

POLICY BRIEF 63

# Strengthening the EU response to prevention and control of Antimicrobial Resistance (AMR)

## Policy priorities for effective implementation

Michael Anderson

Dimitra Panteli

Elias Mossialos

In collaboration with the Belgian Federal Public Service (FPS)  
Health, Food Chain Safety and Environment (HFCSE)

Keywords:

Anti-bacterial agents

Drug resistance, microbial

Drug resistance, bacterial

Health policy

Health governance

Biomedical research

One Health

### What is a Policy Brief?

A policy brief is a short publication specifically designed to provide policy makers with evidence on a policy question or priority. Policy briefs

- Bring together existing evidence and present it in an accessible format
- Use systematic methods and make these transparent so that users can have confidence in the material
- Tailor the way evidence is identified and synthesised to reflect the nature of the policy question and the evidence available
- Are underpinned by a formal and rigorous open peer review process to ensure the independence of the evidence presented.

Each brief has a one page key messages section; a two page executive summary giving a succinct overview of the findings; and a review setting out the evidence. The idea is to provide instant access to key information and additional detail for those involved in drafting, informing or advising on the policy issue.

Policy briefs provide evidence for policy-makers not policy advice. They do not seek to explain or advocate a policy position but to set out clearly what is known about it. They may outline the evidence on different prospective policy options and on implementation issues, but they do not promote a particular option or act as a manual for implementation.

This policy brief is one of a new series to meet the needs of policy-makers and health system managers. The aim is to develop key messages to support evidence-informed policy-making and the editors will continue to strengthen the series by working with authors to improve the consideration given to policy options and implementation.

### © World Health Organization, 2024

(acting as the host organization for, and secretariat of, the European Observatory on Health Systems and Policies)

Some rights reserved. This work is available under the Creative Commons Attribution-NonCommercial-ShareAlike 3.0 IGO licence (CC BY-NC-SA 3.0 IGO; <https://creativecommons.org/licenses/by-nc-sa/3.0/igo>).

Under the terms of this licence, you may copy, redistribute and adapt the work for non-commercial purposes, provided the work is appropriately cited, as indicated below. In any use of this work, there should be no suggestion that the WHO, the European Observatory on Health Systems and Policies or any of its Partners endorses any specific organization, products or services. The use of the WHO and the European Observatory on Health Systems and Policies logo is not permitted. If you create a translation of this work, you should add the following disclaimer along with the suggested citation: "This translation was not created by the World Health Organization (WHO) or the European Observatory on Health Systems and Policies. WHO and the European Observatory on Health Systems and Policies are not responsible for the content or accuracy of this translation. The original English edition shall be the binding and authentic edition".

Any mediation relating to disputes arising under the licence shall be conducted in accordance with the mediation rules of the World Intellectual Property Organization (<http://www.wipo.int/amc/en/mediation/rules/>).

**Suggested citation.** Anderson M, Panteli D, Mossialos E. *Strengthening the EU response to prevention and control of Antimicrobial Resistance (AMR): Policy priorities for effective implementation*. Copenhagen: WHO Regional Office for Europe; 2024. Licence: CC BY-NC-SA 3.0 IGO.

**Cataloguing-in-Publication (CIP) data.** CIP data are available at <http://apps.who.int/iris>.

**Sales, rights and licensing.** To purchase WHO publications, see <https://www.who.int/publications/book-orders>. To submit requests for commercial use and queries on rights and licensing, please contact [contact@obs.who.int](mailto:contact@obs.who.int).

**Third-party materials.** If you wish to reuse material from this work that is attributed to a third party, such as tables, figures or images, it is your responsibility to determine whether permission is needed for that reuse and to obtain permission from the copyright holder. The risk of claims resulting from infringement of any third-party-owned component in the work rests solely with the user.

**General disclaimers.** The designations employed and the presentation of the material in this publication do not imply the expression of any opinion whatsoever on the part of the WHO and the European Observatory on Health Systems and Policies or any of its Partners concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries. Dotted lines on maps represent approximate border lines for which there may not yet be full agreement.

The mention of specific companies or of certain manufacturers' products does not imply that they are endorsed or recommended by the WHO or the European Observatory on Health Systems and Policies or any of its Partners in preference to others of a similar nature that are not mentioned.

Errors and omissions excepted, the names of proprietary products are distinguished by initial capital letters. All reasonable precautions have been taken by the European Observatory on Health Systems and Policies to verify the information contained in this publication. However, the published material is being distributed without warranty of any kind, either expressed or implied.

The responsibility for the interpretation and use of the material lies with the reader. In no event shall the WHO, the European Observatory on Health Systems and Policies or any of its Partners be liable for damages arising from its use.

The named authors alone are responsible for the views expressed in this publication. The views and opinions expressed in Observatory publications do not necessarily represent the official policy of the Participating Organizations.

# Strengthening the EU response to prevention and control of Antimicrobial Resistance (AMR)

Policy priorities for effective implementation

---

<b>Contents</b>	page
Foreword	2
List of contributors	3
Acknowledgements	4
Acronyms	5
List of tables, figures and boxes	6
Key messages	7
Executive summary	8
Policy Brief	
1. Background	10
2. Boosting implementation of effective strategies to combat AMR	16
3. Conclusions	35
4. References	36
5. Annex	45

## **Editor**

Dimitra Panteli

## **Managing Editors**

Jonathan North

Lucie Jackson

The authors and editors are grateful to the reviewers who commented on this publication and contributed their expertise.

## **Authors**

**Michael Anderson**, Health Organisation, Policy, Economics (HOPE), Centre for Primary Care & Health Services Research, The University of Manchester, and LSE Health, Department of Health Policy, London School of Economics and Political Science, United Kingdom

**Dimitra Panteli**, European Observatory on Health Systems and Policies

**Elias Mossialos**, LSE Health, Department of Health Policy, London School of Economics and Political Science, United Kingdom, and European Observatory on Health Systems and Policies

**Print ISSN 1997-8065**

**Web ISSN 1997-8073**

---

## Foreword

In today's complex landscape of public health, few challenges stand as prominently as antimicrobial resistance (AMR). This multifaceted issue not only poses a direct threat to individual health but also reverberates across healthcare systems, agricultural practices and global economies.

AMR's impact on public health is profound and far-reaching. As pathogens develop increasing resistance to antimicrobials, treating infections becomes more difficult, leading to prolonged illnesses, increased mortality rates and heightened healthcare costs. Moreover, the effects extend beyond human health, affecting animal health and welfare, and the environment.

Addressing the menace of AMR demands a united front. A 'One Health' approach, recognizing the interconnectedness of human, animal, plant and environmental health, is essential. By fostering collaboration among diverse stakeholders, including the Directorate-General for Health and Food Safety (DG-SANTE), the European Health Emergency Preparedness and Response Authority (HERA), and other EU institutions, we can develop comprehensive strategies to combat AMR and protect public health.

While the challenges posed by AMR are intimidating, there is reason for optimism. International and national efforts to address AMR have gained momentum in recent years, culminating in the establishment of EU-level targets and the development of robust EU-level and national-level action plans. However, effective implementation remains a significant obstacle, with differences persisting among Member States.

This brief, presented under the auspices of the Belgian Presidency of the Council of the EU, serves as a vital exploration of the obstacles and opportunities inherent in implementing strategies to combat AMR. From enhancing antimicrobial stewardship in hospitals and the community sector to strengthening biosecurity measures in agricultural settings, each step forward requires careful consideration and collaboration across disciplines.

At the heart of our response to AMR lies strong and committed leadership. Leaders at all levels must navigate the complexities of this issue, designating clear roles and responsibilities among relevant stakeholders, and ensure accountability mechanisms are upheld. Further enablers for collective and sustainable actions include enhancing surveillance systems, advocating for responsible antimicrobial use, promoting antimicrobial stewardship programmes, and strengthening infection prevention and control measures.

As we embark on this critical effort, let us remain resolute in our commitment to addressing AMR. By strengthening governance structures and prioritizing AMR on the political agenda, we can pave the way for a healthier future for generations to come.

### **Prof. Dr. Dirk Ramaekers**

Chair Federal Public Service for Public Health, Food Chain Safety & Environment

## List of contributors

**Table A: List of contributors from the Belgian Federal Public Service (FPS) Health, Food Chain Safety and Environment (HFCSE)**

CONTRIBUTOR	ROLE
Zeynep Darici	Expert in European and International policies
Laurane Dubrunfaut	Expert in European and International policies
Thomas Janssens	Policy advisor – One Health coordinator of the National Action Plan on Antimicrobial Resistance (NAP AMR)
Katie Vermeersch	AMR coordinator – Animal Pillar
Vincent Dehon	Biocides policy officer
Melissa Rousseau	AMR coordinator – Environmental Pillar
Jennifer Pirotte	Biocides expert
Miryam Benalla	Division Plant Health – Scientific expert attaché – Plant Pillar
Lieven van Herzele	Division Plant Health – Head of the Division – Plant Pillar
Kristien Braeken	Division Plant Health – Scientific expert attaché – Plant Pillar

**Table B: Members of the Belgian Antibiotic Policy Coordination Committee (BAPCOC) support team**

MEMBER	ROLE
Ivo Deckers	AMR coordinator – Human Pillar / coordinator BAPCOC support team
Annemie Vlayen	Quality and Patient Safety cell leader
An Caluwaerts	Infection Prevention and Control (IPC) focal point
Ann Versporten	Antimicrobial Stewardship (AMS) in hospitals focal point
Florine Croquet	Antimicrobial Stewardship (AMS) in ambulatory care focal point
Harun Yaras	Host coordinator
Heidi Van Den Bossche	Antimicrobial Stewardship (AMS) hospital medicine focal point
Pascaline De Bie	Diagnostic Stewardship (DS) and Hand Hygiene focal point

---

## Acknowledgements

This publication was produced as a collaboration between the European Observatory on Health Systems and Policies, the London School of Economics and Political Science (LSE), and the Belgian Federal Public Service (FPS) Health, Food Chain Safety and Environment (HFCSE). It is being published to support the Belgian Presidency of the Council of the EU high-level meeting on Antimicrobial Resistance. The FPS HFCSE team was involved in the conception and drafting of this policy brief (individual contributors are outlined in Table A on page 3). Various scientific and professional organizations in Belgium along with individual experts have also provided feedback and suggested text for the brief, including the Belgian Antibiotic Policy Coordination Committee (BAPCOC, see Table B on page 3), Sciensano, the Federal Agency for Medicines and Health Products, and the Federal Agency for the Safety of the Food Chain. We would also like to acknowledge the contribution of all the experts from EU Member States and the European institutions who participated in a half-day workshop held in preparation of this brief to discuss implementation challenges for relevant AMR interventions (see 5. Annex). We are also grateful to Dominique L. Monnet (ECDC), and Ernesto Liebana (EFSA) who gave up their time for follow up interviews to provide further feedback. While insights from the workshop and feedback from stakeholders influenced the development of this brief, its contents do not necessarily reflect the views of the individuals or their institutions who participated in those processes.

