

Briefing: Evaluation of the AMR Action Plan 2011-2016

Antimicrobial Resistance

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european public health alliance





Evaluation of the AMR Action Plan 2011-2016

Context

Antimicrobial resistance (AMR) is a severe threat to public health and to the future effectiveness and sustainability of healthcare and health services worldwide. 2016 is a landmark year for global political awareness of the scale and urgency posed by AMR: The AMR Review,¹ commissioned by the UK Prime Minister and published in May, outlined the global impact in terms of loss of life and economic cost to 2050 if no action is taken; at the UN General Assembly in September, Heads of State and Government committed to coordinated action to address the root causes of AMR across human health, animal health and agriculture.²

The European Commission plans to adopt a new Action Plan on Antimicrobial Resistance during the first half of 2017.³ The new Action Plan will set the course for coordinated support to EU Member States and the direction of European policies and programmes to tackle AMR.

In preparation of the new roadmap, the Commission's Health directorate has published an Evaluation⁴ report of the outgoing 2011-2016 Action Plan.⁵ This Briefing summarises EPHA's comments on the Commission's evaluation report and outlines our recommendations for follow up in order to prepare an Action Plan commensurate with the scale, urgency and cost of the AMR challenge in Europe.

We support the overall conclusions of the evaluation. However, in general, the report understates the still-growing threat of AMR and the necessary role for European and intergovernmental institutions (not only EU, European Commission and agencies, but also WHO Europe, OECD, etc.) in tackling it in a coordinated manner. There is plentiful evidence available for the Action Plan to make a stronger case for a more active European policy response.

¹ Review on Antimicrobial Resistance: <https://amr-review.org/home>

² UN General Assembly, [Draft political declaration of the High-Level Meeting](#), 16 September 2016.

³ European Commission, [Roadmap: Commission's Communication on a One-Health Action Plan to support Member States in the fight against Antimicrobial Resistance \(AMR\)](#), 24 October 2016.

⁴ European Commission Staff Working Document, [SWD\(2016\)347 final](#), Evaluation of the Action Plan against the rising threats from antimicrobial resistance, 24 October 2016.

⁵ European Commission, Communication [COM\(2011\)748](#), Action Plan against the rising threats from Antimicrobial Resistance (2011-2016), 15 November 2011.



1. Update the EU figures for the impact and cost of AMR in Europe

The evaluation report and original action plan refer to the estimate of 25,000 avoidable deaths per year in Europe, taken from the ECDC/EMA joint report of 2009.⁶ This figure requires urgent review as it is a drastic underestimate of the real impact of AMR in Europe. The scientific evidence base around AMR has progressed rapidly in recent years. Many national governments, institutions and research programmes (not least EARS-Net⁷) have up-to-date figures which should be drawn together for more accurate EU-wide and wider-Europe estimates.

For example, France alone estimates a death toll of 12,500 people annually from drug-resistant infections.⁸

The ECDC also notes in relation to the 2009 study that “With the increase of AMR noted since these estimates were produced, the numbers are most likely to be considerably higher today.”⁹

The evaluation recognizes that “In 2016, AMR is still a growing global burden” and cites the AMR Review figures that inaction is projected to result in 10 million deaths annually worldwide by 2050, with an associated cost of EUR88trillion to the world economy (p16-17).

An update of the EU figures of the number of people contracting drug-resistant infections is urgently needed, including fatalities, prolonged illnesses, hospitalisations and treatment and the associated costs to health systems and economies across Europe. The current estimate (also from 2009) of EUR1.5billion of healthcare costs and productivity losses resulting from AMR also needs to be updated and is likely to be far higher.

Presenting up-to-date figures to underpin the new Action Plan is of vital importance to ensure that the scale and urgency of the problem is fully understood by policy-makers, health professionals, media and the general public. The evidence base must be accurate so that the policy response will be adequate to begin turning the tide on AMR in every country in Europe.

It is positive that the scope of the evaluation report considers some non-EU countries: Norway, Switzerland, Iceland and Serbia. The conclusions allude to closer cooperation within the WHO European Region, which is to be welcomed. Closer coordination with neighbouring countries should be encouraged and supported by the EU, Commission, Agencies and Member States, as well as other expert institutions including the WHO and OECD.

