

Council of the European Union

> Brussels, 27 April 2023 (OR. en)

Interinstitutional File: 2023/0125(NLE) 8417/23 ADD 2

SAN 216 PHARM 62 VETER 47 ENV 427 PHYTOSAN 21 RECH 149

## **COVER NOTE**

From:	Secretary-General of the European Commission, signed by Ms Martine DEPREZ, Director
То:	Ms Thérèse BLANCHET, Secretary-General of the Council of the European Union
No. Cion doc.:	SWD(2023) 191 final
Subject:	COMMISSION STAFF WORKING DOCUMENT Accompanying the document Proposal for a COUNCIL RECOMMENDATION on stepping up EU actions to combat antimicrobial resistance in a One Health approach

Delegations will find attached document SWD(2023) 191 final.

Encl.: SWD(2023) 191 final

LIFE 5



EUROPEAN COMMISSION

> Brussels, 26.4.2023 SWD(2023) 190 final

# COMMISSION STAFF WORKING DOCUMENT

Accompanying the document

# Proposal for a COUNCIL RECOMMENDATION

on stepping up EU actions to combat antimicrobial resistance in a One Health approach

{COM(2023) 191 final}

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## Glossary

Term or acronym	Meaning or definition
AMC	Antimicrobial consumption
AMR	Antimicrobial resistance
BTSF	Better Training for Safer Food
САР	Common Agricultural Policy
ECDC	European Centre for Disease Prevention and Control
ECRAID	European Clinical Research Alliance on Infectious Diseases
EEA	European Economic Area
EMA	European Medicines Agency
ESAC-Net	European Antimicrobial Resistance Surveillance Network
ESVAC	European Surveillance of Veterinary Antimicrobial Consumption
EU	European Union
EU-JAMRAI	Joint Action on Antimicrobial Resistance and Healthcare-Associated Infections
ЕХРН	Expert Panel on effective ways of investing in health
FAO	The Food and Agriculture Organization
H2020	EU's Research Funding Programme Horizon 2020
HERA	The Commission's Health Emergency preparedness and Response Authority

ICMs	Intersectoral Coordination Mechanisms
IMI	Innovative Medicines Initiative
NAPs	National Action Plans
ND4BB Programme	New Drugs 4 Bad Bugs Programme
OH EJP	The One Health European Joint Programme
OIE/ WOAH (new name replacing OIE)	World Organisation for Animal Health
РАНО	Pan American Health Organization
R&D	Research and Development
R&D&I	Research, Development and Innovation
TAFTAR	Transatlantic Taskforce on AMR
ТВ	Tuberculosis
UN	United Nations
UNEP	United Nations Environment Programme
WHO	World Health Organization

## 1. INTRODUCTION

The purpose of this staff working document is to provide evidence in support of the proposal for a *Council Recommendation on stepping up EU actions to combat antimicrobial resistance in a One Health approach*. The proposed Recommendation aims at strengthening and complementing the 2017 European One Health Action Plan against Antimicrobial Resistance<sup>1</sup> (AMR) (hereafter referred to as '2017 AMR Action Plan') by setting concrete objectives and activities to support the Commission's and the Member States' actions against AMR. It thus aims at complementing and extending the actions implemented at European Union (EU) level, maximising synergies to attain a strong and effective response against AMR across the EU.

AMR means the ability of a micro-organism to survive or to grow in the presence of a concentration of an antimicrobial agent which is usually sufficient to inhibit or kill that micro-organism. AMR is leading to infections being difficult or even impossible to treat and is increasingly threatening, i.a. the ability to perform surgery, the treatment of immunocompromised patients and organ transplantation, and constitutes a threat for cancer therapy. AMR is a One Health<sup>2</sup>, cross-border and cross-cutting issue, and is described as a "slow tsunami" by the World Health Organization (WHO)<sup>3</sup> - a slowly developing but potentially devastating global pandemic. AMR is a growing global burden and it marks a grave societal and economic challenge with cost of inaction projected to result in 10 million deaths globally each year and costs up to 100 trillion USD to the world economy by 2050<sup>4</sup>. In the EU, AMR is estimated to be responsible for over 35,000 deaths per year<sup>5</sup> and annually costs about 1.1 billion euros to the health care systems of EU/ European Economic Area (EEA) countries<sup>6</sup>.

Already in 2001, the EU identified the importance of tackling AMR with the adoption of the 2001 Community strategy against AMR<sup>7</sup>. As from 2006, in the EU, antibiotics are not allowed as additives in animal feed (Regulation (EC) No 1831/2003)<sup>8</sup>. The EU AMR policy was reinforced by the 2011-2016 Commission Action Plan<sup>9</sup> meant to foster action among Member States. Following the evaluation of the action plan<sup>10</sup>, the Commission adopted the 2017 AMR Action Plan, as requested in 2016 by the EU Member States<sup>11</sup>. The 2017 AMR

<sup>6</sup> Antimicrobial Resistance: Tackling the Burden in the European Union, Briefing note

for EU/EEA countries, OECD 2019

<sup>&</sup>lt;sup>1</sup> <u>A European One Health Action Plan against Antimicrobial Resistance (AMR)</u>

<sup>&</sup>lt;sup>2</sup> <u>"One Health"</u> is an integrated, unifying approach that aims to sustainably balance and optimize the health of people, animals, and ecosystems. It recognizes the health of humans, domestic and wild animals, plants, and the wider environment (including ecosystems) are closely linked and interdependent.

<sup>&</sup>lt;sup>3</sup> <u>WHO Director-General opening remarks at the AMR Action Fund Launch</u>

<sup>&</sup>lt;sup>4</sup> For the period 2014-2050 - see <u>Antimicrobial Resistance: Tackling a crisis for the health and wealth of nations</u>, The Review on Antimicrobial Resistance Chaired by Jim O'Neill. December 2014

<sup>&</sup>lt;sup>5</sup> <u>Assessing the health burden of infections with antibiotic-resistant bacteria in the EU/EEA, 2016-2020</u>

<sup>&</sup>lt;sup>7</sup><u>Communication from the Commission on a Community Strategy against antimicrobial resistance</u>

<sup>&</sup>lt;sup>8</sup> <u>Regulation (EC) No 1831/2003 of the European Parliament and of the Council of 22 September 2003 on</u> additives for use in animal nutrition (OJ L 268, 18.10.2003, p. 29–43).

<sup>&</sup>lt;sup>9</sup> <u>Communication from the Commission to the European parliament and the Council Action plan against the rising threats from Antimicrobial Resistance COM/2011/748</u>

<sup>&</sup>lt;sup>10</sup> <u>Commission Staff Working Document on the evaluation of the Action Plan against the rising threats from</u> antimicrobial resistance (2016) 347 final

<sup>&</sup>lt;sup>11</sup> Council conclusions on the next steps under a One Health approach to combat antimicrobial resistance

Action Plan is structured around three overarching pillars and fifteen specific objectives<sup>12</sup> and is motivated by the need for the EU to play a leading role in the fight against AMR and to add value to Member States' actions. It provides a framework for continued, more extensive action to reduce the emergence and spread of AMR. Its overarching goal is to preserve the possibility of effective treatment of infections in humans and animals, by ensuring the development and access to effective antimicrobials inside and outside the EU.

The three pillars on which the 2017 AMR Action Plan is built are:

- 1. **Making the EU a best practice region** in terms of better evidence, coordination, surveillance and control measures;
- 2. **Boosting research, development and innovation** by closing current knowledge **gaps**, providing novel solutions and tools to prevent and treat infectious diseases and improving diagnosis in order to control the spread of AMR;
- 3. Intensifying EU efforts worldwide to **shape the global agenda on AMR** and address the related risks in an increasingly interconnected world.

Under each of these three pillars, concrete activities relating to the specific objectives were set. Progress reports on the 2017 AMR Action Plan are published regularly; the latest progress report was published in March 2022<sup>13</sup>.

Since the adoption of the 2017 AMR Action Plan, important policy actions have contributed to further strengthen the EU's response to AMR, such as:

- the adoption of the Strategic Approach to Pharmaceuticals in the Environment<sup>14</sup>;
- the adoption of the Farm-to-Fork Strategy<sup>15</sup>, the Biodiversity Strategy<sup>16</sup> and the Zero Pollution Action Plan<sup>17</sup>, which all include a target to reduce overall EU sales of antimicrobials for farmed animals and in aquaculture by 50% by 2030;

<sup>&</sup>lt;sup>12</sup> (1) Better evidence and awareness of the challenges of AMR, (2) Better coordination and implementation of EU rules to tackle AMR, (3) Better prevention and control of AMR, (4) Better addressing the role of the environment, (5) A stronger partnership against AMR and better availability of antimicrobials, (6) Improve knowledge on detection, effective infection control and surveillance, (7) Develop new therapeutics and alternatives, (8) Develop new preventive vaccines, (9) Develop novel diagnostics, (10) Develop new economic models and incentives, (11) Close knowledge gaps on AMR in the environment and on how to prevent transmission, (12) A stronger EU global presence, (13) Stronger bilateral partnerships for stronger cooperation, (14) Cooperating with developing countries, (15) Developing a global research agenda.

<sup>&</sup>lt;sup>13</sup> Progress reports on the 2017 AMR Action Plan

<sup>&</sup>lt;sup>14</sup> <u>Communication from the Commission to the European Parliament, the Council and the European Economic</u> and Social Committee - European Union Strategic Approach to Pharmaceuticals in the Environment – <u>COM</u> (2019) 128 final

<sup>&</sup>lt;sup>15</sup> <u>Communication from the Commission to the European Parliament, the Council, the European Economic and</u> Social Committee and the Committee of the Regions - A Farm to Fork Strategy for a fair, healthy and environmentally-friendly food system - COM 2020 (381 final)

<sup>&</sup>lt;sup>16</sup> Communication from the Commission to the European Parliament, the Council, the European Economic and Social Committee and the Committee of the Regions – EU Biodiversity Strategy for 2030 – COM 2020 (380) final

<sup>&</sup>lt;sup>17</sup> Communication from the Commission to the European Parliament, the Council, the European Economic and Social Committee and the Committee of the Regions - EU Action Plan: 'Towards Zero Pollution for Air, Water and Soil' – COM 2021(400)final

- the adoption and implementation of the Regulation on Veterinary Medicinal Products<sup>18</sup>, the Regulation on Medicated Feed<sup>19</sup>, and relating tertiary legislation<sup>20</sup>;
- the EU4Health programme<sup>21</sup>;
- the Horizon Europe programme<sup>22</sup>;
- the reinforcement of the EU health security framework, notably through the adoption of the Regulation on serious cross-border threats to health<sup>23</sup> and the reinforced mandates of the European Centre for Disease Prevention and Control (ECDC)<sup>24</sup> and the European Medicines Agency (EMA)<sup>25</sup>;
- the new Commission Implementing Decision on the monitoring and reporting of AMR in zoonotic and commensal bacteria<sup>26</sup>;
- the building of the European Health Union<sup>27</sup>;
- the creation of the Health Emergency Response Authority (HERA)<sup>28</sup>;
- the adoption of the Pharmaceutical Strategy for Europe<sup>29</sup>;
- the adoption of the EU Global Health Strategy<sup>30</sup>.

