norway¹³</p>	<ul style="list-style-type: none"> • AB use in total pop will be reduced by 30%, measured in DDD6/1000 inhabitants/day, as compared to 2012. • NO will be one of the three European countries that uses the least antibiotics in humans, measured in DDD/1000 inhabitants/day. • Reduction of AB prescriptions from an average today of 450 prescriptions per 1000 inhabitants per year to 250 • Prescription of ABs for respiratory infections will be reduced by 20%, measured in DDD/1000 inhabitants/day, compared to 2012 	<ul style="list-style-type: none"> • Achieved 35% decrease in antibiotics consumption by food-producing animals (1995-2013) • 99% decrease of antibiotic use in aquaculture (1987-1996), after which it remained stable • Norway is among the countries best placed with regard to prescribing narrow-spectrum ABs • LA-MRSA will not be established in the pig population. • ESBL in poultry-production will be reduced to a minimum. • Antibiotics use in terrestrial animals used for food production will be reduced by at least 10% compared with 2013. • AB use in pets will be reduced by at least 30% compared with 2013. • Total AB use in fish farming in 2020 will be at the same or lower levels than for the period 2004-2014, measured in total kilograms of antibiotics.
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2.3 Prevention

Infection prevention and control (IPC) in all healthcare settings and vaccination of animals and risk groups are two of the most important and effective tools to keep infections at bay. In order to increase vaccination rates, it is advantageous to diversify

¹³ Ministry of Health and Care Services (2015). National strategy against antibiotic resistance. Available on ECDC website <https://www.regjeringen.no/contentassets/5eaf66ac392143b3b2054aed90b85210/antibiotic-resistance-engelsk-lavoppløslig-versjon-for-nett-10-09-15.pdf>

the ways in which vaccines are being administered, e.g. by enabling pharmacists to vaccinate against certain diseases such as seasonal influenza¹⁴.

Prevention and health promotion activities should extend beyond vaccination with the aim to keep people and animals healthier and avoid infection. As highlighted in EPHA's Recommendations for the Dutch Council Conclusions, maintaining good health is one of the most effective ways of prevention, which at practical level translates into enabling healthy living for people (good nutrition, healthy environment, physical exercise, reduced stress, etc.), ensuring good animal husbandry practices (e.g. low stocking densities, suitable climate) and promoting environmentally responsible pharmaceutical and agricultural production methods.

Prevention and health promotion are also crucial to stem the global rise of chronic, non-communicable diseases in an ageing European society. The negative effect of antibiotics on the human microbiome, specifically the digestive system, potentially contributing to the pervasiveness of chronic diseases, such as obesity, type-two diabetes and cancer, highlights another reason to focus on prevention¹⁵.

Firm and decisive action in the following areas must be taken to prevent the spread of AMR:

Recommendations

Human health

- 1. Enforce existing legislation on illegal practices properly** Illegal over-the-counter (OTC), online and other non-pharmacy availability of antibiotics in Europe must be investigated, and the laws at EU and national level must be updated to ensure that they are robust enough to eradicate illegal practices. Internet sales are a growing problem, even in low consumption countries like the Netherlands and Sweden. As new technology evolves rapidly, policymakers must keep a close eye on the diversification of purchasing channels in order to determine what further legislative action is required to close any loopholes.
- 2. Introduce electronic decision support systems and boost laboratory capacities.** The uptake and use of e-Prescribing systems and access to shared eHealth records, patient medication records, or pharmaceutical records should be

¹⁴ For example, in a growing number of European countries, community pharmacists can vaccinate individuals against seasonal influenza: PGEU Statement on Pandemic Influenza (2009), <http://bit.ly/2otJycn>

¹⁵ This may have potential links to causative effects in obesity, cancer and diabetes: See <https://bmcmmedicine.biomedcentral.com/articles/10.1186/s12916-016-0605-7>, <http://gut.bmj.com/content/early/2017/03/16/gutjnl-2016-313413>, <http://onlinelibrary.wiley.com/doi/10.1002/ijc.23622/full>, and <http://press.endocrine.org/doi/10.1210/jc.2015-2696>

promoted as such infrastructure can highlight safety issues, interactions, overuse and abuse of medicines.