⁶ ECDC/EMA (2009) [Joint technical report: The bacterial challenge time to react](#), Stockholm.

⁷ <http://ecdc.europa.eu/en/activities/surveillance/EARS-Net/>

⁸ Touraine, M. [Tackling antimicrobial resistance in France](#), *The Lancet*, 1 May 2016.

⁹ ECDC (2015) [Antimicrobial resistance surveillance in Europe 2014](#), Annual report of the European Antimicrobial Surveillance Network (EARS-Net), Stockholm, November 2015. p3.



2. Outline the threat to safe and sustainable provision of healthcare and health services

It is notable that the introductory section of the evaluation report (p4) describes the threat to public health, food safety, food security, animal health and welfare including economic losses in animal production and increase costs in food production, but does not mention the existential threat that AMR poses to the future operation of health services. It misses the vital aspect that failure to act on AMR threatens a return to the “dark ages of medicine”.¹⁰

In particular, with regard to health service costs, there is a need for the next Action Plan period to improve collection of data on the disease-specific and treatment-specific costs of increasing antimicrobial resistance. This applies, for example, to projected impacts for chemotherapy, infectious disease control (including tuberculosis), and healthcare acquired infections. Whilst global figures on AMR impact are becoming more precise, policy-makers, the public and healthcare stakeholders also need to be informed of potential future sectoral impacts.

In preparation for the new Action Plan, it is essential to capture the possible threat to future operation of health services and provision of universal health coverage in Europe and around the world. AMR is specifically mentioned in the outcome statement of the UN Summit of Heads of State and Government which adopted the Sustainable Development Goals (SDGs) in September 2015. World leaders recognized that the progress already made towards the Millennium Development Goals will be undone if AMR is not tackled.¹¹ The new EU AMR Action Plan should be placed in the context of achievement of the SDGs, including the goal to provide universal health coverage, to which all European leaders and the EU have committed.

3. Recognise that AMR prevalence continues to rise, especially multi-drug resistance and resistance to last-line treatments

The evaluation of the Action Plan dodges the question as to whether the EU policy approach so far has been effective in reducing the prevalence and future risk of AMR, despite stating that “the main aim of the Action Plan is to combat increasing threats from AMR by reducing resistant micro-organisms and the number of infections caused by them.” (p6). The evaluation does not reach a clear conclusion as to what progress has been achieved towards this main aim. Whilst the report outlines the state of antimicrobial resistance and microbial infection across Europe up to 2011, citing ECDC surveillance figures, the evaluation of progress 2011-2015 focusses on whether actions were implemented, rather than whether they were actually effective in tackling AMR.

¹⁰ Former UK Prime Minister David Cameron: <https://amr-review.org/>

¹¹ <http://www.reactgroup.org/news/502/126.html>



The evaluation gives scant detail (just 3 paragraphs) of results from ECDC/EARS-Net annual surveillance data of antimicrobial resistance, which should be the core of any evaluation of effectiveness. The report is remarkably brief in the acknowledgement that “the situation is still worrying from gram-negative pathogens and with high and, in many cases, increasing resistance percentages reports from many parts of Europe” and regarding combined resistance “Increasing resistance trends were noted for individual EU/EEA Member States with both low and high resistance percentages.” (p19)

The evaluation concludes that “Available data show that the situation in 2015 is as alarming as it was in 2011” (p32) and that “it was not possible to identify clear trends in the level of AMR for the EU overall during the period 2011-2014 (p19).” However, this is contradicted by the statement that: “The increasing resistance in some antimicrobial groups is, according to the ECDC, an indication of further loss of effective treatment options and a threat to patient safety.” (p19) It is clear that the situation has become *more* alarming during the period of the current Action Plan, the scale and urgency of the threat of AMR has become clearer not least because of the increased availability of evidence.