<sup>&</sup>lt;sup>18</sup> <u>Regulation (EU)</u> 2019/6 of the European Parliament and of the Council of 11 December 2018 on veterinary medicinal products and repealing Directive 2001/82/EC (OJ L 4, 7.1.2019, p. 43–167)

<sup>&</sup>lt;sup>19</sup> <u>Regulation (EU)</u> 2019/4 of the European Parliament and of the Council of 11 December 2018 on the manufacture, placing on the market and use of medicated feed, amending Regulation (EC) No 183/2005 of the European Parliament and of the Council and repealing Council Directive 90/167/EEC (OJ L 4, 7.1.2019, p. 1–23).

<sup>&</sup>lt;sup>20</sup> Implementation of Regulation (EU) 2019/6 on veterinary medicinal products and Regulation (EU) 2019/4 on medicated feed

<sup>&</sup>lt;sup>21</sup><u>Regulation (EU)</u> 2021/522 of the European parliament and of the Council of 24 March 2021 establishing a Programme for the Union's actions in the field of health ('EU4Health Programme') for the period 2021-2027, and repealing Regulation (EU) No282/2014 (OJ L 107, 26.3.2021, p.1).

<sup>&</sup>lt;sup>22</sup><u>Regulation (EU) 2021/695 of the European Parliament and of the Council of 28 April 2021 establishing</u> Horizon Europe – the Framework Programme for Research and Innovation, laying down its rules for participation and dissemination, and repealing Regulations (EU) No 1290/2013 and (EU) No 1291/2013 (OJ L 170, 12.5.2021, p. 1–68)

<sup>&</sup>lt;sup>23</sup> <u>Regulation (EU)</u> 2022/2371 of the European Parliament and of the Council of 23 November 2022 on serious cross-border threats to health and repealing Decision No 1082/2013/EU

<sup>&</sup>lt;sup>24</sup> Regulation (EU) 2022/2370 of the European Parliament and of the Council of 23 November 2022 amending Regulation (EC) No 851/2004 establishing a European centre for disease prevention and control

<sup>&</sup>lt;sup>25</sup> <u>Regulation (EU)</u> 2022/123 of the European Parliament and of the Council of 25 January 2022 on a reinforced role for the European Medicines Agency in crisis preparedness and management for medicinal products and medical devices

<sup>&</sup>lt;sup>26</sup> <u>Commission Implementing Decision (EU)</u> 2020/1729 of 17 November 2020 on the monitoring and reporting of antimicrobial resistance in zoonotic and commensal bacteria and repealing Implementing Decision 2013/652/EU (OJ L 387, 19.11.2020, p. 8–21)

<sup>&</sup>lt;sup>27</sup> <u>Communication from the Communication to the European Parliament, the Council, the European Economic</u> and Social Committee and the Committee of the Regions - Building a European Health Union: Reinforcing the EU's resilience for cross-border health threats - COM(2020) 724 final

<sup>&</sup>lt;sup>28</sup> Commission Decision of 16 September 2021 establishing a Health Emergency Preparedness and Response Authority - C(2021) 6712 final

<sup>&</sup>lt;sup>29</sup> <u>Communication from the Commission to the European Parliament, the Council, the European Economic and Social Committee and the Committee of the Regions - Pharmaceutical Strategy for Europe - COM/2020/761 final</u>

<sup>&</sup>lt;sup>30</sup> EU Global Health Strategy: Better Health for All in a Changing World

Member States have also put in place new policy initiatives that could help to boost the fight against AMR in the EU, notably those policy initiatives brought about by COVID-19 (e.g., joint procurement and diagnostics). In the meantime, progress in research, innovation and technology is expected to positively influence the fight against AMR, for example the phage therapy<sup>31</sup> clinical trials. Behavioural and societal changes are also shaping a new context for AMR as shown by the 2022 Special Eurobarometer on AMR<sup>32</sup>. Although some progress has been achieved since the last Eurobarometer in 2018<sup>33</sup>, reducing the misuse of antimicrobials remains a challenge.

In light of these developments, there was a need to assess the progress in the implementation and outcomes of the 2017 AMR Action Plan, to review its relevance and coherence against the new challenges and opportunities brought by recent and potential future developments and to prioritize the most impactful activities in order to reach concrete outcomes reducing the development and spread of AMR.

### 2. METHODOLOGY

To achieve a solid base for the proposed Council Recommendation, the Commission launched a *study on a future-proofing analysis of the EU AMR Action Plan<sup>34</sup>*. The aim of this study was to assess the outcomes of the 2017 AMR Action Plan to date and to identify priorities to inform improvements for the future. In particular, the study identified recent and potential future scientific, technological, environmental, agricultural and societal developments influencing AMR and analysed the relevance of the 2017 AMR Action Plan, the study considered the fifteen specific objectives under the three pillars and assessed to which extent the activities have been effective in reaching the objectives. For several specific objectives, gaps have been identified between the implemented actions and the Action Plan objectives. This is outlined in section 3 of this staff working document "Achievements of the 2017 AMR Action Plan and Gaps". In its section 4, the impacts of current and future developments on AMR as well as how EU action can be strengthened are considered. Finally, section 5 outlines the recommendations on how the identified gaps and challenges can be addressed.

The study used a mixed methodology involving (1) a document review complemented by an in-depth review of 28 selected activities within the 2017 AMR Action Plan; (2) the development of future scenarios; and (3) consultations with stakeholders through a call for evidence, interviews, a targeted survey and a future scenarios workshop. A synopsis report, summarizing the results of the stakeholder consultations, is provided in Annex 8 of the study on a future-proofing analysis of the 2017 AMR action plan. The documents reviewed captured information on how factors relating to AMR may develop over the next 10 years within thematic areas (science and technology, society, human health, animal health and agriculture, and the environment). A public call for evidence on a "recommendation for

<sup>&</sup>lt;sup>31</sup> A bacteriophage (or phage) is a virus that infects bacteria. The phage therapy uses bacterial viruses (phages) to treat bacterial infections.

<sup>&</sup>lt;sup>32</sup> Eurobarometer 2022, Antimicrobial Resistance.

<sup>&</sup>lt;sup>33</sup> Special Eurobarometer 478: Antimicrobial Resistance (in the EU)

<sup>&</sup>lt;sup>34</sup> <u>European Commission, Directorate-General for Health and Food Safety, Study on a future-proofing analysis</u> of the 2017 AMR action plan : final report, Publications Office of the European Union, 2023 <u>https://data.europa.eu/doi/10.2875/636347</u>

greater action on antimicrobial resistance"<sup>35</sup> was launched on 24 February 2022, which received 161 qualitative feedbacks and 28 relevant documents in 4 weeks. Apart from the document reviews and the call for evidence, the study work consisted of a targeted survey which received 149 responses, 40 targeted interviews, a future scenario workshops with 28 multisectoral stakeholders, in-depth activity review and triangulation of evidence and analysis.

Beyond the future-proofing analysis study, the Commission also took into consideration the following published reports and initiatives launched to prevent and tackle development of AMR:

- The *subgroup of the AMR One Health Network*<sup>36</sup> composed of Member States representatives was tasked to provide technical expertise and opinions on concrete objectives and activities to strengthen EU and Member States' action against AMR. They considered, in particular, the One Health approach covering the area of public health, animal health, plant health and the environment, taking into account the latest policy developments.
- The Commission performed a *review of the Member States existing National Action Plans*<sup>37</sup> (NAPs). The review was a systematic check to ascertain the extent to which Member States have developed NAPs, including how the One Health dimension and governance mechanisms are reflected therein as well as policy objectives per area.
- The *Expert Panel on effective ways of investing in health* (EXPH)<sup>38</sup> was requested to provide a policy-oriented opinion with analysis and recommendations on the One Health dimension of AMR, the impact of new technologies, existing AMR policies and concrete strategies to tackle AMR in the future.
- The latest *EU-JAMRAI report*<sup>39</sup> and the *case study report on AMR*<sup>40</sup> from the evaluation study<sup>41</sup> of the European Framework Programmes for Research and Innovation were also reviewed.
- The Commission launched a *Eurobarometer on AMR*<sup>42</sup>. It comprised a series of surveys among the general public to monitor their levels of knowledge and usage of

<sup>38</sup> Expert Panel on Effective Ways of Investing in Health, Managing antimicrobial

resistance across the health system, 26 October 2022

<sup>&</sup>lt;sup>35</sup> <u>Antimicrobial resistance – recommendation for greater action</u>

<sup>&</sup>lt;sup>36</sup> <u>Final report - Subgroup established under the EU AMR One Health Network to formulate suggestions for AMR Actions</u>

<sup>&</sup>lt;sup>37</sup> Overview report on the review of Member States' One Health National Action Plans against Antimicrobial <u>Resistance</u>. Globally, countries committed to the framework set out in the Global Action Plan (GAP) 2015 on AMR during the 2015 World Health Assembly and committed to the development and implementation of multisectoral national action plans. To ensure global progress, countries need to ensure costing and implementation of national action plans across sectors to ensure sustainable progress.

<sup>&</sup>lt;sup>39</sup> European Joint Action on Antimicrobial Resistance and Healthcare-Associated Infections (EU-JAMRAI), LAYMAN REPORT

<sup>&</sup>lt;sup>40</sup> This case study analysed a portfolio of 188 AMR actions funded under H2020. These actions were directly related to AMR R&D and were a part of a larger portfolio of projects that addressed infectious diseases and that directly and indirectly will also contribute to advancements in AMR R&D.

<sup>&</sup>lt;sup>41</sup> [Publication forthcoming]

<sup>&</sup>lt;sup>42</sup> <u>Eurobarometer 2022, Antimicrobial Resistance.</u> This survey was carried out by the Kantar Public Brussels network in the 27 EU Member States between 21 February and 21 March 2022. In total, 26,511 respondents from different social and demographic groups were interviewed face-to-face at home in their mother tongue.

antibiotics. The 2022 survey represents the fourth in the series of surveys and tracks progress on public use of and knowledge about antibiotics.

On the basis of the results of the future-proofing analysis study and the review of the abovementioned reports, a review of the achievements and remaining gaps of the 2017 AMR Action Plan is presented below. Factors that influence how AMR may develop in the future are also considered to inform recommendations on how actions can be strengthened.