We also extend our thanks to our colleagues at the European Observatory for their support in initiating, researching and producing this brief: Beatrice Durvy, Josep Figueras, Lucie Jackson, Suszy Lessof, Jonathan North and Erica Richardson. Many thanks also to Alison Chapman and Neil Adams for production support.

## Acronyms

AMR	antimicrobial resistance	HAP	hospital-associated pneumonia
AMS	antimicrobial stewardship	HERA	Health Emergency Response Authority
AMU	antimicrobial use	IGZ	Health Care Inspectorate (of the Kingdom of the Netherlands)
API	active pharmaceutical ingredient	IPC	infection prevention and control
ARG	antimicrobial resistance gene	IT	information technology
ARSIA	Association Régionale de Santé et d'Identification Animales	JPIAMR	Joint Programming Initiative on Antimicrobial Resistance
ASP	antimicrobial stewardship programme	MDRO	multidrug-resistant organism
ATP	adenosine triphosphate	MRP	mutual recognition procedure
AWaRe	Access, Watch, Reserve	MRSA	methicillin-resistant <i>Staphylococcus aureus</i>
BAPCOC	Belgian Antibiotic Policy Coordination Committee	MUMS	minor use or minor species
CAUTI	catheter-associated urinary tract infection	NVR	New Veterinary Regulation
CARB-X	Combating Antibiotic Resistant Bacteria Biopharmaceutical Accelerator	OECD	Organisation for Economic Co-operation and Development
CDSS	clinical decision support system	OHHLEP	One Health High-Level Expert Panel
CLABSI	central line-associated bloodstream infection	PNEC	predicted no-effect concentration
CRP	C-reactive protein	POCT	point-of-care testing
DDD	defined daily dose	PPB	plant pathogenic bacteria
DG-SANTE	Directorate-General for Health and Food Safety	PPS	point prevalence survey
DG-RTD	Directorate-General for Research and Innovation	R&D	research and development
EARSS	European Antimicrobial Surveillance System	RCT	randomized controlled trial
EC	European Commission	RSV	respiratory syncytial virus
ECDC	European Centre for Disease Prevention and Control	SME	small and medium-sized enterprise
EEA	European Economic Area	SPC	Summary of Product Characteristic
EFSA	European Food Safety Authority	SSI	surgical site infection
EMA	European Medicines Agency	TARGET	Treat Antibiotics Responsibly, Guidance, Education and Tools
ERA	environmental risk assessment	UN	United Nations
ESVAC	European Surveillance of Veterinary Antimicrobial Consumption	UNEP	United Nations Environment Programme
EU	European Union	USA	United States of America
FAO	Food and Agriculture Organization (of the United Nations)	VAP	ventilator-associated pneumonia
FBO	food business operator	VASC	Veterinary Advisory Service Contract
GARDP	Global Antibiotic Research and Development Partnership	WASH	water, sanitation and hygiene
GDP	gross domestic product	WHO	World Health Organization
GMP	good manufacturing practice	WOAH	World Organisation for Animal Health
GP	general practitioner		
HAI	healthcare-associated infection		

---

## List of tables, figures and boxes

### Tables

<b>Table 1:</b> WHO groupings of AMR interventions to improve antibiotic prescribing behaviours in healthcare settings	16
<b>Table 2:</b> Pathways through which vaccination can reduce AMR	20
<b>Table 3:</b> Selected implementation considerations for key AMR interventions in human health	21
<b>Table 4:</b> Selected implementation considerations for key AMR interventions in animal health	28
<b>Table 5:</b> Selected implementation considerations for key AMR interventions in environmental health	32
<b>Table 6:</b> Policy actions to secure sustainable access to antimicrobials	33

### Figures

<b>Figure 1:</b> Projected trends in antimicrobial resistance in EU/EEA countries among priority antibiotic-bacterium combinations, by line of antimicrobial treatment	10
<b>Figure 2:</b> Overall volume of antibiotics prescribed in OECD countries for human consumption, 2011, 2019 and 2021 (or nearest years)	11
<b>Figure 3:</b> Incentives developed to encourage antimicrobial research and development can be aligned by considering public health and market factors, as well as implementation and feasibility	34

### Boxes

<b>Box 1:</b> Antibiotic use for controlling plant pathogenic bacteria	12
<b>Box 2:</b> WHO AWaRe programme	12
<b>Box 3:</b> Importance of the One Health approach	13
<b>Box 4:</b> EU-level targets to reduce AMR	14
<b>Box 5:</b> Methodology behind the insights in this brief	15
<b>Box 6:</b> Point-of-care testing: a diagnostic tool to help physicians on the spot	17
<b>Box 7:</b> Drive-Antimicrobial Stewardship case study	17
<b>Box 8:</b> Optimizing environmental cleaning in healthcare facilities to reduce AMR	19
<b>Box 9:</b> The EU's veterinary regulation of 2019	24
<b>Box 10:</b> Antimicrobial stewardship programmes (ASPs) and clinical decision support systems (CDSSs) in veterinary medicine	25
<b>Box 11:</b> Biocheck and FarmFit systems	25
<b>Box 12:</b> Research projects to understand spread of AMR in the environment in Belgium	30



## Key messages

Antimicrobial resistance (AMR) is a major global public health challenge. It is driven by inappropriate antimicrobial use and poor infection prevention and control across human, animal, plant, and environmental health settings. With resistance to second and third-line antimicrobials growing the threat is profound. Key messages for policy-makers are that:

- **A paradigm change is needed based on collective responsibility.** National and international commitments to a “One-Health” approach offer some hope and bring sectors, disciplines, and communities together but despite years of policy discussion and much agreement, action has often been sluggish and ineffective.
- **Successful implementation is critical.** The factors that enable it work best in combination and include
  - Strong leadership commitment at all levels
  - Clear roles, responsibilities, and accountability mechanisms
  - Monitoring and surveillance with rapid feedback
  - Multidisciplinary teams and training
  - Tailored targets and benchmarking at multiple levels
  - Reimbursement models that incentivise appropriate antimicrobial use and prevention
  - Educational programmes and the promotion of awareness
  - Adequate funding for research, and
  - Policies which support sustainable innovation and access to effective antibiotics.
- **There are key, evidence-informed interventions that countries can usefully implement**
  1. In human health settings, key measures that work include:
    - Antimicrobial stewardship programmes
    - Clinical decision support systems (CDSS) for prescribers
    - Control of falsified and counterfeit antimicrobials
    - Infection prevention and control
    - Vaccination to prevent the emergence and spread of key pathogens
  2. Key effective interventions in animal health settings include:
    - Regulation and supervision to promote prudent use of antimicrobials
    - Improved biosecurity
    - Vaccination to prevent emergence and spread of key pathogens
    - Food safety compliance programmes
  3. Key steps that can make a difference in environmental health settings include:
    - Improving wastewater treatment facilities
    - Limiting concentration of antimicrobials in discharges from the pharmaceutical industry
    - Improving waste management in agricultural production
- **Policy-makers face barriers to action** including an absence of accountability mechanisms, healthcare and veterinarian staffing shortages, limited diagnostic and surveillance capacity, delayed feedback of surveillance data, misinformation on social media, shortages of essential antimicrobials and vaccines and lack of resources.
- **EU institutions have a key role to play** from legislation, to surveillance, to technical advice. The EU adds particular value in evidence-based guidelines; the efficacy and safety of antimicrobials and vaccines; joint procurement; research funding; and in providing platforms to coordinate policy and share good practices.
- **Action in and by countries continues to be essential** including in strengthening AMR national action plans to achieve EU-level targets. Strong leadership, balancing top-down and bottom-up interventions, optimizing the use of public resources and fostering accountability and responsiveness all support implementation at the national (and sub-national) level.
- **Collaboration is critical and requires suitable (and stronger) governance** mechanisms at the European and global levels to foster effective links across sectors and between European, national, regional and local stakeholders.
- **Keeping AMR on international and national political agendas is crucial**, and countries holding the Presidency of the Council of the EU can play a pivotal role in advancing this agenda.

## Executive summary

Antimicrobial resistance (AMR) leads to increased mortality and disability rates, alongside increased medical costs, prolonged hospital stays and socioeconomic impacts for households, communities and broader society. In 2019, it was estimated that antibiotic resistance directly caused 1.27 million deaths globally. Additionally, antibiotic resistance incurs approximately €1.1 billion in annual healthcare system costs for European Union (EU) and European Economic Area (EEA) countries.

AMR is driven by inappropriate antimicrobial use (AMU), as well as insufficient prevention and control across human, animal, plant and environmental health settings. Inconsistent access to essential antimicrobials and diagnostics further exacerbates the suboptimal treatment of infections. An insufficient antimicrobial research and development (R&D) pipeline also means that the supply of new antimicrobials is not sufficient to combat the increasing threat of AMR.

International and national efforts to tackle AMR have accelerated in recent years, with a significant milestone being the establishment of EU-level targets. However, the implementation of effective strategies varies among EU Member States and generally lags behind. Achieving the desired targets will require strengthening implementation of recommended AMR interventions.

This brief aims to summarize implementation considerations for effective strategies to address AMR. It draws upon guidance from the European Commission (EC), the World Health Organization (WHO), the Food and Agricultural Organization of the United Nations (FAO), the United Nations Environment Programme (UNEP), the World Organisation for Animal Health (WOAH) and the Organisation for Economic Co-operation and Development (OECD) to identify key recommended AMR interventions. Additionally, a workshop with representatives from EU institutions and Member States was conducted to identify implementation considerations. This brief will not cover considerations for effective strategies to address AMR in plant health settings.