Much more is known about the scale and urgency of the AMR crisis today than was the case in 2011 - the case for coordinated policy action is stronger than ever. The evaluation report is too brief on ECDC surveillance data and conclusions, so fails to explicitly recognize that the overall situation in Europe is becoming more urgent, and has accelerated during the period of the Action Plan. This is in marked contrast to press statements by two key agencies of the Commission, ECDC and EFSA, who clearly state that AMR is “on the rise in the EU”.¹²

The ECDC’s 2014 report on Antimicrobial resistance surveillance in Europe states:

*“The ongoing increase in antimicrobial resistance to a number of key antimicrobial groups in invasive bacteria isolates reported to EARS-Net is therefore of great concern.”*¹³

In particular, the evaluation of the 2011-2016 Action Plan does not mention the increase in bacteria resistant to last-line antibiotics. Rising resistance to carbapenems was the central message from ECDC on European Antibiotic Awareness Day in 2015. The evaluation also does not mention the emergent threat of resistance to colistin as a last resort treatment for severe human infections with salmonella.¹⁴

4. Analyse important differences in AMR prevalence resulting from different policies in Member States

Best practice identification and sharing should be a clear part and mandate of the next EU AMR Action Plan. The clear north-south and east-west gradients for every type of infection studied by ECDC illustrates the cross-border threat posed by AMR – lack of action in one region could easily and swiftly undermine progress in all others - and urgent need to transfer effective policies and measures across borders.

¹² EFSA press release, [Antimicrobial resistance on the rise in the European Union](#), EFSA and ECDC warn, 11 Feb 2016

¹³ ECDC (2015) [Antimicrobial resistance surveillance in Europe 2014](#), Annual report of the European Antimicrobial Surveillance Network (EARS-Net), Stockholm, November 2015.

¹⁴ <http://ecdc.europa.eu/en/eaad/antibiotics-news/news-release/Pages/news-release.aspx>



The evaluation report acknowledges that “there still exist considerable disparities between antimicrobial consumption and spread of AMR in animals between Member States” (p41) and “there are huge differences between Member States in the governance and scope of national strategies and action plans, and in the way measures are implemented and assessed. As a consequence, there are also huge differences in antimicrobial consumption and resistance in humans between Member States. Therefore, further support of Member States and understanding of the effectiveness of AMR policies is needed to develop effective AMR policies.”(p41-42)

In preparation for the new Action Plan, the ECDC annual surveillance data provides an opportunity to draw further conclusions. It is important to illustrate impressive progress made in some Member States to reduce both antimicrobial consumption and prevalence of AMR thanks to national policies and action plans. The new EU Action Plan is a vital opportunity to assess which policies are most effective, in line with the EU’s stated goal to support Member States and become a best practice region.

In particular, the preparations for the Action Plan should highlight the decreases in antimicrobial consumption in both humans and animals that were targeted and achieved – and associated decreases in drug resistant infections - in the best performing Member States and propose how to ensure that these targets and best practices are transferred to those countries which risk undermining progress across Europe.

5. Examine and compare trends in antimicrobial consumption / prudent use in humans and animals

The evaluation report is also regrettably light on consumption trends in both humans and animals. It does not note the instructive comparisons between Member States and national action plans and policies. The ECDC data (from ESAC-Net¹⁵) is again overlooked. In particular, figure 4 (p21) presents sales data in tonnes of active ingredients of veterinary antimicrobials for food-producing animals, but as the figures refer to gross national consumption without taking account of the size of the national herd, the comparison is not particularly instructive. The report identifies a decrease in sales over the period 2011-2013, but does not discuss contributory factors. (p20)

The evaluation report concludes that “It is still too early to be able to determine the results from the actions put in place to draw firm conclusions on the effectiveness regarding prudent use in human health” (p29) and likewise for use in animals (p30). It would be useful to cite figures from the impact assessments of recently adopted legislation on animal health and veterinary medicines – what is the expected impact of the legislation on reduction of antimicrobial use and therefore of AMR? Will they be sufficient to ensure minimization of the use of antimicrobials in animals to only essential uses? What contribution will they make to heading off increasing resistance, including to colistin?

¹⁵ ECDC, ESAC-Net database: <http://ecdc.europa.eu/en/healthtopics/antimicrobial-resistance-and-consumption/antimicrobial-consumption/esac-net-database/Pages/database.aspx>



6. Quantify industrial causes of AMR: End pollution in the pharmaceutical supply chain

The evaluation report examines the relevance of the 2011-2016 Action Plan, and concludes that all actions are still relevant to tackling the increasing threat of AMR. Yet there is an important cause of AMR which is not addressed by the outgoing Action Plan, which is also overlooked in the evaluation report: industrial causes of AMR in the supply chain for antimicrobial treatments.