## 3. ACHIEVEMENTS OF THE 2017 AMR ACTION PLAN AND GAPS

The following sections outline the implementation and outcomes of key activities of the 2017 AMR Action Plan. Gaps between implemented activities and the objectives are also reported as identified notably by the study on the future- proofing analysis of the EU AMR Action Plan.

### **3.1 Pillar 1: Making the EU a best practice area**

#### Achievements

To achieve the specific objective 1.1 of **better evidence and awareness of the challenges of AMR**, different actions took place to strengthen One Health surveillance and reporting of AMR and antimicrobial use, benefit from the best evidence-based analysis and data, and increase awareness and understanding of AMR, including:

- the adoption of a new EU implementing decision on monitoring and reporting of AMR in zoonotic and commensal bacteria and on the communicable diseases and related special health issues to be covered by epidemiological surveillance as well as relevant case definitions<sup>43</sup>;
- the adoption of outcome indicators for the surveillance of AMR and antimicrobial consumption in humans and food-producing animals<sup>44</sup>; and
- the support to Member States in their awareness-raising efforts through the annual European Antibiotic Awareness Day<sup>45</sup> and the outputs produced by ECDC, including the ECDC annual updates on AMR and antibiotic consumption surveillance from EU/EEA countries<sup>46</sup>.

Moreover, the Commission has made proposals for the harmonised monitoring of AMR in the environment. The Commission proposal for a recast of the Urban Waste Water Treatment Directive<sup>47</sup> includes the requirement to establish the mandatory surveillance of AMR, at least twice a year, at the inlets and outlets of urban wastewater treatment plants for agglomerations of 100 000 population equivalent and above and, when relevant, in the collecting systems. To that end, the Commission is empowered to adopt an implementing act to establish a harmonised methodology for measuring AMR in urban wastewaters. In the Commission

<sup>&</sup>lt;sup>43</sup> <u>Commission implementing Decision (EU) 2018/945</u> of 22 June 2018 on the communicable diseases and related special health issues to be covered by epidemiological surveillance as well as relevant case definitions

<sup>&</sup>lt;sup>44</sup> <u>ECDC</u>, EFSA and EMA Joint Scientific Opinion on a list of outcome indicators as regards surveillance of antimicrobial resistance and antimicrobial consumption in humans and food-producing animals

<sup>&</sup>lt;sup>45</sup> European Antibiotic Awareness Day (EAAD) 2022

<sup>&</sup>lt;sup>46</sup> European Centre for Disease Prevention and Control, Annual surveillance reports on antimicrobial resistance.

<sup>&</sup>lt;sup>47</sup> Proposal for a revised Urban Wastewater Treatment Directive – COM(2022) 541 final

proposal reviewing the water legislation<sup>48</sup>, microorganisms, genes or genetic material reflecting the presence of microorganisms resistant to antimicrobial agents, in particular microorganisms pathogenic to humans or livestock, have been included in the indicative list of main pollutants<sup>49</sup>. Moreover, the Commission intends to include AMR genes in the next watch list under the Environmental Quality Standards Directive<sup>50</sup>, after the Directive's proposed revision. The Commission proposal reviewing the water legislation also includes a number of antimicrobial substances in the priority substances list under the Water Framework Directive and sets quality standards for those substances both in groundwater and surface water.

To achieve a **better coordination and implementation of EU rules to tackle AMR** (specific objective 1.2) several initiatives were put in place. In particular, the EU launched a joint action to tackle AMR and healthcare-associated infections (EU-JAMRAI)<sup>51</sup>, co-funded by the Third EU Health Programme<sup>52</sup>, to support collaborative activities and policy development by Member States. The EU-JAMRAI conducted a wide range of activities, e.g., producing work packages on the implementation of One Health national strategies and NAPs for AMR, on infection prevention and control and antimicrobial stewardship, contributing to better coordination, better knowledge and increased sharing of information. Additionally, the EU supported the implementation of national One Health action plans through joint Commission/ ECDC visits to Member States upon their request.

To reach the specific objective 1.3 of **better prevention and control of AMR**, the WHO and ECDC have carried out annual infection prevention and control trainings from 2018-2021. In 2018, 2019 and 2020, the training was attended by senior healthcare professionals from 13 countries in the WHO European region. The workshops focussed on a different aspect of infection prevention and control support each year, starting with the infection prevention and control core concepts, and moving on to their implementation and the development of action plans at national level. Regarding better prevention, Member States used the 2015 EU guidelines for the prudent use of antimicrobials for veterinary medicine<sup>53</sup> to inform the understanding of best practices and develop guidelines at national level; the Commission monitored Member States' efforts to encourage this prudent use<sup>54</sup>. Similarly, Member States used the 2017 EU guidelines for the prudent use of antimicrobials in human health<sup>55</sup> to

<sup>&</sup>lt;sup>48</sup> <u>Proposal for a Directive amending the Water Framework Directive, the Groundwater Directive and the</u> <u>Environmental Quality Standards Directive</u>

<sup>&</sup>lt;sup>49</sup> <u>Annex VIII to Directive 2000/60/EC of the European Parliament and of the Council of 23 October 2000</u> establishing a framework for Community action in the field of water policy

<sup>&</sup>lt;sup>50</sup> Directive 2008/105/EC of the European Parliament and of the Council of 16 December 2008 on environmental quality standards in the field of water policy, amending and subsequently repealing Council Directives 82/176/EEC, 83/513/EEC, 84/156/EEC, 84/491/EEC, 86/280/EEC and amending Directive 2000/60/EC of the European Parliament and of the Council

<sup>&</sup>lt;sup>51</sup> The Joint Action 'EU-JAMRAI' was launched in 2017, bringing together 44 participating partners (National Competent Authorities, National Institutes of public health, National veterinary Institutes and universities) and over 45 stakeholders across Member States (in the form of a Stakeholder Forum), including representatives from international organisations, industry, healthcare professional associations and patient associations.

<sup>&</sup>lt;sup>52</sup> EU Health Programme

<sup>&</sup>lt;sup>53</sup> <u>Guidelines for the prudent use of antimicrobials in veterinary medicine. (2015/C 299/04)</u>

<sup>&</sup>lt;sup>54</sup> Overview Report - Measures to tackle Antimicrobial Resistance through the Prudent Use of Antimicrobials in <u>Animals</u>

<sup>&</sup>lt;sup>55</sup> <u>EU</u> Guidelines for the prudent use of antimicrobials in human health (2017/C 212/01)

develop AMR NAPs and implement measures to promote the prudent use of antimicrobials in humans. In addition, Regulation (EU) 2019/6 on Veterinary Medicinal Products<sup>56</sup> and Regulation 2019/4 on Medicated Feed<sup>57</sup> provide since 2022 a stronger mechanism for promoting prudent and responsible use of antimicrobials in all animal species, including companion animals, by means of concrete legal obligations. In line with the requirements of Regulation (EU) 2019/6 on Veterinary Medicinal Products, Member States have to collect relevant and comparable data on the volume of sales and on the use of antimicrobial medicinal products used in animals. Furthermore, Regulation (EU) 2022/2371 on serious cross-border threats to health covers AMR which is defined as one of the serious cross-border threats to reinforce collection of comparable and compatible data and information on AMR and antimicrobial consumption (AMC), in particular through the designation of one or more EU reference laboratories specifically on AMR and the adoption of tertiary legislation focusing on AMR and AMC.

To better address the role of the environment (specific objective 1.4), the Commission identified actions in the 2019 EU Strategic Approach on Pharmaceuticals in the Environment<sup>58</sup> to be taken or further investigated at EU and/or Member State level to address the risks from and contribution of pharmaceutical residues in the environment to AMR. The Strategic Approach also aims to encourage action in third countries where pharmaceutical emissions from manufacturing and other sources are suspected of contributing to the global spread of AMR. There has been some international cooperation on this matter through WHO and United Nations (UN) work, and especially through the Strategic Approach to International Chemicals Management<sup>59</sup>. This has provided frameworks for cooperation and action in third countries. The Strategic Approach also seeks to facilitate the exchange of best practices on the environmentally safe disposal of medicinal products and clinical waste, and the collection of pharmaceutical residues. For this, an ad-hoc working group was established under the Pharmaceutical committee to focus on the above actions of the EU Strategic Approach on Pharmaceuticals in the Environment. Further progress has been made through the publication of EFSA's scientific opinion on the role played by the environment in the emergence and spread of AMR through the food chain<sup>60</sup>.

As described in the 2022 Progress Report on the EU AMR Action Plan<sup>61</sup>, four concrete activities have been undertaken to achieve a **stronger partnership against AMR and better availability of antimicrobials** (specific objective 1.5): (1) The EU has supported work with stakeholders to ensure the availability of human and veterinary antimicrobials and continued

<sup>&</sup>lt;sup>56</sup> <u>Regulation (EU)</u> 2019/6 of the European Parliament and of the Council of 11 December 2018 on veterinary medicinal products and repealing Directive 2001/82/EC (OJ L 4, 7.1.2019, p. 43–167)

<sup>&</sup>lt;sup>57</sup> <u>Regulation (EU) 2019/4</u> of the European Parliament and of the Council of 11 December 2018 on the manufacture, placing on the market and use of medicated feed, amending Regulation (EC) No 183/2005 of the European Parliament and of the Council and repealing Council Directive 90/167/EEC (OJ L 4, 7.1.2019, p. 1–23)

<sup>&</sup>lt;sup>58</sup> Communication from the Commission to the European Parliament, the Council and the European Economic and Social Committee on the European Union Strategic Approach to Pharmaceuticals in the Environment, COM(2019) 128 final

<sup>&</sup>lt;sup>59</sup> <u>Strategic Approach to International Chemicals Management</u>

<sup>&</sup>lt;sup>60</sup> European Food Safety Authority 2021, Role played by the environment in the emergence and spread of antimicrobial resistance (AMR) through the food chain.

<sup>&</sup>lt;sup>61</sup> <u>Progress Report on the 2017 EU AMR Action Plan, Q2 2022</u>

access to established antimicrobials, as well as the provision of incentives to increase the uptake of diagnostics, antimicrobial alternatives and vaccines. A completed action to support this specific objective is the discussion in the In Vitro Diagnostic Technical Group (IVD TG)<sup>62</sup>. (2) In addition, the EU has engaged with and supported collaboration among key stakeholders in the human health, animal health, food, water and environmental sectors to encourage the responsible use of antimicrobials and appropriate handling of waste material through "Better Training for Safer Food" (BTSF) training activities, discussions in the plenary of the advisory group of the food chain and animal and plant health and an EMA information session on AMR. (3) The EU has also assisted Member States and stakeholders in the successful implementation of the safety features (unique identifier) to reduce the scope for falsified medicines and (4) discussed the availability of veterinary antimicrobials to tackle AMR in the Veterinary Pharmaceutical Committee.