Strengthening implementation of AMR interventions in human health settings requires:

- **Antimicrobial stewardship programmes (ASPs):** Strengthening implementation requires strong leadership commitment, combined with clear roles, responsibilities and accountability mechanisms, behavioural science approaches, improved diagnostic capacity and consistent access to antimicrobials.
- **Clinical decision support systems (CDSS) for prescribers:** Supporting implementation requires integration within electronic health records and prescriber software, user-friendly interfaces that minimize alert fatigue, use of updated guidelines, and investment in strengthening health IT infrastructure.

- **Regulation and related supervision to prevent falsified and counterfeit antimicrobials:** Robust traceability systems across supply chains, enhancing custom controls, inspections of pharmacies, and awareness campaigns are required to combat falsified and counterfeit antimicrobials.
- **Infection prevention and control (IPC) programmes:** IPC programmes should be aligned with ASPs and supported by legal and accountability frameworks, as well as monitoring and surveillance with rapid feedback mechanisms.
- **Vaccination to prevent emergence and spread of certain pathogens:** Vaccination should be integrated within AMR national action plans as a key strategic objective, and combined with efforts to address vaccine hesitancy and misinformation to strengthen implementation. There are also opportunities to prioritize which pathogens should be the focus of vaccine R&D, including implications for AMR.

Strengthening implementation of AMR interventions in animal health settings requires:

- **Regulation and related supervision to promote the prudent use of antimicrobials:** Prudent use of antimicrobials in animals could be optimized with sector-specific targets and benchmarking, payment mechanisms that adjust direct profits from antimicrobial sales, strict conditions on use of certain broad-spectrum antimicrobials, and aligning and updating summary product characteristics for veterinary antimicrobials across the EU. ASPs and CDSSs also have a key role in animal health to promote prudent use of antimicrobials.
- **Improved biosecurity to prevent emergence and spread of infection:** Contracts need to be designed to reward veterinarians for giving preventative and biosecurity advice, and the cost benefits of biosecurity need to be routinely reported and emphasized to farmers.
- **Vaccination to prevent emergence and spread of certain pathogens:** Investment is needed to stimulate R&D of novel vaccines in animal health, with an emphasis on unmet needs to reduce AMR and transmission to humans.
- **Food safety compliance programmes:** Food safety messages, such as thorough cooking and good hygiene practices, should be integrated into AMR awareness campaigns, and surveillance of AMR in food should be strengthened.

Strengthening implementation of AMR interventions in environmental health settings requires:

- **Optimizing wastewater treatment to minimize spread of AMR:** While the EU has a clear regulatory framework for wastewater treatment, investment in research and consensus building could help establish which improvements in wastewater treatment facilities should be prioritized to reduce AMR.

- **Limiting dissemination from the pharmaceutical industry:** Current concentration targets for antimicrobials in waste effluent from the pharmaceutical industry are voluntary, and mandating maximum concentration targets at the EU level may improve compliance and consistency of implementation.
- **Improving waste management in agricultural production:** Improvements in agricultural waste management would have multiple benefits including reducing the dissemination of AMR in the environment and promoting sustainable soil management practices, although more evidence is needed on acceptable concentration levels of antimicrobials.

Common enablers for implementation include: the importance of strong leadership commitment, combined with clear roles, responsibilities and accountability mechanisms; ensuring sufficient funding for interventions listed within national action plans; use of targets to drive progress through integrated One Health surveillance systems at the national level; optimizing reimbursement and revenue models to ensure that antimicrobial prescribing is appropriate; enhanced public awareness and training initiatives; and investment in research and evaluation of AMR interventions. Keeping AMR on international and national political agendas is key, and subsequent Presidencies of the Council of the EU could play a pivotal role in advancing this agenda.

## Policy brief

### 1. Background

#### Why is it critical to address AMR now?

Antimicrobials – including antibiotics, antivirals, antifungals and antiprotazoals – are medicines used to prevent and treat infections in humans, animals and plants. AMR refers to the ability of micro-organisms to survive or to grow in the presence of a concentration of an antimicrobial agent which is usually sufficient to inhibit or kill them (EUR-Lex, 2018a). AMR is described by the World Health Organization as one of the top 10 public health challenges worldwide as it poses major threats to modern medicine and global health (WHO, 2019a). The European Commission classifies AMR as one of the top three priority health threats in the EU (European Commission, 2022a).

#### AMR leads to increased mortality and disability.

AMR has made common infections increasingly difficult or impossible to treat, and leads to higher medical costs, prolonged hospital stays and increased mortality. Antimicrobials are not just essential for the treatment of infections, but also facilitate the safe provision of surgery and oncology care. In 2019, it was estimated that 4.95 million deaths worldwide were associated with bacterial AMR, including 1.27 million deaths directly attributable to bacterial AMR. Specifically for the WHO European Region, it is estimated that 541,000 deaths were associated with bacterial AMR in 2019, including 133,000 deaths directly attributable to bacterial AMR (Mestrovic et al., 2022).

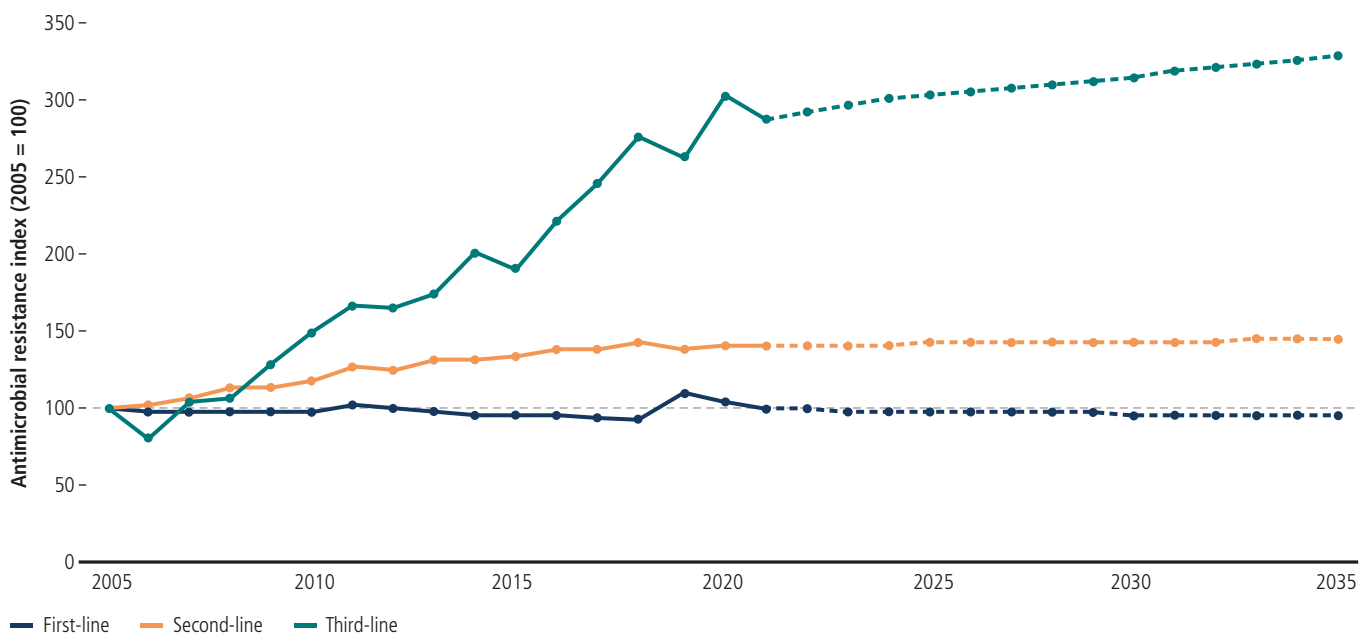
*AMR is responsible for significant costs for individuals, health systems and society.*

Individuals that contract resistant pathogens are at risk of mortality, long-term disability, catastrophic health expenditure and lost income, as well as delay of effective treatment, with suffering and socioeconomic impacts for households and communities. The estimated cost of AMR for healthcare systems in Europe is €1.1 billion per year (OECD, ECDC, EFSA & EMA, 2022). These costs result from several impacts of AMR, including increased hospitalization, greater length of stay, increased treatment costs, and reduced ability to safely provide treatments such as chemotherapy and surgical care. AMR also has significant economic implications for societies at large resulting from reductions in the size and productivity of the workforce, increased healthcare expenditure, and reductions in livestock production and trade. These factors all contribute to reduced gross domestic product (GDP) associated with AMR, with estimates indicating that AMR will cost the global economy up to \$100 trillion by 2050 (Review on Antimicrobial Resistance, 2016).

#### Resistance to second- and third-line antimicrobials is growing.

When an infection does not respond to a first-line antimicrobial treatment (the most effective and safest treatment option for the patient), healthcare professionals turn to more expensive alternatives, such as second- and third-line antimicrobials (the last treatment options available). Resistance to last-resort antimicrobials is growing. Figure 1 shows that AMR to second- and third-line antimicrobials, used when bacteria are resistant to common antimicrobials, is both high and projected to keep increasing in EU/EEA countries.

**Figure 1: Projected trends in antimicrobial resistance in EU/EEA countries among priority antibiotic-bacterium combinations, by line of antimicrobial treatment**



Source: OECD, 2023a.

Note: Historical data go from 2005 to 2020, and forecasts start in 2021.

### What are the main drivers of AMR?

The emergence of AMR is multifactorial and dynamic, and driven by factors such as inappropriate use of antimicrobials, suboptimal prevention of infection, and an insufficient antimicrobial pipeline. The drivers of AMR involve stakeholders working across human, animal, plant and environmental health.