The AMR Review's 2015 report *Antimicrobials in Agriculture and the Environment: Reducing Unnecessary Use and Waste* (commissioned by the office of the UK Prime Minister and including Treasury officials and medical experts from the Wellcome Trust) identified pollution in the medicines supply chain as a major cause of the spread of AMR and called on the pharmaceutical industry to take action to tackle it. Poor waste disposal practices, including dumping of active antimicrobial compounds into the local environment near production facilities, especially in India and China, have been shown to be commonplace in the supply chains of both major pharmaceutical brands and generics producers.

As described in our briefing '*Drug resistance through the back door*' together with Changing Markets: "The substantial quantities of antibiotics released from polluting factories, which frequently combine with runoff from farms and human waste in water bodies and sewage treatment plants, provide a perfect breeding ground for drug-resistant bacteria[...] Experts view the promotion of antibiotic resistant bacteria as "by far the greatest human health risk" posed by the presence of pharmaceutical residues in the environment and note that, in addition to fostering the spread of resistant pathogens, antibiotic residues can also turn harmless environmental bacteria into carriers of resistance."¹⁶

The Action Plan evaluation report dedicates just three lines to the environmental spread of AMR caused by contaminated food and water systems. Whilst the report mentions that a strategic approach to pharmaceuticals in the environment is under development by the European Commission (Directive 2013/39/EU) (p23), there is no mention at all of industrial causes of AMR from antimicrobial manufacturing facilities in global supply chains. This cause of AMR has been highlighted in many recent studies, including the AMR Review, and repeatedly raised by stakeholders including EPHA, SumofUs,¹⁷ Changing Markets and Ecostorm,¹⁸ Nordea Asset Management¹⁹ and Healthcare Without Harm²⁰ during consultations.

The industrial pollution aspect and need for internationally coordinated follow up is recognized by parts of the pharmaceutical industry, for example in the Davos Declaration and Industry Roadmap statement released alongside of the UN General Assembly in

¹⁶ EPHA and Changing Markets (2016) [Drug Resistance through the Backdoor: How the Pharmaceutical Industry is fueling the rise of Superbugs through Pollution in its Supply Chains](#)

¹⁷ SumOfUs (2015), *Bad Medicine: How the pharmaceutical industry is contributing to the global rise of antibiotic-resistant superbugs*, June 2015.

¹⁸ Changing Markets and Ecostorm (2016) *Superbugs in the supply chain*, October 2016

¹⁹ E.g. Nordea Asset Management (2016) *Impacts of Pharmaceutical Pollution on Communities and Environment in India*, March 2016.

²⁰ <https://noharm-europe.org/articles/news/europe/european-antibiotic-awareness-day-2015>



September 2016.²¹ In the roadmap, thirteen major companies committed to “Reduce the environmental impact from the production of antibiotics, including a review of the companies’ manufacturing and supply chains, and work with stakeholders to establish a common framework for assessing and managing antibiotic discharge”.

Whilst this is an important recognition of the problem and significant commitment to clean up supply chains, it is however essential to note that some of the worst offender brands and their suppliers identified in the SumOfUs, Changing Markets and Ecostorm reports are not amongst the signatories. This implies that binding measures would be the only way to ensure a coordinated and sufficiently stringent approach that puts a stop to the incentive to cut corners in the supply chain.

The new Action Plan must tackle industrial and environmental causes of AMR, as part of the political commitment to the One Health approach. Action under the new Plan will be essential as there is no reference to the anticipated Pharmaceuticals in the Environment Strategy in the European Commission work programme for 2017, entitled *Delivering a Europe that Protects, Empowers and Defends*.²²

The evaluation report correctly recognizes that “The implementation of the roadmap was, however, too sector specific. When the action plan was adopted, the initiatives regarding the transmission of AMR via the environment were limited. As a consequence, this area received less attention in the Action Plan” (p41) and “the scope of environmental action should be expanded” (p41). A strong focus on the environmental causes - and in particular industrial causes - of AMR must not be overlooked if the new Action Plan is to be credible and effective.

7. Evaluate the added value and highest impact of EU funds

The evaluation report notes that the 2011-2016 Action Plan was not supported by any EU funding. As part of the Action Plan preparation and with a view to the future EU Multi-annual Financial Framework, an overview of all EU funds allocated and still available to tackle AMR would be instructive. How can public funds be used most effectively in future?