#### Identified gaps

Monitoring systems for AMR are not operational in all Member States which hampers achieving better evidence and awareness of the challenges of AMR. In particular, harmonised outcome indicators for evaluating progress made at national level are not in place. While a target on the reduction of the overall EU sales of antimicrobials for farmed animals and in aquaculture by 2030 has been included in the Farm to Fork Strategy, there is currently no AMR target in the human health sector. Generally, differences across Member States continue to exist in both areas, mostly due to varying degrees of resources available, traditional views and national methods of working. Therefore, progress is less than expected, especially in countries with fewer resources. Indeed, according to the EXPH, although most EU Member States have NAPs in place, too few are fully implemented. Furthermore, in its overview report of 17 November 2022<sup>63</sup>, the Commission found that the NAPs vary considerably in content, detail and core components. For instance, the operational, monitoring and evaluation parts, are generally not well developed, nor available in other documents cross-linked to NAPs. Finally, awareness-raising efforts among stakeholders and the general public are not sufficiently tailored to respond to specific national needs and country settings.

Activities and actions to **better address the role of the environment** are still largely ongoing and have overall been less developed than in other dimensions of the One Health approach. A relevant gap is a persistent lack of communication around research on environmental issues. This may be because relevant knowledge is not widely communicated with relevant stakeholders, and AMR discourse may not include researchers working on AMR and environment<sup>64</sup>. In addition, there is insufficient awareness of the existing body of evidence emerging on the role of the natural environment in AMR.

<sup>&</sup>lt;sup>62</sup> <u>Register of Commission Expert Groups and Other Similar Entities, In Vitro Diagnostic Technical Group</u>

<sup>&</sup>lt;sup>63</sup> <u>Overview report on the review of Member States' One Health National Action Plans against Antimicrobial</u> <u>Resistance</u>

<sup>&</sup>lt;sup>64</sup> European Commission, Directorate-General for Health and Food Safety, Study on a future-proofing analysis of the 2017 AMR action plan : final report, Publications Office of the European Union, 2023, https://data.europa.eu/doi/10.2875/636347

Regarding **the availability of existing antimicrobials**, the EU-JAMRAI<sup>65</sup> identified shortages of existing antibiotics in EU Member States and third countries as a serious problem. Due to antibiotic resistance patterns and prescribing habits, the markets of some essential antibiotics are small, including those for children. Those shortages of older and newer generic antibiotics lead to more broad-spectrum use of antibiotics which in turn increases the risk of AMR. One major barrier to continued access is insufficient transparency of where active pharmaceutical ingredients are manufactured. National medicines agencies and procurers lack the tools to work proactively to avoid antibiotic shortages. In addition, the world supply of active pharmaceutical ingredients is highly concentrated in a few countries, outside of the EU/EEA.

### **3.2** Pillar 2: Boosting research, development and innovation

#### Achievements

To **improve knowledge on detection, effective infection control and surveillance** (specific objective 2.1), the activities supported by the Commission include research into the development and testing of interventions that prevent the development and spread of AMR, improve the understanding of the epidemiology of AMR, support the development of new tools for early (real-time) detection of resistant pathogens in humans and animals, and support new eHealth solutions. The activities have produced promising outputs, especially in terms of developing stewardship tools to combat AMR (i.e., a digital antimicrobial stewardship smartphone application to combat AMR, the AB-Assistant project<sup>66</sup>) as well as new methods to advance research for AMR detection (i.e., WORLDCOM project<sup>67</sup>).

Research was also supported for the **development of new antimicrobials and alternative products** for humans and animals as well as the repurposing of existing antimicrobials or on the development of new combination therapies (specific objective 2.2). In particular, 12 relevant projects have been funded in 2018 through the EU's research funding programme Horizon 2020 (H2020)<sup>68</sup>. Furthermore, reporting activities referring to many projects have been completed or are currently ongoing, including reporting activities on eight projects funded in the context of the EU's two public-private partnerships, i.e. the Innovative Medicines Initiative<sup>69</sup> (IMI) (funded under the 7th Framework Programme for Research and Innovation) and the IMI2 (funded under H2020). These EU-funded initiatives have supported the New Drugs for Bad Bugs (ND4BB)<sup>70</sup> Programme and the Antimicrobial resistance

69 https://www.imi.europa.eu/about-imi

<sup>&</sup>lt;sup>65</sup> <u>European Joint Action on Antimicrobial Resistance and Healthcare-Associated Infections (EU-JAMRAI),</u> <u>Incentivizing antibiotic access and innovation.</u>

<sup>&</sup>lt;sup>66</sup> <u>A digital antimicrobial stewardship smartphone application to combat AMR: the AB-assistant (AB-assistant)</u>

<sup>&</sup>lt;sup>67</sup> WORLDCOM: Development of new tools for real-time detection of zoonotic bacteria and antimicrobial resistance in veterinary, human and environmental sources. The WORLDCOM project, supported by the One Health European Joint Programme (OH EJP), developed new methods and tools for detection of AMR zoonotic pathogens in agriculture and environmental settings.

<sup>&</sup>lt;sup>68</sup> Horizon 2020 Call topics SC1-BHC-14-2019 on stratified host-directed approaches to improve prevention, treatment and/or cure of infectious diseases; and Horizon 2020 Call topics SC2-SFS-11-2018-2019 on antimicrobials and animal production.

<sup>&</sup>lt;sup>70</sup> <u>https://www.imi.europa.eu/projects-results/project-factsheets/nd4bb</u>. The ND4BB had multiple streams, including ENABLE, which aimed to develop attractive antimicrobial candidates for extensive preclinical studies and First-in-Human clinical trials, as well as TRANSLOCATION focused on drug discovery,

Accelerator<sup>71</sup> (AMR accelerator). Two specific projects, DRIVE-AB<sup>72</sup> (funded under the IMI ND4BB) and Phagovet<sup>73</sup> (funded under H2020), have produced outputs contributing to increased knowledge, including at the international level, and understanding of limitations and possibilities in the context of the development of new therapeutics and alternatives to antibiotics. In particular, DRIVE-AB outputs have enabled the development of pilots on pull incentives across Europe and internationally, while Phagovet contributed to advancing research in the area of phage-based products as alternatives to antibiotics. Furthermore, the Commission has been supporting different research projects for the establishment of a European-wide sustainable clinical research network for infectious diseases (ECRAID)<sup>74</sup> to efficiently generate evidence to improve the diagnosis, prevention and treatment of infections.

The EU has also provided continued support and funding for research into the **development** of new preventive vaccines for humans and for animals (specific objective 2.3). Several projects have been funded for this activity under H2020, including the SAPHIR<sup>75</sup> project on novel vaccine strategies for animal production and the TBVAC2020<sup>76</sup> project on advancing novel and promising tuberculosis (TB) vaccine candidates from discovery to preclinical and early clinical development. The outputs produced by TBVAC2020 and SAPHIR are being used by actors involved in the development of new vaccines, including by academic institutes, research laboratories and pharmaceutical companies.

In addition, the EU has supported research into the development of **novel diagnostics** (specific objective 2.4), in particular on-site tests in humans and animals. Seven projects were initiated in the context of the One Health European Joint Programme (OH EJP) including on new diagnostics tools on AMR. Furthermore, two projects that have been funded under

COMBACTE focused on drug development for gram positive bacteria, and COMBACTE-CARE, COMBACTE-MAGNET, and iABC focused on drug development for gram-negative bacteria.

<sup>&</sup>lt;sup>71</sup> <u>https://www.imi.europa.eu/projects-results/project-factsheets/amr-accelerator</u>

<sup>&</sup>lt;sup>72</sup> The project DRIVE-AB conducted research on specific bottlenecks affecting the development of antibiotics and evaluated possible solutions: <u>Driving re-investment in R&D and responsible antibiotic use (DRIVE-AB)</u>.

<sup>&</sup>lt;sup>73</sup> The project Phagovet has been conducting research on alternatives to antibiotics in poultry production and is producing promising initial results in terms of proving safety and efficacy of phage-based products: <u>A cost-effective solution for controlling Salmonella and Escherichia coli in poultry production (Phagovet)</u>.

<sup>&</sup>lt;sup>74</sup> <u>https://www.ecraid.eu/</u>. One of the outputs consisted of a Business Plan serving as the implementation basis for a coordinated, permanent, and pan-European infrastructure for clinical research on infectious diseases, ECRAID<sup>74</sup>. This infrastructure, that builds upon the COMBACTE programmes, has now been established, it provides a platform, first of its kind in Europe, to offer a single point of access to a pan-European clinical research network for infectious diseases.

<sup>&</sup>lt;sup>75</sup> <u>Strengthening Animal Production and Health through the Immune Response (SAPHIR).</u> The outputs of the SAPHIR project include six laboratory-tested, promising candidate vaccines to protect against six major pathogen strains affecting cattle, pigs and poultry, with one already licensed to a pharmaceutical company for commercial development and other companies interested in two others.

<sup>&</sup>lt;sup>76</sup> <u>Advancing novel and promising TB vaccine candidates from discovery to preclinical and early clinical development (TBVAC2020).</u> The project TBVAC2020 identified 13 promising new TB vaccines candidates and established a unique global platform for TB biomarker research and development resulting in a rich pipeline of biomarkers, while also contributing to better knowledge sharing and exchange with more than 120 publications in scientific journals.

H2020 have produced significant outputs: the FAPIC<sup>77</sup> project on developing a fast assay for pathogen identification and characterization and the PoC-ID<sup>78</sup> project on Point-of-Care diagnostics for infectious diseases. In addition, projects of H2020 contributed to advancing the AMR research and innovation field by bringing diagnostic tools and alternative therapies for infection treatment closer to the market.

Under specific objective 2.5 to **develop new economic models and incentives**, actions are ongoing to increase the evidence base for understanding the societal costs and benefits of different strategies for fighting AMR, and to support research into the development of new economic models, exploring and analyzing financial incentives to boost the development of new therapeutics, alternatives, vaccines and diagnostics. Different research projects have been funded under these activities, including the DRIVE-AB project funded under the IMI ND4BB Programme described in specific objective 2.2. The reporting activity related to this project was conducted in the context of the 2017 AMR Action Plan and completed in 2018. The DRIVE-AB project significantly contributed to advancing research into the development of new economic models to boost the development of new antibiotics. It produced significant results as it has researched and assessed economic incentives gathered from different industries and identified incentives applicable to the antibiotic development.