#### Inappropriate antimicrobial use in human, animal and plant health drives increased AMR.

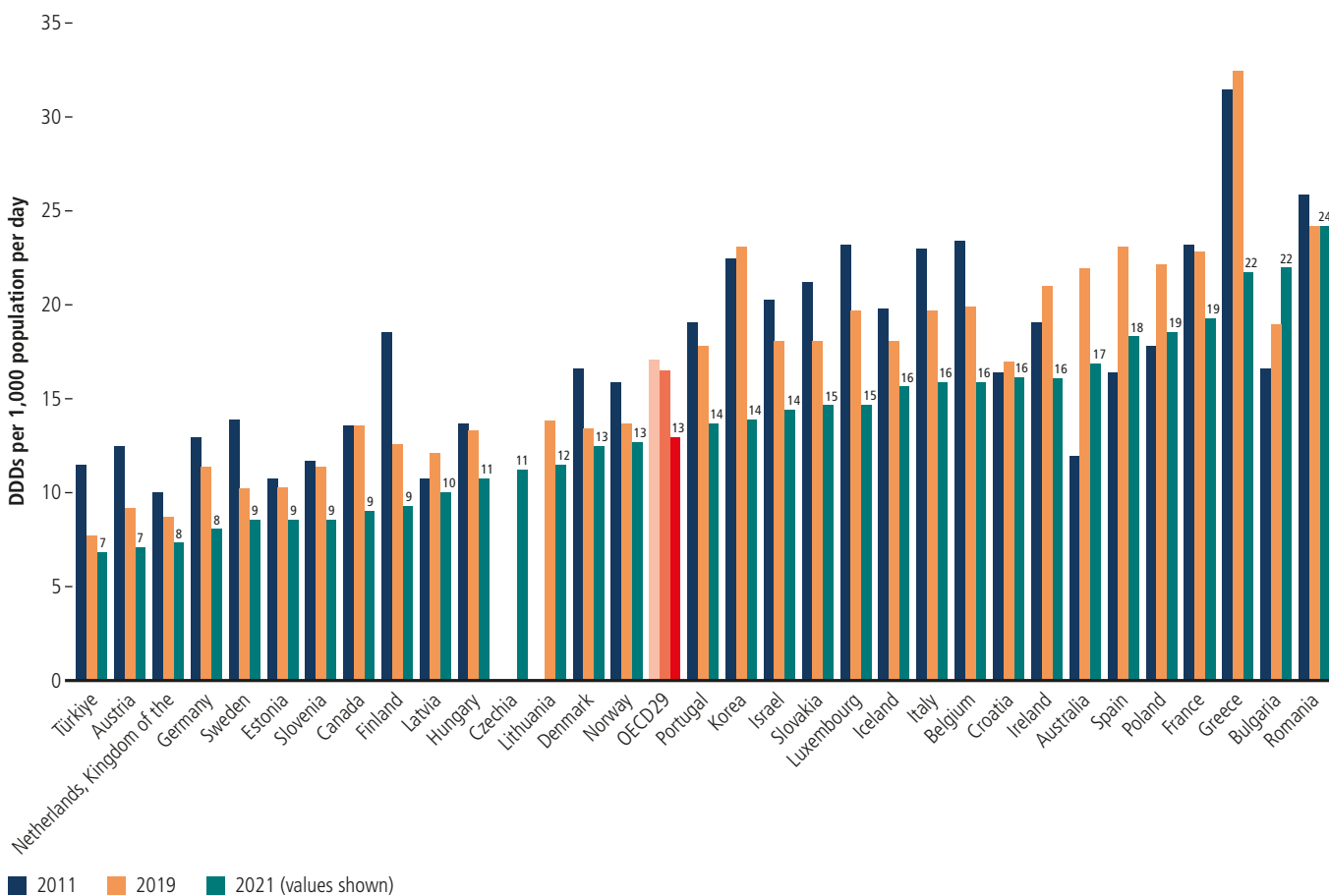
Wrong antimicrobial choices, inadequate dosing and unnecessarily extended treatment drive AMR within human, animal and plant health settings (Agyeman et al., 2022). This is because antimicrobials can exert a ‘selective pressure’ on pathogens, where random mutations create resistant pathogens that survive antimicrobial treatment to then multiply and spread.

The overall volume of antimicrobials prescribed in human health settings in 2021 varied three-fold across OECD countries (Figure 2). The observed variation might be explained, on the supply side, by differences in the guidelines and incentives that govern primary care prescribers and, on

the demand side, by differences in attitudes and expectations regarding the optimal treatment of infectious illness.

Worldwide, it is estimated that approximately two-thirds of all antimicrobials are used in animals rather than humans (Tiseo et al., 2020). The European Commission’s Farm to Fork Strategy aims to reduce the overall sales of antimicrobials in farm animals and aquaculture in the EU by 50%, down to 59.2mg/PCU in 2030 compared to 118.3mg/PCU in 2018 (European Commission, 2020a). According to the Thirteenth European Surveillance of Veterinary Antimicrobial Consumption (ESVAC) report, aggregated sales declined significantly in 2022 and, according to the latest available data, over half of the targeted 50% reduction has already been achieved. However, total sales and trends vary greatly between the different reporting countries, from 2.1mg/PCU to 254.7mg/PCU (EMA, 2023). Differences in the composition of the animal population and production systems, as well as in disease incidence, prescription practices, daily doses used and treatment duration, may explain some of the variation in total sales between Member States (EMA, 2022). Increasingly, the extent of antibiotic use in plants has also been acknowledged (Box 1, page 12).

Figure 2: Overall volume of antibiotics prescribed in OECD countries for human consumption, 2011, 2019 and 2021 (or nearest years)



Source: OECD, 2023b.

Note: Data exclude products used in the treatment of addiction.

Defined daily dose (DDD) is the assumed average maintenance dose per day for a drug used for its main indication in adults. For instance, the DDD for oral aspirin equals 3 grammes, the assumed maintenance daily dose to treat pain in adults. DDDs do not necessarily reflect the average daily dose actually used in a given country. For more details, see Norwegian Institute of Public Health, 2023.

**Box 1: Antibiotic use for controlling plant pathogenic bacteria**

Like humans and animals, plants are affected by bacterial diseases, e.g. the fireblight or Rosaceae caused by *Erwinia amylovora*, Pierce's disease caused by *Xylella fastidiosa* or the bacterial blight of rice caused by *Xanthomonas oryzae*. These diseases remain difficult to control and may cause impactful epidemics. Yet, there is a lack of data on the use of antibiotics as plant protection products worldwide, despite growing concerns on the possible contribution to AMR in crops commonly used as feed and food.

Based on a recent study by UCLouvain, co-funded by the European Food Safety Authority (EFSA) (Verhaegen et al., 2024), up to 39 countries use antibiotics such as kasugamycin, gentamicin, streptomycin, oxolinic acid, oxytetracycline, validamycin and zhongshengmycin. This work also demonstrated the lack of robust publicly available data, the rapid changes of use over time and the unofficial use of antibiotics in some areas. Moreover, antibiotic resistance genes (ARGs) have been identified in plant pathogenic bacteria (PPB) (Verhaegen et al., 2023). Streptomycin resistance is the most frequently reported in PPB, in 18 different countries. The ability of ARGs to spread among the plant-associated phytomicrobiome, via mobile genetic elements, is a source of concern from a One Health perspective. For instance, the Tn5393 transposon and its variants, carrying streptomycin resistance genes, have been found in the human pathogen *Salmonella enterica* and *Klebsiella pneumoniae*. This emphasizes the need to develop alternative control measures for controlling PPB, for which some are already commercially available while many more are under development.

Produced by: Verhaegen M<sup>a</sup>, Mahillon J<sup>a</sup>, Stancanelli G<sup>b</sup>, Streissl F<sup>b</sup> and Bragard C<sup>a</sup>.

<sup>a</sup> Earth&Life Institute – Applied Microbiology, UCLouvain, Belgium.

<sup>b</sup> Environment, Plants & Ecotoxicology (PLANTS) Unit, European Food Safety Authority, Parma, Italy.

***Insufficient prevention and control of infection is a key contributor to increased AMR.***

Infection prevention and control is key to reducing the risk and spread of AMR in human, animal and environmental health settings. A review of antibiotic-resistant infections in EU/EEA countries between 2016 and 2020, found that around 70% of cases of infections were healthcare-associated infections (HAIs) (ECDC, 2022). IPC is also at the core of a number of other major global health priorities, including health emergencies and the International Health Regulations, patient and health worker safety, AMR action plans, sepsis prevention, Water, Sanitation and Hygiene (WASH), and integrated people-centred, high-quality care.

In 2021–2022, a detailed global survey on the minimum requirements for national IPC programmes in human health settings carried out by WHO showed that an active IPC programme (a functioning programme with annual workplans and budget) existed in about half of the participating countries (WHO, 2022a). However, very few met all minimum requirements for IPC. Relevant gaps were limited availability of a budget specifically dedicated to IPC, limited support at the national level for IPC training roll-out and monitoring of its effectiveness, and lack of expertise to conduct IPC monitoring (WHO, 2022a).

From the animal health perspective, IPC is achieved through a variety of measures, including biosecurity

measures, good animal husbandry, vaccination, access to WASH, and monitoring and surveillance. Despite evidence that implementation of biosecurity measures can reduce AMU (Postma et al., 2016 ; Diana et al., 2020), there remains variation in implementation of recommended standards across Member States (Filippitzi et al., 2018; Souillard et al., 2024).

***Several pathways contribute to the transmission and dissemination of AMR in the environment.***

The environment is a major reservoir and driver of AMR. Resistant micro-organisms and their resistance genes enter the soil, air, water and sediments through various ways, including: (i) industrial and municipal wastewater (including hospital effluents); (ii) sewage sludge and spreading of animal manure; and (iii) aquaculture systems (Samreen, Malak & Abulreesh, 2021). The application of biocides, pharmaceuticals and plant protection products, such as fungicides, have also led to the selection of resistant micro-organisms, which causes serious challenges to the natural environment. Surveillance and monitoring of AMR in the environment is therefore crucial to understand the role played by antimicrobial residues in the emergence and spread of AMR, the levels on environmental contamination and the risk posed to human and animal health (Niegowska, 2021).

***Inconsistent access to essential antimicrobials contributes to suboptimal treatment of infections.***

In addition to developing new antimicrobials, ensuring access to essential medications is vital for combating AMR. Numerous countries lack access to both new and pre-existing antimicrobials. In 2019, healthcare systems in the EU reported more than 1300 instances of antimicrobial shortages (European Commission, 2021a). This scarcity forces clinicians to resort to second-choice antimicrobials, potentially leading to prolonged infections and escalating the threat of AMR. WHO categorizes antimicrobials into three distinct tiers: 'Access', 'Watch' and 'Reserve', each determined by its potential for inducing resistance (Box 2).

**Box 2: WHO AwaRe programme**

In 2017, WHO introduced the Access, Watch, Reserve (AwaRe) system to classify antimicrobials based on their impact on AMR, priority for antimicrobial stewardship (AMS) and activity against multidrug-resistant organisms (MDROs) (Sharland et al., 2018).

**Access** antimicrobials are antimicrobials active against a limited number of pathogens. They generally have fewer side-effects, a lower potential for the selection of AMR and a lower cost.