- 3. Oblige prescribers, pharmacists and other health professionals to inform patients about rational use** and available alternatives to antibiotics. In addition, there should be mandatory check-ups for patients using antimicrobials for longer periods of time to ensure treatment compliance and avoid “home rationing”.
- 4. Propose a standardized system of antibiotic labelling and packaging** to inform consumers of appropriate use, disposal, and risks associated with misuse. Harmonise pack sizes across Europe so that they correspond to the prescribed course duration and usage, will make it more difficult for people to maintain personal “supply cupboards” at home

Animal health and agriculture

- 1. Support farmers in the transition from intensive to sustainable animal husbandry practices**, as intensive farming is exacerbating the AMR problem¹⁶. The AMR Now publication released by the Dutch government during their EU Council Presidency provides an overview of good farming practices put in place by animal keepers who have reduced stocking densities and increased outdoor access, improved system design and selection of breeds less susceptible to infection. These tried and tested measures have improved the living conditions of farm animals, and with it reduced the need for antibiotics without compromising productivity.
- 2. Extend the standards and restrictions of antimicrobial use outlined in Council Regulation (EC) No 834/2007¹⁷ and Commission Regulation (EC) No 889/2008¹⁸ to apply to non-organic farming** as well as organic farming. This would ensure that farming practices are altered so that antibiotics can be used as a treatment for disease, and not as a preventative measure.
- 3. Promote increased vaccination in agriculture and aquaculture** (which is e.g. widely practised in Norway), and scale up best practices via the One Health-AMR Network to overcome the technical and economic challenges involved.
- 4. Facilitate dialogue between Chief Veterinary Officers, veterinarians, farmers and the animal health industry**, to inspire responsible use of antimicrobials and

¹⁶ Alliance To Save Our Antibiotics (2015). *Antimicrobial Resistance - why the irresponsible use of antibiotics in agriculture must stop*. Available at: <http://www.saveourantibiotics.org/media/1466/antibiotics-alliance-40pp-report-2015-final-artwork-1.pdf>

¹⁷ European Council (2007). *Council Regulation (EC) No 834/2007*. Available at: <http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:L:2007:189:0001:0023:EN:PDF>

¹⁸ European Commission (2008). *Commission Regulation (EC) No 889/2008*. Available at: <http://eur-lex.europa.eu/eli/reg/2008/889/oj>

tackle AMR in order to convert key animal health stakeholders into antibiotic stewards.

Research and development

- 1. Direct a greater proportion of public funding towards universities, research centres, and initiative such as the Drugs for Neglected Diseases initiative (DNDi)** for the development of new antimicrobials and diagnostic tests. Due to the low commercial value of antimicrobials, it is unrealistic to rely on profit-driven industry to lead research and development in this field.
- 2. Support research to better understand how people and animals can be enabled to lead healthy lives, physically and psychologically, whilst minimising the use of antimicrobial drugs.** It is important that health professionals – especially GPs - are aware of the full range of treatment options at their disposal since antibiotics should only be prescribed as a last resort. Developing evidence-based recommendations on the use of alternatives to antibiotics is beneficial as integrative settings may have lower rates of antibiotics prescription¹⁹.
- 3. Provide funding for – and encourage companies to invest in - diagnostic tools, including rapid diagnostic tests.** The UK Review on AMR has noted that, due to reliance on empirical diagnosis, viral infections are often misdiagnosed as bacterial infections and vice versa²⁰. More refined tests will enable more precise prescribing, thereby reducing unnecessary use of antibiotics.
- 4. Support more research, including from the disciplines of social science and behavioural psychology, into the various reasons for irrational and unnecessary consumption and prescribing,** which are often culturally, socially and economically determined. The EU should enable research into assessing and comparing behavioural change interventions for antimicrobial prescribing that take into account cultural differences, as well as translational research into how antimicrobials are being used.