Continued efforts have led to progress in terms of closing knowledge gaps on AMR in the environment and on how to prevent AMR evolution and transmission (specific objective 2.6). The Commission has supported research into knowledge gaps on the release of resistant microorganisms and antimicrobials into the environment and their spread. Many actions have been taken to further develop knowledge on AMR in the environment, including the NEREUS<sup>79</sup> action which, amongst other, conducted a multinational survey of cefotaximeresistant coliforms in urban wastewater treatment plants, a reflection paper from EMA<sup>80</sup> which reviewed currently available data on antimicrobials in the environment and their role in the transmission of antimicrobial resistance genes, and the PREMIER<sup>81</sup> project which seeks to develop a database with environmental information on pharmaceuticals and a novel information and assessment guiding system to support regulators, water managers and other stakeholders in identifying and managing any potential environmental risks associated with the patient use of medicines. Another action described in the 2022 Progress Report on the 2017 AMR Action Plan is the development of technologies that enable efficient and rapid degradation of antimicrobials in wastewater and the environment and reduce the spread of AMR. Actions taken to further develop such technologies include the LIFE Programme<sup>82</sup>

<sup>&</sup>lt;sup>77</sup> <u>Fast Assay for Pathogen Identification and Characterization (FAPIC).</u> The FAPIC project developed two automated instruments based on specifications and assay protocols, one of which has been clinically validated. The tools provide a better understanding of the genetic mechanisms that bacterial pathogens use to evade an antibiotic therapy.

<sup>&</sup>lt;sup>78</sup> <u>Platform for ultra-sensitive Point-of-Care diagnostics for Infectious Diseases (PoC-ID)</u>. The PoC-ID project produced new microelectronic based sensors in a point-of-care in vitro diagnostic (PoC-ID) benchtop device which provides accurate analysis results in only approximately 6 minutes. Such novel devices can be applied in diagnosis, monitoring of therapeutic responses research of pathogen-host interaction and personalised medicine and represent a significant step towards low cost and fast detection of specific biomarkers.

<sup>79</sup> NEREUS Cost Action

<sup>&</sup>lt;sup>80</sup> <u>Reflection paper on antimicrobial resistance in the environment: considerations for current and future risk</u> assessment of veterinary medicinal products, EMA

<sup>&</sup>lt;sup>81</sup> <u>PREMIER: Prioritisation and risk evaluation of medicines in the environment, Innovative Medicines Initiative</u>

<sup>&</sup>lt;sup>82</sup> LIFE Programme, European Climate Infrastructure and Environment Executive Agency.

which helped develop and promote methods to address pharmaceuticals and other emerging contaminants in Wastewater treatment plants, and NEREUS<sup>83</sup> which i.a. sought to understand the contribution of biological processes to antibiotic resistance spread into the environment. Such research actions provide strong knowledge bases to develop needed technology in the area. The activities show that progress has been achieved in terms of closing knowledge gaps on AMR in the environment and on how to prevent transmission.

#### Identified gaps

In its 2019 special report<sup>84</sup> on AMR, the European Court of Auditors noted that despite providing a strategy for the Commission to support research, the 2017 AMR Action Plan does not address some specific challenges for AMR research in the development of new antibiotics, given in particular the long timelines required for R&D, as well as challenges in integrating long term research priorities and sustaining activities across programming periods. The EU-JAMRAI report<sup>85</sup> also identified gaps, pointing at a lack of research in the environmental field, food safety area, infection prevention and control and on how to improve clinical trials for antimicrobials.

In addition, incentives may not be sufficient to encourage innovation and investment in antimicrobials, medical countermeasures against AMR, and innovation in wastewater management such that they are brought to the market. Fragmentation of the type and target of incentives across Member States makes it difficult for incentives to be effective.

None of the innovative solutions to stimulate the development of novel antibiotics (i.e., economic incentives in the context of the DRIVE-AB project) have been implemented at EU or at national level. Furthermore, limited access to new and pre-existing antibiotics is driving resistance development because of prolonged infections, greater use of broader spectrum antibiotics, and the creation of market opportunities for substandard and falsified antibiotics. Thus, there is still room for push and pull incentives to encourage the development of innovative novels antimicrobials, as well as the access to antimicrobials (new and existing ones), medical countermeasures such as preventive vaccines against certain resistant pathogens, a stronger focus on public-private partnerships and greater attention to the development of novel diagnostics.

The EU-JAMRAI report<sup>86</sup> identified gaps with regards to EU infection prevention and control programmes, in particular a lack of active involvement of hospital administrators and clinical department heads, insufficient cooperation between hospital administrators, infection prevention and control teams and public health authorities, and a lack of human and budgetary resources.

<sup>&</sup>lt;sup>83</sup> <u>NEREUS Cost Action ES1403. 2018.</u> Deliverable 15 Harmonized protocols for effect-based in vitro biotests (bioassays) able to serve as routine tools for analysis and evaluation of the efficiency of the various treatment technologies to remove toxicological hazards and evaluate the quality of the wastewater to be reused.

<sup>&</sup>lt;sup>84</sup> <u>Special report No 21/2019</u>: Addressing antimicrobial resistance: progress in the animal sector, but this health threat remains a challenge for the EU

<sup>&</sup>lt;sup>85</sup> <u>European Joint Action on Antimicrobial Resistance and Healthcare-Associated Infections (EU-JAMRAI),</u> LAYMAN REPORT

<sup>&</sup>lt;sup>86</sup> <u>European Joint Action on Antimicrobial Resistance and Healthcare-Associated Infections (EU-JAMRAI),</u> <u>LAYMAN REPORT</u>

Furthermore, the current European monitoring system does not cover AMR surveillance in sick animals, as pointed out in the EU-JAMRAI report. This is of limited help to veterinary practitioners and policymakers seeking to improve antimicrobial prudent use in animal health.

## 3.3 Pillar 3: Shaping the global agenda

#### Achievements

To **promote a stronger EU global presence** (specific objective 3.1), the EU has played an active role in collaborating with international organisations. The Commission has been contributing to the normative work of the WHO, the World Organisation for Animal Health (WOAH), the Food and Agriculture Organisation of the United Nations (FAO) and Codex Alimentarius on the development of ambitious international frameworks and standards, norms, guidelines and methodologies related to AMR. The Commission has also been working towards continued high-level political attention and commitment to AMR action, including in UN forums, the G7 and G20, and collaborating with the United States, Canada, Norway and the United Kingdom within the Transatlantic Taskforce on AMR<sup>87</sup> (TAFTAR). Combatting AMR in the context of the One Health approach has also been included in the EU Global Health Strategy as a priority<sup>88</sup>, highlighting that international cooperation is needed to ensure a coordinated response to AMR from the global community.

Activities relating to the specific objective 3.2 of **forming stronger bilateral partnerships for stronger cooperation** include the EU-JAMRAI which successfully created bilateral partnerships across EU Member States focusing on AMR, as well as the engagement with major global players and strategic countries (e.g., Brazil, China and India) towards achieving the objectives of the WHO global action plan on AMR<sup>89</sup>. The EU has been working to develop stronger partnerships with third countries and has delivered initiatives to increase networking and collaboration to address the global issue of AMR. Actions undertaken in the context of this activity include events<sup>90</sup> with India on AMR in veterinary medicine, animal health and the environment (in 2017 and 2021), which created opportunities to enhance cooperation between the EU and India, as well as the publication of a report<sup>91</sup> regarding national policies and measures against AMR in third countries (2018), and the ongoing quadripartite collaboration project between FAO, WOAH, PAHO/WHO and UNEP "Working together to fight Antimicrobial Resistance (2019-2023)"<sup>92</sup>. This collaboration supports the implementation of national action plans in seven South American countries (Argentina, Brazil, Chile, Colombia, Paraguay, Peru and Uruguay).

The Commission is **cooperating with developing countries** (specific objective 3.3) on the development of AMR strategies in the area of food safety and animal health through regional

<sup>&</sup>lt;sup>87</sup> Transatlantic Taskforce on Antimicrobial Resistance (TATFAR)

<sup>&</sup>lt;sup>88</sup> EU Global Health Strategy: Better Health for All in a Changing World

<sup>&</sup>lt;sup>89</sup> Global action plan on antimicrobial resistance, WHO 2016

<sup>&</sup>lt;sup>90</sup> <u>EU-India Dialogue Seminar on the Use of Veterinary Medicine and AMR</u>

<sup>&</sup>lt;sup>91</sup> <u>Non-EU Countries' National Policies and Measures on Antimicrobial Resistance Report (2018).</u> As part of the report, a questionnaire was sent to 128 EU delegations in non-EU countries. Amongst the 77 countries that replied to the questionnaire, 13 were form East Asia and Pacific and 19 from Latin America & Caribbean.

<sup>&</sup>lt;sup>92</sup> <u>The Quadripartite Collaboration Project (FAO, OIE, PAHO/WHO, UNEP)</u> "Working together to fight <u>Antimicrobial Resistance (2019-2023)</u>"

training workshops on AMR. Third countries participate in an AMR One Health training within the BTSF programme<sup>93</sup>. Additionally, between 2017 and 2022, DG INTPA supported two projects<sup>94</sup> with the WHO to pilot a package of activities to foster the development and implementation of antimicrobial stewardship (AMS) programs in hospitals in Sub-Saharan African countries and to conduct surveys to identify the frequency of substandard and falsified (SF) antimicrobial medicines to inform the development of tools to support future SF surveillance programs in low resources countries.

By providing essential information on the status of research, including research developments and existing initiatives and opportunities, the EU is contributing to a **global research agenda** (specific objective 3.4). The EU further supports research facilities working on AMR around the world, facilitating research coordination, knowledge exchange and capacity development.

#### Identified gaps

Support to low and middle-income countries in implementing their actions against AMR remains insufficient concerning the strengthening of the knowledge and evidence base, infection prevention and control, quality and use of antimicrobials, as well as sharing best practices from the EU such as antimicrobial stewardship teams.

### 4. FUTURE-PROOFING ANALYSIS AND CHALLENGES

This section assesses how current and future developments might influence AMR, to what extent the 2017 AMR Action Plan is relevant and coherent in light of these developments, and how it can be complemented to better address future challenges.

#### 4.1 Science, technology and innovation

While knowledge of AMR has improved over time, there are still areas where basic and applied research may significantly change our understanding of the threats posed by AMR and the ways to address them in the future. Basic research has led to knowledge of the connections between animal, human and environmental health, but it has not yet led to a precise understanding of how AMR is transferred between the environment, humans and animals. New discoveries made through basic research in the next ten years could shape how well the mechanisms by which resistance is transferred are understood and what policy actions can be taken to address it. Future research into AMR with a One Health approach which is at the heart of the 2017 AMR Action Plan will continue to be relevant, as new evidence will emerge on how One Health domains are linked and regarding the important role of the environment in transfer of resistance. Further areas of research where discoveries may be relevant are for example genetic and microbiome factors associated with AMR.

Similarly, technological advancements may change how AMR is addressed. Advancements in laboratory techniques over the next ten years may allow for more rapid identification of

<sup>&</sup>lt;sup>93</sup> BTSF Academy, Courses One Health, Antimicrobial Resistance

<sup>&</sup>lt;sup>94</sup> PP-AP/2017/387-116 and P-AP/2018/402-050 Pilot Projects "Mapping the Global Threat posed by Antimicrobial Resistance".

pathogens, resistance and virulence, which could help avoid spread of resistant pathogens, reduce the need for antimicrobials and better target their use when necessary<sup>95</sup>.