**Watch** antimicrobials generally have a higher potential for the selection of AMR than Access antimicrobials and are more commonly indicated for use in sicker patients in the hospital facility setting. Their use should be carefully monitored to avoid overuse. **Reserve** antimicrobials are last-resort antimicrobials, and their use should be mostly limited to treat severe infections caused by multidrug-resistant pathogens in healthcare facilities.

In 2022, the AwaRe classification was supplemented by the AwaRe antimicrobial book, which contains detailed information on how to use antimicrobials on the WHO Model List for essential medicines for over 30 infections and surgical prophylaxis (Sharland et al., 2018, 2022; WHO, 2022b; Zanichelli et al., 2023).

For most common infections, the 'Access' category is adequate, as these antimicrobials exhibit minimal resistance development. Resorting to less effective antimicrobials due to shortages worsens resistance and may necessitate the use of broader-spectrum alternatives, which carry their own resistance risks. However, it is concerning that even staple 'Access' antimicrobials like amoxicillin face regular shortages. Alarming, by 2020, eight nations within Europe had not achieved the WHO's benchmark of ensuring that 'Access' antimicrobials constituted 60% of their consumption (WHO, 2019b).

### ***The antimicrobial R&D pipeline is insufficient to meet the challenge of AMR.***

In recent decades, only a few new antimicrobials have been developed, with most lacking novel features. This makes them vulnerable to developing resistance. In 2022, WHO described the current antimicrobial pipeline as insufficient to combat rising AMR (WHO, 2022c). Obstacles for antimicrobial R&D are substantial. Large pharmaceutical companies have exited antimicrobial R&D due to high failure rates, scientific challenges and lower profitability compared to other medicines. Consequently, academic institutions and small and medium-sized enterprises (SMEs) are now leading antimicrobial R&D. However, many SMEs face economic hardships upon launching new antimicrobials. Even with push incentives that lead to innovative preclinical approaches, SMEs struggle to get funding, especially during high-risk initial stages. These enterprises are in pursuit of strategies that would guarantee more consistent financial backing from the investors (Anderson, Panteli & Mossialos, 2023).

### ***What has been done to tackle AMR so far at the international level?***

Given the multiple drivers of AMR described in the previous section, developing policy responses to the drivers of AMR requires a 'One Health' approach (Box 3).

### ***All countries are expected to implement and update AMR national action plans with a One Health approach.***

Over the past 20 years, both international and national efforts to address AMR have increased substantially. Two significant global milestones mark this progress. First, the initiation of the World Health Organization Global Action Plan on Antimicrobial Resistance in 2015 (WHO, 2015), which called upon all nations to formulate national action plans by 2017. Second, the United Nations (UN) General Assembly reached a political consensus on AMR in 2016, with participating countries signing a declaration that involved committing to develop and implement multisectoral national action plans across human, animal and environmental health in accordance with the 'One Health' approach (UN, 2016).

At the EU level, as early as 1998, the European Commission established the European Antimicrobial Surveillance System (EARSS) and in 2001 the Community Strategy against AMR was published (EUR-Lex, 2001). The EU Council's recommendations on the prudent use of antimicrobial

### **Box 3: Importance of the One Health approach**

'One Health' has been developing as a concept over the past 20 years (Gibbs, 2014), following the increasing realization that effective response to emerging zoonotic diseases requires intersectoral and interdisciplinary collaboration.

In 2022, the One Health High-Level Expert Panel (OHHLEP) from the United Nations' agencies released a formal definition of One Health: "One Health 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. The approach mobilizes multiple sectors, disciplines and communities at varying levels of society to work together to foster well-being and tackle threats to health and ecosystems, while addressing the collective need for healthy food, water, energy, and air, taking action on climate change, and contributing to sustainable development" (Mettenleiter et al., 2023). The One Health Joint Plan of Action (2022–2026) includes several actions related to AMR and has been launched at global level by the Quadripartite Alliance, which brings together four leading organizations: the Food and Agriculture Organization of the United Nations (FAO), the United Nations Environment Programme (UNEP), the World Health Organization (WHO) and the World Organization for Animal Health (WOAH) (FAO, UNEP, WHO & WOAH, 2022).

Among global public health challenges, the fight against AMR is one where the benefits of the One Health approach have been most frequently highlighted. The European One Health Action Plan against Antimicrobial Resistance (AMR), released in 2017, represents a landmark initiative uniting human health, animal health and environmental sectors in a collaborative effort to combat AMR (European Commission, 2017). This comprehensive plan lays out a strategic framework to safeguard public health, animal health and the environment. Implementing a One Health approach to combat AMR involves collaboration between human health, animal health and environmental sectors to address the interconnectedness of antimicrobial use and resistance in these domains.

agents in human medicine followed in 2002 (EUR-Lex, 2002). As of 2006, the use of antibiotics for promoting growth in animals was banned in all EU countries (EUR-Lex, 2003a). These policies were reinforced by the 2011–2016 Commission Action Plan against the rising threats from AMR, designed to foster action among Member States (EUR-Lex, 2011). This was subsequently enhanced through the implementation of the 2017 EU One Health Action Plan against AMR, aiming to position the EU as a beacon of best practices, invigorate research, development and innovation, and influence the global discourse on AMR (European Commission, 2017). In 2019, the New Veterinary Regulation (NVR) followed, banning the prophylactic use of antibiotics in groups of animals, restricting metaphylactic use of antimicrobials in animals, and providing for the possibility to restrict the use of certain antimicrobials to human use only (EUR-Lex, 2018a).

### ***EU-level targets for AMR in human and animal health were set out in 2023 and 2020, respectively.***

Over the years, several Presidencies of the Council of the EU have focused on AMR as a policy priority (Anderson et al., 2019). The 2024 Belgian Presidency of the Council of the European Union was preceded by the Swedish (Jan–Jun 2023) and the Spanish (Jul–Dec 2023) Presidencies.

The three Presidencies had a common goal to keep the fight against AMR high on the political agenda of the next European Commission. On 13 June 2023, under the Swedish Presidency, the Council adopted the Commission's proposal for recommendations on stepping up EU actions to combat AMR (General Secretariat of the Council, 2023). After its adoption, the Recommendation was published in the Official Journal of the European Union (EUR-Lex, 2023). A major development contained within the Council Recommendations was the definition of targets to reduce antimicrobial consumption and AMR in human health (Box 4). The Commission intends to report on the progress of this Recommendation four years after its adoption. These targets also complement the aforementioned EU-level targets to reduce overall EU sales of antimicrobials for farmed animals and in aquaculture included in the Farm to Fork Strategy (European Commission, 2020a) and in the Zero Pollution Action Plan (European Commission, 2021b).

#### Box 4: EU-level targets to reduce AMR

##### PROPOSED TARGETS FOR AMR AND ANTIMICROBIAL CONSUMPTION IN HUMAN HEALTH (2023)

- Decrease of 20% in the total consumption of antimicrobials in humans in the EU by 2030 (using 2019 as baseline).
- 65% of the total consumption of antimicrobials in humans being from the 'Access' group, as per the AwaRe classification of the WHO by 2030.
- By 2030, reduce by 15% bloodstream infections due to methicillin-resistant *Staphylococcus aureus* (MRSA); by 10% bloodstream infections due to third-generation cephalosporin-resistant *Escherichia coli*; and by 5% bloodstream infections due to carbapenem-resistant *Klebsiella pneumoniae* (using 2019 as a baseline).

##### TARGETS FOR ANTIMICROBIAL USE IN ANIMALS (2020)

- 50% reduction of overall EU sales of antimicrobials for farmed animals and in aquaculture by 2030 (using 2018 as a baseline).

Source: Targets from (General Secretariat of the Council, 2023) and (European Commission, 2020a).

#### What does this brief add?

Despite increasing awareness of the detrimental effects of AMR and the complexity of its drivers, progress in terms of policy implementation has been slow. The purpose of this policy brief is to identify key enablers and barriers to sustainable implementation of recommended interventions to tackle AMR in human, animal and environmental health settings in line with the One Health approach and to provide a basis for future policy action. We acknowledge that plant health is also an important aspect of the One Health approach that is not covered within this policy brief but should be the subject of future research and policy discussion.

The brief zooms in on 12 interventions (five in human health, four in animal health and three in environmental health) identified through a targeted review of international policy documents from the WHO (WHO, 2015), European Commission (European Commission, 2017), UNEP (UNEP, 2023), WOAAH (OIE, 2016; WOAAH, 2022), FAO (FAO, 2016, 2021) and OECD (OECD, 2023b) (see Box 5). These are:

- Human health:
  1. Antimicrobial stewardship programmes to promote prudent antimicrobial use.
  2. Clinical decision support systems for prescribers.
  3. Regulation and related supervision to prevent falsified and counterfeit antimicrobials.
  4. Infection prevention and control programmes.
  5. Vaccination to prevent emergence and spread of certain pathogens.
- Animal health:
  1. Regulation and related supervision to promote the prudent use of antimicrobials.
  2. Improved biosecurity to prevent emergence and spread of infection.
  3. Vaccination to prevent emergence and spread of certain pathogens.
  4. Food safety compliance programmes.
- Environmental health:
  1. Optimizing wastewater treatment to minimize spread of AMR.
  2. Limiting dissemination from the pharmaceutical industry.
  3. Improving waste management in agricultural production.



**Box 5: Methodology behind the insights in this brief**

A targeted literature review of international policy documents from the WHO (WHO, 2015), the European Commission (European Commission, 2017), UNEP (UNEP, 2023), WOAAH (OIE, 2016; WOAAH, 2022), FAO (FAO, 2016, 2021) and OECD (OECD, 2023b) was carried out in November 2023. These international organizations were selected because they have carried out seminal work on AMR, and their reports synthesize evidence derived from existing literature and expert consensus during the development of their policy documents.

Relevant operational, regulatory and financial enablers and barriers were identified in the literature and discussed during a workshop held virtually in February 2024. In total, representatives from 18/27 Member States attended. The majority of Member State representatives were AMR experts from their respective countries, with expertise in human, animal and environmental health. The remaining attendees were representatives from key EU institutions, including the European Centre for Disease Prevention and Control (ECDC), European Medicines Agency (EMA), EFSA, Directorate-General for Health and Food Safety (DG-SANTE), HERA, Directorate-General for Research and Innovation (DG RTD), and WHO EURO. A full list of representatives is provided in supplementary material (Annex).