To date, over EUR1billion of public funds has been made available for R&D projects under the AMR Joint Programming Initiative (JPI-AMR).²³ As yet, the overall results of this huge public investment have not been collectively evaluated. It would be essential to know, for example, how many new antimicrobial types and diagnostic tools are in the development pipeline as a result of the EU funding contribution and how close are they to being authorized for use? How much of this development was made possible by EU funding that would not have otherwise taken place?

The work on the forthcoming action plan should also evaluate the effectiveness of and future need for EU funding into effective alternatives to antimicrobials, in fields outside conventional pharmaceutical and medical technology research and development.

²¹ IFPMA: [Davos Declaration](#) and [Industry Roadmap to combat AMR](#), 2016

²² European Commission Work Programme 2017 : Delivering a Europe that protects, empowers and defends http://ec.europa.eu/atwork/key-documents/index_en.htm

²³ European Commission, Press release, 28/10/2016 http://europa.eu/rapid/press-release_IP-16-3567_en.htm



In stark contrast to the vast funding support for drug development there were no supporting funds for implementation of the Action Plan. The annual budget for the ECDC's ARHAI (AMR and Healthcare-associated infections) programme is under EUR1.5million and yet is intended to cover surveillance, analysis, risk identification and support to Member States. Could EU funds be more usefully directed towards improving understanding of evidence-based best practices into how countries can reliably advance in achieving more prudent use of antimicrobials in the health sector? Some resources from Structural Funds have recently been made available to Portugal to increase laboratory capacity, but these opportunities are under-used in relation to the urgency of the problem and lack of infrastructure and capacity to stop the spread of AMR.

The preparations for the Action Plan should consider how the EU can best support national governments to use EU funds including structural and regional development funds in the fight against AMR.

Conclusions – Make a stronger case for EU AMR action

The urgency and scale of the AMR threat in Europe are systematically understated in the Commission's evaluation and background report. Nevertheless, the broad thrust of the conclusions are valid. In light of the above points, the following conclusions of the report (and that of the background report undertaken by RAND) are extremely relevant and should be the main focus of preparations for the Action Plan and future European action:

“the AMR problem is persisting and continued action is needed to combat it.”(p28)

“antimicrobial resistance is a public health concern which cannot be handled by Member States if they work in isolation. This calls for coordinated national responses. Furthermore, the scale and scope of the problem, covering both human medicine and animal health, with environmental as well as macro-economic implications, requires a critical mass of countries cooperation at EU and global level and effective monitoring instruments to facilitate evidence-based policy-making. Coordinated EU action against AMR is therefore justified.”(p28)

“the EU should build on progress already made and continue to play an active role in the area of AMR. The contractor recommends that additional coordinated support should be provided to Member States to encourage and support them in the development and implementation of national action plans and to encourage regional collaboration. Furthermore, it is recommended that the monitoring of AME is taking a more holistic approach, linking data on resistance to and usage of antimicrobials to prescribing trends and



other factors: better tracking AMR-related costs and benefits; considering the use of targets and related indicators, including, as appropriate country-specific targets and indicators; and continuing to monitor public awareness.” (p40-41)

“the scope of environmental action should be expanded and the EU should also continue international cooperation in particular with the WHO to determine potential for a global approach and to improve the monitoring and surveillance across the European region.” (p41)

Whilst we contest that progress has been sufficient as evidenced by the increasing threat of AMR and insufficient actions taken at national level, there has indeed been notable progress in the areas of governance, monitoring and surveillance from the European level since 2009. As outlined above, the new Action Plan will need to additionally include the industrial cause of AMR from environmental pollution, to ensure that all aspects are considered under a One Health approach.

The question as to whether EU action so far has been ‘appropriate’ merits further reflection. The evaluation report looked at this from the perspective of whether actions taken have been in line with the Action Plan. A better question is: Were the actions taken sufficient to reverse the trend of accelerating AMR? To which the answer is clearly No, according to the EU’s own evidence base as presented in ECDC reports. It is essential that Member States and EU institutions recognize this and that the Commission steps up to play a much stronger role – commensurate with the scale and urgency of the AMR challenge - from 2017.

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), and the Better Regulation Watchdog.

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