The slow progress in developing new antimicrobials for human health, in particular due to scientific challenges and high risk of failed R&D efforts, is a key issue in the fight against AMR and there are very few novel antimicrobials currently in pharmaceutical pipelines. Since 2017, only 11 antibiotics have been approved (by either the Commission or the US Food and Drug Administration or both). With some exceptions, the newly approved agents have limited clinical benefit over existing treatment, as over 80% are from existing classes where resistance mechanisms are well established and rapid emergence of resistance is foreseen<sup>96</sup>. Currently 43 antibiotics and combinations with a new therapeutic entity are in the clinical antibacterial pipeline, but only few of them meet at least one of the WHO innovation criteria (absence of known cross-resistance, new binding site, mode of action and/or class). The development and availability of novel antimicrobials and other medical countermeasures (e.g., vaccines, phage therapy and alternative treatments) for both human and animal health in the next ten years will be pivotal in combating AMR.

#### How can EU activities be strengthened?

There is a need to further strengthen research, development and innovation (R&D&I) activities, also around specific mechanisms by which resistance is transferred between the One Health dimensions (human, animal and environment). Furthermore, given the emergence of resistant strains, there is a need for a new generation of safe and effective antimicrobials, alongside alternative treatments and vaccines to mitigate the spread of AMR. Therefore, continued support and increased funding to R&D&I to support technological developments needs to be strengthened. This should also include further financial and technical support, as well as coordination and infrastructure such as universities and clinical research networks.

To strengthen the One Health approach, there is a need for additional evidence from basic and applied research (e.g., in genetics, transfer of resistance and the role of the environment) clarifying how the One Health approach should be understood and applied in practice. More cross-disciplines research, including social sciences, and collaboration can further encourage the uptake of the One Health approach. Part of this includes the need for integrated, joined up surveillance of AMR as it relates to human health, animal health and the environment.

### 4.2 Society, awareness and education

Although many Europeans are aware of the risks related to AMR<sup>97</sup>, evidence points to the need for continued educational efforts, especially in relation to awareness of AMR among the public and key stakeholders (e.g., healthcare providers, farmers, veterinarians). The 2022

<sup>&</sup>lt;sup>95</sup> Bassetti, M., Poulakou, G., Ruppe, E. et al. (2017). Antimicrobial resistance in the next 30 years, humankind, bugs and drugs: a visionary approach. Intensive Care Med 43, 1464–1475. <u>https://doi.org/10.1007/s00134-017-4878-x</u>

<sup>&</sup>lt;sup>96</sup> <u>World Health Organisation 2021, 2020 Antibacterial agents in clinical and preclinical development: an</u> <u>Overview and Analysis</u>

<sup>&</sup>lt;sup>97</sup> Elena-Alexandra Alexa (Oniciuc), Eleni Likotrafiti, Alberto Garre, Lorena Ruiz, Miguel Prieto, Avelino Alvarez-Ordóñez, A European questionnaire-based study on population awareness and risk perception of antimicrobial resistance, FEMS Microbiology Letters, Volume 366, Issue 17, September 2019, fnz221, https://doi.org/10.1093/femsle/fnz221

Eurobarometer<sup>98</sup> showed that Europeans' knowledge about antibiotics leaves room for improvement. Only half of those questioned are aware that antibiotics are ineffective against viruses, and there are still great differences between citizens awareness among Member States. In addition, almost one in ten Europeans are taking antibiotics without prescription. A large majority (79%) of Europeans say they would like further information on antibiotics, a sharp increase compared to 2018. Close to one in three mention wanting more information regarding the medical conditions for which antibiotics are used and a large majority of Europeans do not remember getting any information in the last year about not taking antibiotics unnecessarily.

Political will and public awareness of AMR may also be challenging, particularly in light of trends around misinformation and distrust, and due to competing priorities during times of crisis and economic downturn. As human health is largely a national competence, political will among policy makers at Member State level will likely impact how AMR is dealt with. Programmes aimed at raising awareness and educating the public and key stakeholders about AMR may influence AMR-related behaviours into the future<sup>99</sup>. The EU-JAMRAI report<sup>61</sup> also stresses that promoting behaviour change is the biggest challenge in the fight against AMR.

### How can EU activities be strengthened?

The results of the 2022 Special Eurobarometer on AMR demonstrate the need to improve awareness-raising activities on AMR at all levels to increase knowledge and influence behavioural change. Although awareness raising and education are primarily the responsibilities of Member States, the 2017 AMR Action Plan could be strengthened by supporting national and local efforts to educate all the relevant stakeholders, including the public, healthcare providers, veterinarians and farmers, about AMR. For example, this can include supporting Member States in creating and distributing information to the public about not requesting antimicrobials for common colds and how to appropriately dispose antimicrobials. For the healthcare providers it is important to provide better information on appropriate diagnosis for human health and to ensure core competencies for infection prevention and control. Education efforts should also include veterinarians and farmers, and material about basic hygiene, wastewater treatment and environmental aspects of AMR. It is also important to promote continuous dialogue and collaboration between the human, veterinarian and environmental sectors.

### 4.3 Human health

The use of antimicrobials, vaccines, diagnostics and other medical countermeasures may differ between Member States (e.g., due to differences in capacities within healthcare systems). Future disease trends (e.g., more or fewer outbreaks or pandemics in the future) may also influence AMR and the amount of antimicrobials used over the next ten years.

<sup>&</sup>lt;sup>98</sup> Eurobarometer 2022, Antimicrobial Resistance.

<sup>&</sup>lt;sup>99</sup> Charani, E., Mendelson, M., Ashiru-Oredope, D., Hutchinson, E., Kaur, M., McKee, M., Mpundu, M., Price, J. R., Shafiq, N., & Holmes, A. (2021). Navigating sociocultural disparities in relation to infection and antibiotic resistance-the need for an intersectional approach. JAC-antimicrobial resistance, 3(4), dlab123. https://doi.org/10.1093/jacamr/dlab123

Surveillance of resistance in humans and monitoring of the use of antimicrobials in human health will remain a key priority to be dealt with in the future. The ability to collect consistent data across geographies is crucial to understand how pathogens and resistance spreads among human populations, to assess the severity of AMR-related threats and to create timely and targeted responses to outbreaks. The 2017 AMR Action Plan supports existing surveillance and monitoring systems, which remain relevant despite challenges with implementation. Currently the capacities to conduct surveillance of antimicrobial use and AMR in humans differ between Member States, hampering EU and global efforts around surveillance.

The COVID-19 pandemic presents challenges and opportunities, and the future will be influenced by the degree to which we are able to build on lessons and progress made during the pandemic. This includes joint procurement, wastewater surveillance, the use of diagnostics in clinical care, breakthroughs in the development of vaccines and the use of genomic monitoring as a tool to understand the epidemiology underlying the global and local emergence, selection and transmission of AMR.

#### How can EU activities be strengthened?

Although human health is largely a Member State competence, there may be areas where the EU is well positioned to increase coherence across Member States. Potential areas that could be strengthened include the support for Member States to encourage antimicrobial stewardship, the uptake of vaccines, diagnostics and other medical countermeasures, and infection prevention and control measures, particularly where capacity is lacking. In order to improve access to existing antibiotics, diversifying manufacturing capacity, greater intelligence gathering and surveillance across the supply-chain, stockpiling, and joint procurement efforts need to be supported at EU level.

Supporting Member States in shifting healthcare systems towards prevention is important in the fight against AMR, to prevent individual infections and prevent the spread of AMR in healthcare settings, in particular in long-term care facilities.

There is a need for joined approaches to monitoring and surveillance that link AMR in humans, animals and the environment. This would provide further insight into the One Health approach and can provide more information to decision makers. In order for this approach to be successful, Member States need to collaborate when reviewing integrated data and incorporating insights into policy and practice. Furthermore, integrated systems for surveillance and monitoring of AMR and AMC at all levels (e.g., hospitals, long-term care facilities, community/ primary care level) to support the prudent use of antimicrobials in human health are needed. Setting clear targets at EU and national level on the consumption of antimicrobials in humans and the spread of AMR, in particular regarding critical resistant pathogens that pose the highest burden and threat to public health in the EU, would bring clarity on the necessary level of effort, allow for targeted support where necessary and allow monitoring the process made in the coming years. Targeted support may be needed in particular for Member States that lack capacity to effectively perform surveillance and monitoring. The Commission can play a role in encouraging Member States to support the uptake of best practices with respect to surveillance and monitoring, e.g., complying with the

protocols established by ECDC<sup>100</sup> to report Member State data to the European Antimicrobial Resistance Surveillance Network (EARS-Net)<sup>101</sup>.

#### 4.4 Animal health and welfare

Poor animal welfare has an impact on animal health and is associated with higher antimicrobial use in animals<sup>102</sup>. The over-use of broad-spectrum antimicrobials in animals and the lack of good diagnostic techniques and vaccines for animals could worsen AMR in the future.

Improving animal welfare of food-producing animals may contribute to decrease the occurrence and transmission of infectious diseases in farming, contributing to a reduction of antimicrobial use. The degree to which the Farm to Fork Strategy's target of decreasing EU antimicrobial sales for farmed animals and aquaculture by 2030 is successful will also likely influence AMR.

However, progress has also been made in the EU with respect to animal and agricultural use of antimicrobials and medical countermeasures, which will have a positive impact on AMR. such as the list of antimicrobials reserved for human use<sup>103</sup> and the Regulations on Veterinary Medicinal Products and Medicated Feed which restrict antimicrobial use in animals to what corresponds to prudent and responsible use and requires Member States to gather data on antimicrobial sales and use of antimicrobials in animals. Acknowledging the international dimension of AMR, the Regulation on Veterinary Medicinal Products also requires that operators in third countries do not use (i) antimicrobials in animals for the purpose of promoting growth or to increase yield and (ii) antimicrobials from the list of those reserved for human use, for animals and animal products intended for human consumption to be exported to Union. The latest annual report<sup>104</sup> on European Surveillance of Veterinary Antimicrobial Consumption (ESVAC) shows that, since 2011, European countries have substantially reduced sales of veterinary antibiotics in animals. According to data from 25 countries that continuously provided input for the full 2011-2021 period, overall sales of veterinary antibiotics decreased by 47% in this interval, reaching the lowest value ever reported. Despite those advances in Europe, global consumption of antimicrobials from food are estimated to increase by 67% between the years 2010 and  $2030^{105}$ .

Furthermore, surveillance and monitoring of AMR in animals and the food chain has progressed in recent years, e.g., with the publication of annual EU Summary reports on zoonotic infections, food-borne outbreaks and AMR produced by EFSA in cooperation with ECDC, and the EFSA baseline survey reports on the prevalence of AMR in the EU in

<sup>&</sup>lt;sup>100</sup> European Centre for Disease Prevention and Control, Surveillance and disease data for antimicrobial resistance.