The following sections summarize key implementation considerations for the selected interventions and outline roles and responsibilities of EU institutions and Member States where applicable. They are predominantly based on the insights gathered during the participatory approach described in Box 5, but also consider the detailed study of the barriers to effective development and implementation of national policies on AMR funded by the European Commission (European Commission et al., 2023) and the WHO Roadmap on Antimicrobial Resistance for the WHO European Region 2023–2030 (WHO Regional Office for Europe, 2023). They also incorporate case studies from Belgium to highlight what is possible at the national level.

## 2. Boosting implementation of effective strategies to combat AMR

The following sections briefly discuss key implementation enablers and barriers for the selected interventions, and how different actors can engage at the national and EU levels in the areas of human, animal and environmental health, and with regard to ensuring access to effective antimicrobials. The main findings are summarized in Tables 3, 4 and 5 (on pages 21–23, 28–29 and 32, respectively).

### 2.1. Human health

#### 2.1.1 Antimicrobial stewardship programmes

Antimicrobial stewardship programmes are organizational or system-wide healthcare strategies that promote the appropriate use of antimicrobials through the implementation of evidence-based interventions (WHO, 2019c). These programmes encompass a diverse array of persuasive, restrictive and structural interventions (see Table 1), with most being multicomponent in nature. One structural intervention, point-of-care testing (POCT), is receiving increasing attention as a clinically- and cost-effective antimicrobial stewardship

tool (Box 6, page 17). ASPs are known to be effective in both inpatient (Davey et al., 2017) and outpatient settings (Edeghere, Wilson & Hyde, 2010). Research has also shown that ASPs that involve a pharmacist are more effective than those that do not (Saha, Hawes & Mazza, 2019; Monmaturapoj et al., 2021; Kooda, Canterbury & Bellolio, 2022; Lee & An, 2022). It has been estimated that ASPs can prevent more than 3.7 million additional days of hospitalization annually in OECD countries (OECD, 2023b). These findings highlight the significance of investing in ASPs as a sustainable and cost-effective strategy to address AMR and improve overall healthcare efficiency.

Member States are responsible for designing policies that encourage the implementation of ASPs, however the ECDC plays a crucial role in conducting surveillance and country visits, and in providing training and education. The EC has also published EU Guidelines for the prudent use of antimicrobials in human health (EUR-Lex, 2017) and funds AMS initiatives (Box 7, page 17). The Health Emergency Response Authority (HERA)'s mandate to support development of diagnostics and strengthen laboratory and surveillance capacity has the potential to contribute substantially over the next few years.

**Table 1: WHO groupings of AMR interventions to improve antibiotic prescribing behaviours in healthcare settings**

INTERVENTION TYPE	EXAMPLE INTERVENTIONS
<b>Persuasive (education)</b> = strategies that rest on provider education and feedback efforts to induce behaviour change	<ul style="list-style-type: none"> <li>• Educational meetings (e.g. basics on antibiotic use, case-based discussions, morbidity and mortality, significant event analysis, lectures on specified topics)</li> <li>• Distribution of and training on educational material (e.g. clinical practice guidelines)</li> <li>• Using local key opinion leaders/champions to advocate for key messages</li> <li>• Reminders provided verbally, on paper or electronically</li> <li>• AMS e-learning resources made available to all personnel</li> <li>• AMS education as part of undergraduate and continuing education for all healthcare professionals</li> </ul>
<b>Persuasive (feedback)</b> = strategies that limit opportunities to use antibiotics	<ul style="list-style-type: none"> <li>• Audit with feedback to prescribers on their prescribing practice</li> <li>• AMS as a component of ward rounds (e.g. real-time feedback with educational component)</li> <li>• Patient handover meetings between two shifts with real-time feedback by consultants</li> <li>• Local consensus processes for changes in antibiotic treatment or surgical prophylaxis</li> </ul>
<b>Restrictive</b> = strategies that target organizational elements of care	<ul style="list-style-type: none"> <li>• Formulary restrictions</li> <li>• Restricted prescribing of identified antibiotics (e.g. expert approval prior to prescription)</li> <li>• Compulsory order forms for targeted antibiotics</li> <li>• Automatic stop orders (e.g. after a single dose of surgical prophylaxis)</li> <li>• Selective susceptibility reporting from the laboratory</li> </ul>
<b>Structural</b> = often IT interventions	<ul style="list-style-type: none"> <li>• Rapid laboratory testing made available (such as point-of-care C-reactive protein (CRP) testing)</li> <li>• Therapeutic drug monitoring</li> </ul>

Source: Adapted from WHO, 2019c.

**Box 6: Point-of-care testing: a diagnostic tool to help physicians on the spot**

Point-of-care testing encompasses diagnostic tools that can be used where healthcare is provided or near the patient, such as C-reactive protein (CRP) testing. This is increasingly used by many providers aiming to reduce unnecessary AB prescription (Sanders et al., 2008; Falk & Fahey, 2009). The usual tests performed in laboratories often take too long (typically 48–72 hours) to be helpful for immediate prescription, whereas POCT can help the clinicians evaluate in a few minutes the probability of the need for antibiotics (Roos et al., 2019). Even though most infections managed in primary care are from viral origins, it remains particularly challenging for the general practitioner (GP) to discriminate them from bacterial etiologies or to exclude bacterial secondary infection, and consequently to decide if there is a need to prescribe antibiotics (Vicentini et al., 2022). In paediatric settings, the use of POCT in the first line has proved to be efficient in guiding clinical decisions and therefore significantly reducing the prescription and use of antibiotics, although more studies are needed to assess these findings (Vicentini et al., 2022; Brigadoi et al., 2023). In adult patients, POCT has been described as a cost-effective and clinically effective antimicrobial stewardship tool. A Cochrane review of six randomized controlled trials (RCTs) concluded that the use of CRP POCT was associated with a 22% reduction in antibiotic prescribing in adults with acute respiratory tract infections (Aabenhus et al., 2014). Even though a significantly higher reconsultation rate within the 30 days has been shown, the benefits of the technique outweigh this potential harm (Martínez-González et al., 2020).

Source: Provided by Belgian Antibiotic Policy Coordination Committee (BAPCOC).

**Box 7: Drive-Antimicrobial Stewardship case study**

A novel project implementing quality improvement and implementation science is the 'Data-driven implementation of a behavioural Antimicrobial Stewardship approach with expert consultancy for appropriate antimicrobial use in Europe ('drive-AMS')', a European project funded by the EU4Health Programme (European Commission, 2022b). The 'drive-AMS' project aims to reduce inappropriate AMU through supporting effective implementation of AMS interventions with a step-wise behaviour change approach. This combines three key elements: 1) measurement of antimicrobial prescribing, resistance and HAIs through the web-based Global-point prevalence survey (PPS) (Pauwels et al., 2021); 2) thorough training on understanding AMS principles; and 3) implementation through the development of locally based SMART AMS projects based on Global-PPS results, identified capabilities, opportunities and motivation, and supported by expert advice for the local project implementation. The drive-AMS project runs from November 2022 until October 2025, and foresees a continuation of national DRIVE-AMS courses, extending capacity (train the trainer) to other EU countries, continuing Global-PPS support and sustaining expert support to EU and non-EU countries.

**Strengthening implementation of antimicrobial stewardship programmes requires strong leadership commitment; clear roles and responsibilities; accountability mechanisms; behavioural science approaches; improved diagnostic capacity; and consistent access to antimicrobials.**

ASPs are complex interventions with varying success of implementation within and between Member States. There is substantial value in using behavioural science approaches to understand which AMS interventions are more effective than others in different settings and contexts (and why that is the case) (Borek et al., 2022). Several multicomponent AMS interventions with behavioural change techniques have resulted in significant reductions in antimicrobial prescribing (Borek et al., 2020). Examples include online communication skills training (Butler et al., 2012; Little et al., 2013); guidelines and Treat Antibiotics Responsibly, Guidance, Education and Tools (TARGET) resources (McNulty et al., 2018); feedback to high prescribers in primary care (Hallsworth et al., 2016); use of interactive booklets for parents/carers of children presenting with respiratory tract infections (Francis et al., 2009); and evidence-based practice protocols for risk classification and management of sore throats (Cox & Jones, 2001).

Strong leadership commitment is required from healthcare managers and leaders to ensure that AMS remains a high-level organization priority, and leadership training courses may help achieve this goal. Because clinicians may resist implementation of ASPs if these are perceived as being externally imposed, implementation may be more sustainable if development and implementation of ASPs are clinician driven, or at the very least incorporate active stakeholder engagement. Developing AMS centres of excellence can facilitate the sharing of good practice examples and the use of accreditation as an additional incentive to improve the quality of AMS standards (British Society for Antimicrobial Chemotherapy, 2023).

A significant barrier to AMS is shortages of essential antibiotics, which can limit the optimal choice of antibiotic. These frequently occur in Member States because of small markets, limited manufacturing capacity and supply-chain issues, all largely predicated by financial constraints (Anderson et al., 2023). Sustainable procurement policies can help address this challenge. The limited uptake of rapid diagnostics can be attributed to high costs, poor awareness and limited integration into clinical guidelines.

From a regulatory perspective, regulations that have been used effectively to reduce AMU in animal health could provide impetus for stronger regulation of AMU in human health. This would require actions by Member States, as oversight of health systems is a competence of Member States rather than the EC. For example, the Health Care Inspectorate (IGZ) in the Kingdom of the Netherlands has a mandate to monitor whether ASPs have been implemented

in each healthcare facility (HAI, 2023). Furthermore, the pharmaceutical industry may influence the prescribing habits of clinicians. There is a role for regulation (i.e. mandatory industry disclosure) and sanctions (i.e. prohibition or restriction) to prevent inappropriate payments or rewards from pharmaceutical companies to clinicians that may influence their prescribing habits (Mitchell et al., 2021; Zarei et al, 2023). Restrictive lists of certain antibiotics, which require prior approval by infectious disease specialists before prescribing by any clinician, can also improve the quality of prescribing (Davey et al., 2017).