2.4 Environmental policy dimension of AMR

Together with partner organisations, EPHA has stressed the importance of addressing the environmental dimension of AMR, in particular environmental pollution and irresponsible waste disposal generated by the suppliers of multinational pharmaceutical companies during the manufacturing process of antibiotics.

¹⁹ EUROCAM (2015, 2nd ed.). *The Role of Complementary and Alternative Medicine in reducing the problem of antimicrobial resistance*, pp. 10-11. Available at: <http://bit.ly/2pZfwxF>

²⁰ Review on Antimicrobial Resistance (2016), op.cit.

Irresponsible manufacturing processes are encouraged by a lack of transparency in global supply chains, which contributes to soaring drug resistance rates worldwide²¹.

The Commission's Evaluation Report notes that activities meant to implement a One Health approach under the first Action Plan were "too sector specific". It recognises that the environmental dimension of the One Health "received less attention in the first Action Plan" (p.41) despite the promise of action 8 (multilateral cooperation) to "initiate cooperation on reduction of the environmental pollution by antimicrobial medicines particularly from production facilities"²². The Evaluation thus recommends that "the scope of environmental action should be expanded" (ibid.).

The release of the long-overdue EU strategy on Pharmaceuticals in the Environment is again absent from the Commission's 2017 Work Programme. Environmental policy is a necessary area for EU legislative action to contain AMR, e.g. by following the example of Directive 2013/39 on priority substances in the field of water policy, which sets minimum standards²³.

It is important to redress the balance since local people and animals, especially those living in unsanitary environments, come into contact with water, soil and plants that have been contaminated due to toxic effluents and API-laden (active pharmaceutical ingredients) discharges arising from the production process of antibiotics. It is a vicious cycle: resistant bacteria in the environment spread to human pathogens, which then arrive in Europe via international travel and trade.

Recommendations

- 1. Ensure transparency of global supply chains, and include mandatory environmental risk assessments** in Good Manufacturing Practice (GMP) rules (as supported by the government of Sweden), to stem the global rise of "superbugs"²⁴.
- 2. Support research into the various transmission dynamics of AMR via the environment** and the establishment of appropriate surveillance mechanisms. Only few projects have been launched in this area over the last decade.

²¹ SumOfUs (2015). *Bad Medicine: How the pharmaceutical industry is contributing to the global rise of antibiotic-resistant superbugs*. Available at: https://s3.amazonaws.com/s3.sumofus.org/images/BAD_MEDICINE_final_report.pdf

²² European Commission (2016) *Evaluation of the Action Plan against the rising threats from antimicrobial resistance*, op.cit. p.11.

²³ Garde, A. (2016), *EU competence to tackle antimicrobial resistance*, p. 15. Available at: <https://epha.org/wp-content/uploads/2016/11/EU-law-and-competence-to-tackle-antimicrobial-resistance-final.pdf>

²⁴ Changing Markets (2016). *Superbugs in the Supply Chain: How pollution from antibiotics factories in India and China is fueling the global rise of drug-resistant infections*. Available at: https://epha.org/wp-content/uploads/2016/10/Superbugsinthesupplychain_CMreport.pdf

- 3. Require Environmental Risk Assessment** as a mandatory part of the marketing authorisation process for antimicrobials, as well as a requirement for public R&D funding.
- 4. Propose a complete ban of antibiotic residues in ground and surface water** in the European Commission's Pharmaceuticals in the Environment strategy.
- 5. Require and support site inspections of pharmaceutical factories** based outside of the European region to be carried out by European medical agencies thoroughly and with greater frequency to ensure that companies comply with GMP rules.

While it is encouraging that the pharmaceutical industry recognises and is addressing the issue, for example as part of the Eco-Pharmaco-Stewardship framework²⁵, it remains to be seen how effective the measures announced in the Davos Declaration²⁶ and in the Industry Roadmap presented at the United Nations General Assembly²⁷ will be, whether they will stimulate more responsible production processes in countries where polluting factories and suppliers are based (e.g. China and India), and whether it will set a precedent for other multinationals to follow suite. The experience in other public health areas (alcohol, tobacco, nutrition, etc.) has shown that industry self-regulation is significantly less effective than governmental action.