<sup>&</sup>lt;sup>101</sup> European Antimicrobial Resistance Surveillance Network (EARS-Net).

<sup>&</sup>lt;sup>102</sup> Rodrigues da Costa, M., & Diana, A. (2022). A Systematic Review on the Link between Animal Welfare and Antimicrobial Use in Captive Animals. Animals, 12(8), 1025. MDPI AG. <u>https://doi.org/10.3390/ani12081025</u>

<sup>&</sup>lt;sup>103</sup> Commission Implementing Regulation (EU) 2022/1255 of 19 July 2022 designating antimicrobials or groups of antimicrobials reserved for treatment of certain infections in humans, in accordance with Regulation (EU) 2019/6 of the European Parliament and of the Council

<sup>&</sup>lt;sup>104</sup> European Medicines Agency, Sales on veterinary antimicrobial agents in 31 European countries in 2021, Trends from 2010 to 2021, Twelfth ESVAC report

<sup>&</sup>lt;sup>105</sup> Bloomer, E. and McKee, M. (2018). Policy options for reducing antibiotics and antibiotic-resistant genes in the environment. Public Health Pol. 39, p389-406. <u>https://doi.org/10.1057/s41271-018-0144-x</u>

specific animal populations<sup>106</sup>. Moreover, in the context of the Regulation on Veterinary Medicinal Products, tertiary legislation has been adopted to define specific requirements for the collection of data on the sales of veterinary antimicrobials and on the use of antimicrobials per animal species. The implementation of this legislation aims to allow for improved data quality and comparability with a view to set up targeted measures to tackle AMR. However, there remain differences in how Member States conduct surveillance and monitoring that may create challenges in integrated surveillance which may impact harmonisation at EU-level in the future.

#### How can EU activities be strengthened?

Access to information, as well as resources and funding to support good practice, will be influential in how AMR is dealt within the animal health and agricultural sector in the future. The 2017 AMR Action Plan may be strengthened by implementing ways to promote prevention of infections in animals, rather than focusing only on treatment. Ensuring higher standards for animal welfare leads to improved animal health, which helps decrease antibiotic use.

Although EU legislation regarding AMR surveillance in animals already exists with the Veterinary Medicinal Products and Medicated Feed Regulations and the new Commission Implementing Decision on the monitoring and reporting of AMR in zoonotic and commensal bacteria, addressing variation between Member States in how antimicrobials are used and AMR in animals is monitored would be useful in the fight against AMR. For example, there may be opportunities to ensure that all Member States implement consistent monitoring and surveillance systems (e.g., consistent methods and inclusion of the same species and pathogens)<sup>107</sup>. As mentioned in relation to human health, there is also a need for surveillance and monitoring systems that link human health, animal health and the environment.

#### 4.5 Environment

Climate change may create an environment more conducive to AMR, as increase in temperature correlates with an increase in AMR infections in humans<sup>108</sup> and periods of drought can also contribute to poor water sanitation and increased risks of AMR<sup>109</sup>. Climate change may also shift the disease burden in Europe by increasing zoonotic transmission and vector-borne diseases, which may affect demand for antimicrobials. Likewise, the loss of soil biodiversity may facilitate the transmission of AMR even though more study is needed to understand this interrelation better<sup>110</sup>.

<sup>&</sup>lt;sup>106</sup> European Food Safety Authority, Antimicrobial resistance.

<sup>&</sup>lt;sup>107</sup> Mesa Varona, O., Chaintarli, K., Muller-Pebody, B., Anjum, M. F., Eckmanns, T., Norström, M., Boone, I., & Tenhagen, B. A. (2020). Monitoring Antimicrobial Resistance and Drug Usage in the Human and Livestock Sector and Foodborne Antimicrobial Resistance in Six European Countries. Infection and drug resistance, 13, 957–993. <u>https://doi.org/10.2147/IDR.S237038</u>

 <sup>&</sup>lt;sup>108</sup> McGough, S. F., MacFadden, D. R., Hattab, M. W., Mølbak, K. and, Santillana, M. (2020). Rates of increase of antibiotic resistance and ambient temperature in Europe: a cross-national analysis of 28 countries between 2000 and 2016. Euro Surveill. 25 (45), pii=1900414. <u>https://doi.org/10.2807/1560-7917.ES.2020.25.45.1900414</u>
<sup>109</sup> Burnham J. P. (2021). Climate change and antibiotic resistance: a deadly combination. Therapeutic advances in infectious disease, 8, 2049936121991374. <u>https://doi.org/10.1177/2049936121991374</u>
<sup>110</sup> TU Dresden, Chair of Limnology: ANTIVERSA.

The release of effluents (medical, industry, agricultural and urban wastewater treatment facilities etc.) and waste into the environment can impact genetic material and antimicrobial compounds in water and soils pathways, which in turn can contribute to the development of resistance. This is a global issue, as there are different standards in the EU and third countries where manufacturing takes place. Furthermore, advances in statistical forecasting and wastewater surveillance will improve the surveillance of AMR in the environment in the future.

In the context of plant production, some pesticides are used as antimicrobial substances, namely antibiotics used against bacterial diseases and fungicides used against fungal diseases. There is growing concern that some of those plant protection products select for AMR among pathogens important to plant, human and animal health<sup>111</sup>.

#### How can EU activities be strengthened?

Despite wastewater treatment and the partial elimination of antimicrobial residues, final treated effluents, even after disinfection, can contain antimicrobials<sup>112</sup>. Therefore, along with the prudent use of plant protection products or biocidal products, a shift towards prevention (reducing antimicrobials in the environment) could change how AMR in the environment is dealt with and eventually reduce the risk of environmental transmission to humans and animals.

Furthermore, as outlined by the AMR One Health Network subgroup, strengthened data collection and surveillance systems of the environment and in wastewater will improve our understanding of the role of the environment in the spread of AMR. There is also a need to harmonised methods to conduct environmental and wastewater monitoring to ensure that Member States provide comparable results. Supporting Member States to monitor AMR more effectively in the environment (through environmental and wastewater surveillance) will be useful to ensure that practices are similar across all Member States.

### 5. RECOMMENDATIONS ON HOW TO ADDRESS THE CHALLENGES

The 2017 AMR Action Plan has been central to tackling AMR in the EU and beyond. It should be continued and strengthened to address the future challenges likely to be posed by this complex public health issue.

### 5.1 Further develop Member State National Action Plans

NAPs to tackle AMR should continue to be in place in all Member States and should focus more on the One Health dimension of AMR, particularly on the environment. As shown by the review of Member States' NAPs, the environment is currently included in only half of the One Health NAPs<sup>113</sup>. Although research on AMR and international collaborative work are already covered in most NAPs, more could be done to raise the profile of work to improve

<sup>&</sup>lt;sup>111</sup> FAO 2020, Antimicrobial Resistance (AMR) in relation to pesticide use in plant production.

<sup>&</sup>lt;sup>112</sup> Célia M. Manaia (2022) Framework for establishing regulatory guidelines to control antibiotic resistance in treated effluents, Critical Reviews in Environmental Science and Technology, DOI: 10.1080/10643389.2022.2085956

<sup>&</sup>lt;sup>113</sup> Overview report on the review of Member States' One Health National Action Plans against Antimicrobial Resistance

the knowledge on the role of the environment for AMR. Member State NAPs should therefore include measures to prevent, monitor and reduce the spread of AMR in the environment.

Furthermore, NAPs should well describe the intersectoral coordination mechanisms (ICMs), including a clear composition and mandate of the ICMs since they are essential for the development and implementation of One Health NAPs.

To ensure effective implementation of NAPs, Member States should implement specific measures to achieve overarching measurable goals and indicators, and regularly evaluate the outcomes and progress towards achieving these goals. As outlined in the review of Member States' NAPs, efforts to improve data collection and integration across sectors are key to strengthen knowledge and to achieve targets. In addition, Member States should provide sufficient human and financial resources. This would address concerns about the sustainable implementation of NAPs and the arrangements in place in Member States to ensure that the strategic objectives are achieved effectively<sup>114</sup>.

### 5.2 <u>Improving AMR surveillance and monitoring</u>

Environmental and wastewater surveillance and monitoring should be improved to facilitate the understanding of the evolution, dissemination and transmission of AMR within, to, and from the environment to enable more informed decision-making for mitigation strategies to address the spread of AMR. In addition, the capacity of Member States to comply with existing AMR surveillance and monitoring activities should be enhanced, especially where capacity is insufficient or lacking. The EU could create mechanisms to share data across relevant functions (e.g., human health, the environment, wastewater and animal health), which will be facilitated by the establishment of aligned approaches to data collection and indicators. One of the recommendations of EU-JAMRAI<sup>115</sup> relates to action on surveillance: in order to achieve real time surveillance, the EU-JAMRAI identifies as priorities institutional support, unified coordination of microbiological and antimicrobial consumption data sources, more homogeneous indicators, dedicated human resources and modern and integrated IT systems. The subgroup established under the AMR One Health Network also highlighted the strengthening of data collection and AMR surveillance as a priority.

### 5.3 <u>Improving patient safety and supporting infection prevention and control</u>

With over 70% of the AMR burden linked to healthcare-associated infections, it is important to strengthen the standards for infection prevention and control in healthcare and community settings and long-term care facilities at national level to reinforce patient safety. This is also highlighted in the EU-JAMRAI recommendations<sup>116</sup> which underline the urgent need to foster research on infection prevention and control to improve health security. Further research in the area of patient environment and behavioural science will have wide-ranging benefits including lowering the number of hospitalised patients, hindering antibiotic

<sup>&</sup>lt;sup>114</sup> Overview report on the review of Member States' One Health National Action Plans against Antimicrobial Resistance

<sup>&</sup>lt;sup>115</sup> European Joint Action on Antimicrobial Resistance and Healthcare-Associated Infections (EU-JAMRAI), LAYMAN REPORT

<sup>&</sup>lt;sup>116</sup> European Joint Action on Antimicrobial Resistance and Healthcare-Associated Infections (EU-JAMRAI), LAYMAN REPORT

resistance, and strengthening global health preparedness for future pandemics. Core elements for a common infection prevention and control framework at EU level need to be developed. Infection prevention and control also needs to be strengthened in animal health, including in aquaculture. There is a need to improve the health and welfare of food-producing animals to decrease the occurrence and spread of infectious diseases in farming and thereby reduce the need for antimicrobial use in animals.