### *2.1.2 Clinical decision support systems for prescribers*

With the rise of electronic health records, electronic prescribing, portable devices and other advancements in information technology (IT), significant opportunities have emerged to facilitate the creation of current and robust decision-making tools and guidelines tailored to specific clinical contexts. This could be achieved through the utilization of computerized clinical decision support systems (Rittmann & Stevens, 2019). These systems can simplify access to necessary decision-making data, provide timely reminders and cues during patient interactions, aid in diagnosing and ordering, and alert clinicians to emerging patterns in patient data. Overall, literature shows that CDSSs have a significant impact on different outcomes, notably on the decrease of antibiotic consumption and narrowing the spectrum of antibiotic usage (Rittmann & Stevens, 2019; Hojat et al., 2022). Some evidence suggests that CDSSs have a positive impact on the mortality of patients (Roos et al., 2019). Investing in high-quality health information technology platforms and electronic prescribing are key enablers for sustainable implementation of CDSSs in healthcare settings (Rittmann & Stevens, 2019; Hojat et al., 2022).

If CDSSs are classified as a medical device, then the EMA is responsible for assessing quality, safety and efficacy. Whether a CDSS is classified as a medical device is dependent upon whether it just provides information or whether it is considered to be software that is used for the purpose of treatment and diagnosis of disease (Jones, Thornton & Wyatt, 2021). While this is a grey area, CDSSs are considered a medical device in most cases. National health authorities are responsible for appraisal and evaluation of CDSSs, regulation of CDSS providers and integration of CDSSs into national guidance. Purchasing of CDSSs may be the responsibility of national health authorities or local healthcare organizations.

**Supporting implementation of CDSSs requires integration within electronic health records and prescriber software, user-friendly interfaces that minimize alert fatigue, comprehensive data, and investment in strengthening health IT infrastructure.**

Supporting implementation of CDSSs requires investment in strengthening health IT infrastructure, staff training and ongoing maintenance. If they are to be successfully implemented, it is imperative that CDSSs are user-friendly, minimize alert fatigue and are integrated into electronic health records and prescriber software where possible. For CDSSs to be effective they also need comprehensive data

on clinical indications, past medical history, laboratory results and ideally on invasive devices (e.g. central or peripheral intravenous lines and urinary catheters). CDSSs also need a structured process to guarantee the integration of up-to-date guidelines within relevant algorithms. However, privacy concerns and compliance with data protection regulations may present barriers to the implementation of CDSSs and integration into electronic health records. Clinicians may have concerns regarding liability when following CDSSs if there are subsequent medical errors and patient safety incidents.

### *2.1.3 Regulation and related supervision to prevent falsified and counterfeit antimicrobials*

The provision of falsified and counterfeit medicines is a significant challenge in the EU because of access to online pharmacists and imports of such products (OECD & EUIPO, 2020). Falsified antibiotics can prolong infections and create more potential for AMR to emerge. Counterfeit antibiotics, on the other hand, are made by someone other than the genuine manufacturer, by copying or imitating an original product without authority or rights (and therefore without certainty around quality and safety). The WHO Global Surveillance and Monitoring System for Standard and Falsified Medical Products has identified several instances of substandard or falsified antibiotics in Europe and internationally (WHO, 2017). The EU Falsified Medicines Directive, adopted in 2011, aims to strengthen the legal framework for ensuring the safety and authenticity of medicines, including antibiotics, by introducing measures to prevent the entry of falsified medicines into the legal supply chain (European Commission, 2024a).

The EMA supports the implementation of the EU falsified medicines directive (2011/62/EU) through several actions, including: unique identifiers and anti-tampering devices on medicines; creation of an EU-wide system to verify authenticity of medicines at point of dispensing; monitoring supply-chain and good distribution practice; and introducing a system of obligatory logos for legally operating online pharmacies (European Commission, 2024a). National regulatory authorities and law enforcement agencies are responsible for conducting inspections and sanctioning actors involved in falsified or counterfeit medicines.

**Robust traceability systems across supply chains, enhancing custom controls, inspections of pharmacies, and awareness campaigns are required to combat falsified and counterfeit antimicrobials.**

Member States need to invest in improving the frequency of inspections of pharmacies and enhance custom controls to prevent illegal importation of counterfeit or falsified antibiotics and other drugs. Developing awareness and educational campaigns to inform the public of the risks involved in purchasing prescription-only medicines from unregulated online pharmacies is crucial. The EMA also needs to provide clear guidance to Member States around which other countries have 'equivalent' regulatory frameworks to prevent falsified and counterfeit medicines, to inform procurement decisions on antimicrobials from non-EU countries.

### 2.1.4 Infection prevention and control programmes

Infection prevention and control plays a crucial role in reducing AMR by implementing measures to limit the spread of resistant pathogens and infections, thus decreasing the need for antimicrobial treatment. The WHO has published guidance on core aspects of IPC that cover eight components: (1) IPC programmes; (2) IPC guidelines; (3) IPC education and training; (4) Surveillance; (5) Multimodal strategies; (6) Monitoring/audit of IPC practices and feedback; (7) Workload, staffing and bed occupancy (acute healthcare facilities only); and (8) Built environment, materials and equipment for IPC at the facility level (acute healthcare facilities only) (WHO, 2016). IPC programmes involve several interventions, such as standard hygiene measures (i.e. hand washing), the isolation of infected patients, active screening of incoming patients, and the prevention of HAIs. The prevention of HAIs requires the implementation of multimodal strategies, including bundles for catheter-associated urinary tract infection (CAUTI), central line-associated bloodstream infection (CLABSI), surgical site infection (SSI), hospital-associated pneumonia (HAP) and ventilator-associated pneumonia (VAP) (Tacconelli et al., 2014). Environmental cleaning is also a key component of IPC programmes (Box 8), with growing evidence on its role in reducing patient colonization with hospital-associated infections and multidrug-resistant microorganisms (Peters et al., 2022). IPC teams typically monitor compliance with protocols and guidelines, and often include specialist nurses and doctors (Zingg et al., 2015).

#### Box 8: Optimizing environmental cleaning in healthcare facilities to reduce AMR

Interventions to improve environmental cleaning of healthcare facilities involve education and training, local guidelines and processes, and monitoring and evaluation with adenosine triphosphate (ATP) bioluminescence and fluorescent markers (Storr et al., 2017; Browne & Mitchell, 2023). Environmental cleaning of healthcare facilities is known to be a clinically- and cost-effective strategy to reduce AMR (Rice et al., 2023), but more can be done to strengthen its implementation (Dancer, 2023). First, there is an unmet need for evidence-based and universally agreed standards for hard surface cleanliness for different surface types and clinical contexts. Second, guidelines and educational frameworks need to be developed that define adequate staffing for optimal environmental cleaning and their training needs. Third, a systematic monitoring framework needs to be developed to review compliance with universally agreed standards. Finally, and most importantly, the essential role of cleaners in patient safety needs to be promoted and valued by healthcare managers and leadership.

Source: Provided by Belgian Antibiotic Policy Coordination Committee (BAPCOC).

The ECDC conducts country visits, provides technical advice to Member States, and performs surveillance of HAIs and AMR across the EU. Its extended mandate includes monitoring of Member States' IPC programmes to identify gaps and provide recommendations (ECDC, 2023a). The 2023 EU Council Recommendations on stepping up EU actions to combat AMR call for the EC, in conjunction with the ECDC, to develop IPC guidelines in human health

(General Secretariat of the Council, 2023). At the same time, the EU's Joint Programming Initiative on Antimicrobial Resistance (JPIAMR) plays a crucial role in coordinating research efforts and sharing best practices among Member States. National health authorities are responsible for developing national IPC policies and guidelines, providing funding for IPC programmes and conducting surveillance of HAI and AMR in their respective healthcare systems.

#### IPC programmes should be aligned with ASPs, and supported by legal and accountability frameworks, as well as monitoring and surveillance with rapid feedback mechanisms.

There are significant synergies between ASPs and IPC programmes, and ideally these initiatives should be aligned at organizational level to leverage the complementary expertise of stewardship and IPC healthcare professionals and to ensure objectives are aligned (Knobloch et al., 2021). Ensuring healthcare providers have appropriate resources to invest in multidisciplinary IPC teams, diagnostic and laboratory capacity, and educational and training initiatives is key. Behaviour science techniques, such as tailored targets (for HAI and AMR rates), educational and awareness initiatives, cues (e.g. signs) placed in workplaces, computerized alert systems, financial incentives and sanctions, and performance feedback and benchmarking are all strategies that can also be used to improve compliance with recommended IPC measures (Haustein et al., 2011; Edwards et al., 2012; Vokes, Bearman & Bazzoli, 2018; Kim et al., 2020; Norman, 2021).

Political leadership that is committed to enabling IPC can play a key role in providing strategic direction and ensuring that IPC remains a high-level priority across healthcare systems (including hospital, primary and long-term care facilities) and broader society (WHO, 2023). The 2023 WHO Global Strategy on IPC emphasizes how sustainable implementation of recommended IPC components can be supported through legal and accountability frameworks, regulations and accreditation systems (WHO, 2023). This also requires monitoring and surveillance systems with rapid feedback mechanisms, and clear roles and responsibilities across the healthcare system to help facilitate accountability mechanisms.

### 2.1.5 Vaccination to prevent emergence and spread of certain pathogens

Vaccination is a key strategy to limit the development and transmission of AMR through multiple pathways (Table 2, page 20). These go beyond just prevention of infection, but also include reduced infection severity and secondary bacterial infections. Vaccines also have the benefit of being highly specific to their targeted pathogen; this means that they can be developed to target specific strains of a pathogen that are most pathogenic or prone to developing resistance. However, the potential benefit of vaccines to reduce AMR is often underestimated because clinicians and policy-makers sometimes only consider a subset of the pathways by which vaccines can affect antimicrobial use and resistance (Lipsitch & Siber, 2016; Atkins et al., 2018).

**Table 2: Pathways through which vaccination can reduce AMR**

<b>PATHWAY</b>	<b>RATIONALE</b>
<b>Preventing infections by focal pathogens</b>	Vaccines may reduce the incidence of infection by a resistant pathogen. This can occur both through direct protection to those vaccinated, and through indirect protection resulting from reduced exposure to the infection in the unvaccinated (herd immunity).
<b>Bystander effects</b>	Any vaccines that lead to changes in antibiotic use could potentially have an impact on AMR in organisms not targeted by the vaccine. For example, an effective and widely used vaccine that reduces the number of influenza infections should result in population-wide reductions in antibiotic use.
<b>Infection severity effects</b>	Vaccines that reduce the risk of symptomatic infection without reducing the risk of carriage/asymptomatic infection can lead to reductions in the proportion of infections which require treatment with antimicrobials.
<b>Subtype selection effects</b>	Some vaccines may target subtypes of a pathogen population which are more likely to be resistant. As a result, overall resistance may decrease.
<b>Interspecific effects</b>	Vaccination against one organism could reduce transmission of another, leading to declines in both resistant and sensitive phenotypes. For example, influenza or respiratory syncytial virus (RSV) infections may increase the risk of secondary bacterial infections and patients with certain viral infections may transmit more bacterial pathogens.
<b>Selective targeting effects</b>	Vaccination could lead to differential effects if targeted to certain population groups. For example, if a resistant strain of a given pathogen transmits preferentially in hospitals, targeting the hospital population with a vaccine could have a greater overall effect on the resistant strain, leading to declines in resistance in both hospital and community.