Also in this case, the fact that the “main offender” companies singled out in investigative reports of antibiotics pollution in the supply chain are not signatories to the Davos Declaration show that voluntary commitments are insufficient to reverse the current race to the bottom: effective and mandatory regulatory measures are necessary.

2.5 Agriculture Policy

Given the EU's significant competences in the veterinary sector, the agricultural dimension of AMR has been addressed by the first Action Plan through proposals for a new regulatory framework on veterinary medicinal products and medicated feed, as well as the so-called “Animal Health Law”. Among other provisions, the former reinforces data collection on antimicrobials in the veterinary sector, stipulates warnings and guidance for improved product labelling, restricts the use of certain critically important antimicrobials for humans, and introduces incentives for

²⁵ For more information, see <http://www.efpia.eu/documents/164/61/Eco-Pharmaco-Stewardship-EPS-A-holistic-environmental-risk-management-program>

²⁶ *Declaration by the Pharmaceutical, Biotechnology and Diagnostics Industries on Combating Antimicrobial Resistance (Jan 2016)*. Available at:

https://amr-review.org/sites/default/files/Declaration_of_Support_for_Combating_AMR_Jan_2016.pdf

²⁷ IFPMA (2016). *Industry Roadmap for Progress on Combating Antimicrobial Resistance*.

<http://www.ifpma.org/wp-content/uploads/2016/09/Roadmap-for-Progress-on-AMR-FINAL.pdf>

developing new antimicrobials in the veterinary sector. The latter will, *inter alia*, enable EU interventions on animal pathogens that show AMR while also stipulating responsibilities for animal keepers regarding responsible use of veterinary medicines and offering healthy living conditions for their animals.

In spite of these welcome legislative actions, and the changes they may bring in the future, antibiotics are currently still too widely used in farming – amounting to an estimated 70% of all antibiotics used. Overuse in animals has dire consequences for human health in accelerating drug resistance in bacteria and their transmission through food, water and the environment.

As is the case in human medicine, there are significant differences in consumption between European countries in animal health, and surveillance data is incomplete. For example, while the use of antibiotics as growth promoters has been banned in the EU in 2006, routine prophylactic use is still commonplace – e.g. in hatcheries – and such preventative deployment must be phased out entirely²⁸.

Recommendations

- 1.** Ban the routine preventive mass medication of groups of animals with antibiotics via feed or water, regardless of whether treatments occur for prophylactic or metaphylactic reasons, as proposed by the European Parliament's Committee for Environment, Public Health and Food Safety (ENVI) report on the proposed Regulation on Veterinary Medicinal Products.
- 2.** Ban the use of critically important antibiotics for preventative use and group treatments. To preserve the efficacy of colistin, carbapenems, and other last-line antibiotics, these drugs should be reserved for human use.
- 3.** Set binding limits for antimicrobial use in meat and dairy producing animals in order to incentivise proper diagnosis of infection, as well as less intensive husbandry practices.
- 4.** Prohibit veterinarians from selling antibiotics, in order to remove the economic incentive to prescribe antimicrobial therapies to livestock.

2.6 Refining existing Action Plan areas

As acknowledged in the Commission's Evaluation Report, a number of initiatives were only emerging when the 2011-2016 Action Plan was drawn up; hence some elements were underrepresented or missing, and the implementation was sector

²⁸ Alliance to Save Our Antibiotics (2015), *Antimicrobial resistance -why the irresponsible use of antibiotics in agriculture must stop* Available at: <http://www.saveourantibiotics.org/publications/>

specific. Five years later, there is broad agreement that AMR is a complex, global societal challenge that blurs geographic and policy boundaries– it is thus important to ensure that the follow-up Action Plan takes a more holistic stance than its precursor.

Trade

International mobility and trade allow resistant bacteria to transcend geographic space. Resistance that originates in other parts of the world can easily end up in the European food chain, animals (including pets), people and ecosystems. The deepening of globalisation must take AMR into account, and it is important in this context that Europe's international trade agreements are coherent with the EU and WHO Action Plans so that they do not hinder European countries' ability to take further measures at national level.