### 5.4 <u>Strengthening research, development and access of antimicrobials</u>

To further support AMR research, development of and access to antimicrobials, there is scope for coordination, joint procurement for the stockpiling of antimicrobials and AMR medical countermeasures, push incentives to research and innovation, support to European and Member State research infrastructure (e.g. data infrastructures, clinical and research networks), greater support for the identification of innovative business models and strategic pooling of incentives at EU level. The EU may consider opportunities to pool resources and take collective EU action, while respecting Member State competence, to create a harmonised, multi-country pull incentive scheme in form of revenue guarantee, market entry rewards or milestone payments to incentivize the development and access<sup>117</sup> to antimicrobials, complementary to the regulatory framework applicable to the medicinal products for human use. Member States and the Commission should regularly review the scheme implemented and the impact on the development and accessibility. This would contribute to strengthening the EU's role in establishing best practices on incentives. Increased direct funding of AMR-relevant R&D and support to Member State R&D infrastructure (e.g., data infrastructure, R&D networks and partnerships) are crucial aspects. The approach should be considered not only for novel antimicrobials, but also for existing ones on the market including recently authorized antimicrobials, as well as off-patent antimicrobials, and potentially other relevant medical countermeasures relevant to combat AMR.

In the opinion on managing antimicrobial resistance across the health system of the EXPH, it is recommended that Member States should focus research on understanding why policies and practices on their territories continue to create risks of AMR and the Commission should support exchange of the knowledge thus generated.

### 5.5 <u>Reinforcing EU action at global level</u>

As AMR is a global issue, actions beyond the EU-level have also to be continued and strengthened. The EU should continue to participate in and lead global initiatives to address issues such as inappropriate antimicrobial use in human and animal health, AMR-related surveillance, and prescription practices, particularly in low- and middle-income countries. To support this, the EU should support the development and implementation of standards by international bodies (e.g., WHO, WOAH). In particular, the EU should work towards the inclusion of concrete provisions on AMR following a One Health approach in the future WHO international agreement on pandemic prevention, preparedness and response<sup>118</sup>. More broadly, technical capacity as well as human and financial resources may also need to be

<sup>&</sup>lt;sup>117</sup> European Joint Action on Antimicrobial Resistance and Healthcare-Associated Infections (EU-JAMRAI), Policy Brief Improving Access to Essential Antibiotics

<sup>&</sup>lt;sup>118</sup> World Health Organization 2022, Pandemic prevention, preparedness and response accord

strengthened at various levels and Member States should report data on AMR and AMC to the Global Antimicrobial Resistance and Use Surveillance System (GLASS).

### 5.6 <u>Strengthening awareness, education and training about AMR</u>

The report on Member States' NAPs showed that awareness campaigns are included in all NAPs and good examples of collaborative awareness campaigns were identified. The need to adjust the narrative to convey the urgency and importance of AMR is reflected in actions targeting communication strategies and education and continuous professional development in a One Health approach, covering all the relevant professional groups in place in Member States.

Nevertheless, more can be done to ensure that knowledge produced is used effectively and is communicated across disciplines and sectors, remaining aware that specific stakeholders will require different ways of communicating such knowledge. Awareness campaigns for the public and health professionals should focus amongst others on the collection and safe disposal of unused, expired and leftover antimicrobials, as well as on the release of antimicrobials into the environment and its role in the emergence of more resistant strains. The EU should continue to support collaboration and coordination among Member States, for example by building on EU-JAMRAI. At the same time, the EU should also offer more specialised support to countries with fewer resources through trainings, networking events, and *ad-hoc* mutual learning activities. Such actions should be designed as to embed the One Health approach, bringing together stakeholders from across sectors as much as possible to engage in a meaningful and comprehensive way regarding AMR. The EU could also create resources to support evidence-based behaviour change initiatives in Member States aimed at the general public and key stakeholders (e.g., healthcare professionals and providers, veterinarians, farmers). Similarly, the EU should continue supporting countries to ensure that communication and education is a corner stone of their NAP on AMR. At the same time, the EU should continue training and awareness raising activities following the One Health approach in the context of the BTSF initiative.

### 5.7 <u>Promoting prudent use of antimicrobials</u>

Overuse and misuse of antibiotics remain a challenge. Improving public awareness on the role of antibiotics and of AMR is crucial to the achievement of these objectives. Some of the key findings of the 2022 Eurobarometer<sup>119</sup> highlight in particular that fewer Europeans have reportedly taken antibiotics in the last year than in the 2018 survey<sup>120</sup>. This trend is also reflected in data from ECDC, showing show a decrease in the total antibiotic consumption in humans by more than 15% between 2019 and 2020<sup>121</sup>. There has also been a small improvement in Europeans' knowledge of antibiotics since 2018. However, the EU should further promote a widespread adoption of best practices in antimicrobial stewardship. This can include the development of EU guidelines for the treatment of major common infections and the choice of appropriate antibiotics, including the need to ensure their most optimal and prudent use.

<sup>&</sup>lt;sup>119</sup> Eurobarometer 2022, Antimicrobial Resistance

<sup>&</sup>lt;sup>120</sup> Special Eurobarometer 478: Antimicrobial Resistance (in the EU)

<sup>&</sup>lt;sup>121</sup> European Centre for Disease Prevention and Control 2021, Reported decrease in antibiotic consumption across EU/EEA during COVID-19 pandemic.

### 5.8 <u>Further integrate the environment in AMR policy</u>

Other types of monitoring and surveillance are needed to understand how AMR develops in the environment in the presence of antimicrobial residues and/or what risks AMR pollution poses to human and animal transmission risk through crop irrigation, drinking water or recreational use of natural waters.

It is important to synthesize and review evidence on the environmental dimension of AMR and create opportunities to translate this evidence into policy and practice across sectors and different types of stakeholders. The subgroup of the AMR One Health Network<sup>122</sup> recommends developing EU guidelines and regulations to control through harmonized surveillance and manage environmental pollution, notably from wastewater treatment plants and manufacturing sites. The subgroup also concludes that there is a need to strengthen data collection and surveillance systems of the environment. In line with the One Health approach, environmental monitoring of AMR in freshwater and wastewater is essential to further understand the role that the environment plays in the emergence and spread of AMR, the levels of environmental contamination and the risks posed to human health. Monitoring is also essential to complement clinical data by providing sampling material from a large population. Actions in relation to the environment, notably concerning research and monitoring, as well as specific measures on soil and manure management should be included in Member State NAPs.

### 5.9 <u>Continue to support Member States and facilitate cooperation</u>

The EU is already using a range of tools at its disposal to support Member States in addressing AMR at national level; these support mechanisms should continue. Still, some Member States lack the knowledge and resources to sufficiently tackle the problem. The EU should consider whether there are further instruments, including financial and technical support that can be leveraged to strengthen capacity within Member States (e.g., mutual learning and best practice exchange between Member States). The EU-JAMRAI recommendations<sup>123</sup> further point to the need to enhance cooperation between Member States, highlighting that an extended and strengthened AMR One Health Network as well as cooperation with AMR stakeholders and relevant agencies (e.g., EFSA, EMA, ECDC, and EEA) is crucial to achieve this purpose and make Europe a best practice region.

## 5.10 <u>Strengthen the framework for action through targets and indicators</u>

The importance of introducing EU indicators and targets is reflected in the EU-JAMRAI recommendations and in the opinion of the EXPH, which underlines the need to prioritise the development of a comprehensive set of indicators and structured data to measure progress on tackling AMR, ensuring that they are integrated with relevant regulatory data collection requirements. The development of indicators and targets would provide clarity and alignment on goals and objectives and, through future monitoring and evaluation, help to identify where additional support is most needed. This will also contribute to a more robust evaluation of

<sup>&</sup>lt;sup>122</sup> Final report - Subgroup established under the EU AMR One Health Network to formulate suggestions for <u>AMR Actions</u>

<sup>&</sup>lt;sup>123</sup> European Joint Action on Antimicrobial Resistance and Healthcare-Associated Infections (EU-JAMRAI), LAYMAN REPORT

future AMR Action Plans, including of cost-effectiveness, by providing a clear framework for analysis and supporting data obtained through regular monitoring.

While an aspirational target for the reduction of the overall EU sales of antimicrobials for farmed animals and in aquaculture by 2030 has been included in the Farm to Fork Strategy and the contribution of Common Agriculture Policy (CAP) support measures to the reduced use of antimicrobials in farmed animals should be monitored<sup>124</sup>, there is currently no AMR related target in the human health sector at EU level. Therefore, the Commission, in cooperation with the ECDC, should introduce concrete targets both at EU and Member States level to reduce the unnecessary use of antimicrobials.

Furthermore, AMR action should be strengthened through specific and measurable EU-level targets on AMC and AMR and linked to related indicators that define progress, with efforts focused on those countries with the greatest challenges in meeting those targets. The recommended targets at Union level can be complemented by national targets that cover other AMR-related aspects such as IPC, antimicrobial stewardship, prescription practices and training.

## 6. CONCLUSION

Since its adoption and until now, the 2017 AMR Action Plan has made progress towards achieving its main objectives and, based on the reports reviewed and feedback gathered, has had an overall positive effect in making the EU a best practice region, boosting research, development and innovation by closing current knowledge gaps, and intensifying EU efforts worldwide to shape the global agenda on AMR. To date, experience shows that the 2017 AMR Action Plan is still overall fit for purpose.

Notwithstanding this, the future-proofing analysis drawing on scientific literature and reports and outcome assessment of the 2017 AMR Action Plan, which includes numerous consultations of all relevant parties, has led to identification of aspects that deserve particular attention in the short term. While much progress has been achieved in the veterinary sector, it is now crucial to further integrate the One Health approach, better address human health, support Member States in their efforts against AMR and increase actions in the environmental and global domains. The activities implemented under the 2017 AMR Action Plan need to be extended and complemented to maximize synergies to attain a stronger response to AMR across the EU and beyond. Based on this assessment, further support is put forward in the proposal for a Council recommendation, which focuses on specific topics, i.e., (1) NAPs against AMR, (2) surveillance and monitoring of AMR and AMC, (3) infection prevention and control, (4) antimicrobial stewardship and prudent use of antimicrobials, (5) recommended targets for AMC and AMR, (6) awareness, education and training, (7) research and development; incentives for innovation and access to antimicrobials and other AMR medical countermeasures, (8) cooperation and (9) global action.

<sup>&</sup>lt;sup>124</sup> On the basis of result indicator R.43 (share of livestock units concerned by supported actions to limit the use of antimicrobials) of the CAP Strategic Plan Regulation (Regulation (EU) 2021/2115 of the European Parliament and of the Council of 2 December 2021 establishing rules on support for strategic plans to be drawn up by Member States under the common agricultural policy (CAP Strategic Plans) and financed by the European Agricultural Guarantee Fund (EAGF) and by the European Agricultural Fund for Rural Development (EAFRD) and repealing Regulations (EU) No 1305/2013 and (EU) No 1307/2013 (OJ L 435, 6.12.2021, p. 1-186).