Recommendations

- 1. Safeguard that international trade agreements between the EU and third countries support the goals of the WHO Global Action Plan and the follow-up EU Action Plan.** For example, transatlantic agreements like TTIP and CETA must consider and promote the work of the Transatlantic Taskforce on AMR (TATFAR), which in turn must take into account the follow-up EU Action Plan²⁹.
- 2. Insist that the European ban on growth promotion in agriculture must be upheld** and adopted in non-European countries as well.
- 3. Use international health diplomacy as a lever** to make sure that the results of high-level negotiations (G20/ G7, UNGA, WHO, etc.) must be taken into account in trade agreements.

It is hoped that the new Joint Action on AMR and HCAI, led by France, will further add value by underlining the importance of public health at the core of the One Health approach and integrating many different stakeholder perspectives, including those of civil society.

Industrial research and policy

The pharmaceutical industry is a strategic actor when it comes to taking action on AMR. The sector has benefited from significant amounts of EU funding.

Recommendations

²⁹ As to why trade agreements like CETA could contribute to AMR, see <https://epha.org/ceta-and-amr/>

- 1. Include an ex-post evaluation of the overall results of public expenditure** for projects coordinated by the Joint Programming Initiative on AMR and IMI in the follow-up EU Action Plan on AMR.
- 2. Develop de-linkage models (price/sales volumes) that work for both patients and for industry.** A new innovation model for medicines is needed, and this becomes even more urgent when it comes to the need to develop new – and conserve the effectiveness of old – antibiotics.
- 3. Work with the pharmaceutical industry and suppliers** to ensure they commit and contribute to the fight against unlicensed / illegal OTC and Internet sales of antibiotics.

2.7 Education and awareness-raising

Population knowledge of prudent antimicrobial use is still lacking despite growing awareness in many countries. The latest Eurobarometer survey revealed that a mere 43% of Europeans are aware that antibiotics do not work against viral infections, and only 56% knew that they are ineffective against cold and flu, that unnecessary use can make them ineffective, and that they can generate side effects³⁰.

Recommendations

- 1. Introduce harmonised quality standards in EU-wide curricula for health professionals in the area of AMR,** which highlights the risks related to inappropriate prescribing, dosage, use, and disposal. The education and training of healthcare professionals and students is essential given that they play an important role in shaping patients' attitudes towards antimicrobials.
- 2. Increase funding to promote the European Antibiotics Awareness Day (EAAD) action throughout the year** on drug-resistant infections, their consequences and how to prevent them from spreading further³¹. This can be done by consistently tying the EAAD to national and international campaigns and educational activities. The ECDC's high quality reports, infographics and factsheets (aimed at health professionals, experts and the general public) also merit wider dissemination.

³⁰ TNS Opinion & Social (2016). Special Eurobarometer, *Antimicrobial Resistance*. Available at: http://ec.europa.eu/dgs/health_food-safety/amr/docs/eb445_amr_generalreport_en.pdf

³¹ ECDC (2016). *European Antibiotic Awareness Day*. Available at: <http://ecdc.europa.eu/en/eaad/Pages/Home.aspx>

- 3. Develop and support educational interventions, following the example of the e-Bug platform³²** so that all members of society can be reached. Shaping behaviour from childhood and throughout adulthood is vital in helping individuals become more aware of the value of antimicrobials as a public good.
- 4. Create harmonised quality standards in EU-wide curricula for health professionals in the area of AMR**, which highlights the risks related to inappropriate prescribing, dosage, use, and disposal. The education and training of healthcare professionals and students is essential given that they play an important role in shaping patients' attitudes towards antimicrobials.
- 5. Support health professionals with positive incentives** to encourage all prescribers to become advocates of prudent use and practise the “as little as possible, as much as necessary” axiom. More national initiatives like the NHS England General Practice Resilience Program and the Danish yellow card system, which are linked to corrective action mechanisms, are needed. The EU should promote and disseminate these via the One Health Network.
- 6. Establish multidisciplinary common antimicrobial stewardship programmes, facilitated by the EU throughout Europe**, both on- and offline to encourage joint ownership of the problem.

³² e-bug. Available at: <http://www.e-bug.eu>

3. Conclusion

“AMR is not a disease for which we should expect ultimately to develop a cure. Instead it is a silent pandemic that is here to stay”³³ - ReAct

A rise in multi-drug resistant ‘superbugs’ poses a serious risk to public health, national healthcare systems and economies worldwide. Efforts to contain AMR prevalence and preserve the effectiveness of antimicrobials are essential and the entire world is looking to Europe as the global best practice region for research and policy for inspiration and direction.

While European governments retain sole competence for the organisation of national healthcare systems, and the Treaties restrict the EU’s role in health policy matters, AMR disrupts the normal order. As a severe and urgent cross-border threat to health, it calls for exceptional and coordinated Europe-wide measures. The EU has a number of soft and hard law tools at its disposal to improve the situation and protect human health, for the benefit of future generations’ health and wealth. Notably, the EU’s legislative powers can be put to good effect in the areas of food safety, consumer protection, agricultural/fishery and environmental policy. A model of enhanced cooperation could be an option to challenge the specific threats to patient safety arising from AMR³⁴.

In addition, a stronger appreciation of what AMR means for public health, including the future sustainability of European health systems and achieving universal health coverage as a declared goal of the SDGs, must be anchored in the next Action Plan. Combating AMR is not only about warding off a particular health threat; it is about all that follows as a consequence. AMR is relevant to almost every target under SDG3: global health risks, universal health coverage, access to safe health services, maternal and child mortality, ending epidemics of communicable diseases, reducing preventable deaths in relation to non-communicable diseases, vaccine coverage, soil and water contamination. A number of NGOs, especially ReAct³⁵, have made a strong case why sustainable international development cannot be achieved without taking on AMR,

Recognising that public health policies and budgets are both a recipient and a driver of AMR, many crucial actions need to be taken outside the sector, but public health actors must be empowered to analyse all pertinent linkages and share their expertise of managing cross-border threats.

³³ ReAct Europe (2016), *Antimicrobial resistance—a threat to the world’s sustainable development*. p. 162. Available at: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4967260/>

³⁴ Garde, A. (2016), op, cit., p. 12

³⁵ ReAct Europe (2016), op.cit.

The European Commission's follow-up Action Plan on AMR must be as ambitious and clear as possible, supported with SMART objectives and ex-ante, mid-term and ex-post impact assessments. It should serve as a blueprint for the development and revision of national action plans designed to overcome specific challenges experienced in countries³⁶. Given the persisting disparities between countries in antibiotic consumption and AMR prevalence, EU support must be stepped up across the board. Through common targets, dedicated resources, as well as policies and governance mechanisms that exploit the EU public health mandate to the fullest, Europe can ensure that successful national practices and policies do not remain isolated cases. There is no reason why what has been achieved in the Netherlands, Sweden, Denmark and other countries cannot be adapted to suit other settings.

The lack of political will and expertise in certain countries, as well as challenges related to resources, structural or cultural issues, must be addressed head-on. Only a pan-European commitment will preserve antimicrobials as a public good: to safeguard the survival of people, animals and the environment, in Europe and globally.

Transparency and open dialogue between all relevant actors, sectors and countries is a prerequisite. In the end, nobody will gain from AMR, and inaction or lack of capacity in one country or region will risk lives everywhere. This is why supranational action and coordination at European level is indispensable.

³⁶ ECDC (2016). Antimicrobial resistance strategies and action plans. Retrieved from http://ecdc.europa.eu/en/healthtopics/Healthcare-associated_infections/guidance-infection-prevention-control/Pages/antimicrobial-resistance-strategies-action-plans.aspx

About EPHA

EPHA is a change agent – Europe's leading NGO advocating for better health. We are a dynamic member-led organisation, made up of public health NGOs, patient groups, health professionals, and disease groups working together to improve health and strengthen the voice of public health in Europe. EPHA is a member of, among others, the Social Platform, the Health and Environment Alliance (HEAL), SDG Watch, the European Medicines Agency PCWP and the Better Regulation Watchdog.

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