Source: Adapted from Jit, Anderson & Cooper, 2020.

The EMA is responsible for assessing the quality, safety and efficacy of vaccines. The ECDC monitors vaccine schedules and coverage across Member States, hosts the 'European Vaccine Information Portal' (with the EC and EMA) (European Vaccination Information Portal, 2024) and maintains the 'Vaccine Monitoring Platform' (with the EMA) (ECDC, 2023b). The EC (through HERA) also has a mandate to coordinate joint procurement of certain vaccines (i.e. influenza) for Member States when required (European Commission, 2022c). National health authorities are responsible for developing vaccination schedules, procurement and distribution of vaccines, monitoring coverage rates, and conducting public awareness and promotion campaigns.

**Vaccination should be integrated within AMR national action plans as a key strategic objective, combined with efforts to address vaccine hesitancy and misinformation.**

Vaccination is often not included as a strategic objective in AMR national action plans (van Heuvel et al., 2022). The 2023 EU Council Recommendations on stepping up EU actions to combat AMR include vaccination as a key policy to address AMR (General Secretariat of the Council, 2023). However, there also needs to be increased recognition of the essential role of vaccination in combating AMR by high-level policy-makers at the Member State level. Addressing vaccine hesitancy and misinformation through public awareness campaigns is crucial; collaboration with social media influencers can be used to enhance vaccination messages and counter misinformation. Reimbursement models can be adapted to ensure financial incentives exist for healthcare providers to comply with vaccinations

schedules (NICE, 2022). From a regulatory perspective, ensuring that the benefits of vaccines in combating AMR are routinely included in their assessment and appraisal by health technology assessment bodies would help ensure that the value of vaccines is appropriately quantified (Postma et al., 2022). More could also be done to prioritize which pathogens should be the target of R&D of new vaccines, including the implications for AMR. While mapping of the preclinical and clinical pipeline already exists (Frost et al. 2023), prioritization needs to consider evidence on which pathogens may be vulnerable to replacement with other pathogens or non-vaccine serotypes following vaccination and subsequent implications for AMR. Finally, Member States frequently experience shortages of vaccines because of limited suppliers, supply-chain issues, or poor stock management (Filia et al., 2022). Sustainable procurement policies discussed in Table 3 (pages 21–23), could be considered to overcome this challenge.

Table 3: Selected implementation considerations for key AMR interventions in human health

INTERVENTION	ROLE FOR EU	ROLE FOR MEMBER STATES	OPERATIONAL CONSIDERATIONS	FINANCIAL CONSIDERATIONS	REGULATORY CONSIDERATIONS
<b>Human health</b>					
<p><b>Antimicrobial stewardship programmes</b></p>	<ul style="list-style-type: none"> <li>• ECDC conducts surveillance of AMU, conducts country visits and provides training</li> <li>• JPIAMR coordinates research efforts and shares best practices among Member States</li> <li>• EC has produced guidelines on prudent use of antimicrobials in human health (with the ECDC), and funds AMS initiatives (i.e. DRIVE-AMS)</li> <li>• EC supports development of diagnostics, and strengthening laboratory and surveillance capacity</li> <li>• EC to fund research in effectiveness of ASP interventions and rapid diagnostic tools</li> </ul>	<ul style="list-style-type: none"> <li>• National health authorities invest in ASPs, develop guidelines and educational programmes, conduct surveillance of AMU and feedback to prescribers, and evaluate stewardship interventions</li> <li>• Setting specific targets for AMU at regional and organizational levels</li> <li>• More targeted interventions for organizations with higher AMU rates</li> </ul>	<ul style="list-style-type: none"> <li>• Centres of excellence can share examples of best practice, and accreditation can create incentives to improve standards</li> <li>• Clinician-driven initiatives are often more effective, as clinicians sometimes resist political influence</li> <li>• Knowledge transfer needed on ASP best practices across Europe</li> <li>• Behavioural science approaches can be used to strengthen implementation (i.e. goal setting, behaviour monitoring, feedback, social support, social comparison, incentives and sanctions)</li> </ul>	<ul style="list-style-type: none"> <li>• Shortages of essential antibiotics frequently occur because of small markets, limited manufacturing capacity and supply-chain issues</li> <li>• Uptake of rapid diagnostic tools is influenced by poor awareness, high costs and limited integration into clinical guidelines</li> <li>• Investment is needed in multidisciplinary teams and training programmes</li> </ul>	<ul style="list-style-type: none"> <li>• Stronger regulations should be considered to improve accountability for appropriate AMU and implementation of ASPs</li> <li>• Regulations and sanctions to limit the influence of pharmaceutical industry on prescribers may be considered</li> <li>• Restricted lists, verified by specialists before prescriptions (i.e. prior approval processes), can induce significant local-level changes</li> </ul>
<p><b>Clinical decision support systems (CDSS) for prescribers</b></p>	<ul style="list-style-type: none"> <li>• EC funds R&amp;D of CDSSs (i.e. through initiatives such as Horizon Europe)</li> <li>• If classified as a medical device, the EMA is responsible for assessing quality, safety, efficacy of CDSSs (including post-market authorization monitoring of effectiveness)</li> </ul>	<ul style="list-style-type: none"> <li>• Funding for implementation and R&amp;D of CDSSs</li> <li>• Appraisal and regulation of CDSSs</li> <li>• Integration of CDSSs into guidelines</li> </ul>	<ul style="list-style-type: none"> <li>• CDSSs should be user-friendly, minimize alert fatigue and be integrated into electronic health records and prescriber software</li> <li>• CDSSs need a structured process to guarantee the use of up-to-date guidelines</li> <li>• CDSSs need comprehensive data regarding clinical indications, past medical history, laboratory results, and from invasive devices (i.e. intravenous lines and urinary catheters)</li> </ul>	<ul style="list-style-type: none"> <li>• Resources are required to strengthen health IT infrastructure, for staff training, and for ongoing maintenance</li> </ul>	<ul style="list-style-type: none"> <li>• Privacy concerns and compliance with data protection regulations may present barriers to implementation of CDSSs and integration into electronic health records</li> <li>• Clinicians may have concerns regarding liability when following CDSSs</li> </ul>

continued on next page

Table 3: Selected implementation considerations for key AMR interventions in human health *continued*

INTERVENTION	ROLE FOR EU	ROLE FOR MEMBER STATES	OPERATIONAL CONSIDERATIONS	FINANCIAL CONSIDERATIONS	REGULATORY CONSIDERATIONS
<b>Regulation and related supervision to prevent falsified and counterfeit antimicrobials</b>	<ul style="list-style-type: none"> <li>EC introduced the falsified medicines directive (2011/62/EU)</li> <li>EMA supports the implementation of this directive, including:               <ol style="list-style-type: none"> <li>Unique identifiers and anti-tampering devices on medicines</li> <li>EU-wide system to verify authenticity of medicines at point of dispensing</li> <li>Monitoring supply-chain and good distribution practice</li> <li>Obligatory logos for legally operating online pharmacies</li> </ol> </li> </ul>	<ul style="list-style-type: none"> <li>National regulatory authorities and law enforcement agencies are responsible for conducting inspections and sanctioning actors involved in falsified or counterfeit medicines</li> <li>National legislators are responsible for transposing the directive into national law</li> </ul>	<ul style="list-style-type: none"> <li>Public awareness campaigns are essential to discourage the use of falsified antimicrobials</li> <li>Member States may consider enhancing customs controls and inspections to prevent illegal importation of counterfeit or falsified antibiotics and other drugs</li> </ul>	<ul style="list-style-type: none"> <li>Ensuring adequate resources for robust traceability systems across supply-chains of medicines, and regular inspections of pharmacies</li> </ul>	<ul style="list-style-type: none"> <li>Establishing whether non-EU countries have 'equivalent' regulatory frameworks to prevent falsified and counterfeit medicines when importing medicines</li> </ul>
<b>Infection prevention and control programmes</b>	<ul style="list-style-type: none"> <li>EC to develop IPC guidelines in conjunction with ECDC</li> <li>ECDC offers technical expertise, provides training, develops guidelines, conducts country visits, and conducts surveillance of HAIs and AMR across Member States</li> <li>JPIAMR coordinates research efforts and shares best practices among Member States</li> <li>EC with ECDC could set specific targets for AMR in each Member State</li> <li>EC could support the strengthening of national public health agencies in Member States</li> <li>EC to fund research into effectiveness of IPC measures</li> </ul>	<ul style="list-style-type: none"> <li>National health authorities develop policies, produce guidelines, enforce financial and legal frameworks, provide funding for IPC programmes, and conduct surveillance of HAI and AMR</li> <li>National health authorities also develop incentives and sanctions to encourage reduction in HAIs</li> <li>Setting specific targets for AMR at regional and organizational levels</li> <li>More targeted interventions for organizations with higher HAI rates</li> </ul>	<ul style="list-style-type: none"> <li>IPC applies across the healthcare system (hospital, primary and long-term care), and broader society</li> <li>IPC programmes must have multidisciplinary input, and involve sustained audit and feedback mechanisms to ensure accountability</li> <li>IPC activities should coordinate and integrate with other health priorities and programmes, and vice-versa (e.g. patient safety and quality of care, occupational health and safety, health emergencies, biosafety and biosecurity)</li> </ul>	<ul style="list-style-type: none"> <li>Staffing shortages, and limited laboratory and diagnostic capacity hinder implementation of IPC programmes</li> </ul>	<ul style="list-style-type: none"> <li>Legal and accountability frameworks, regulations, accreditation systems, financial incentives, targets and public benchmarking can be effective strategies to scale up core components of IPC programmes, reduce HAIs and promote organizational changes</li> </ul>

*continued on next page*



Table 3: Selected implementation considerations for key AMR interventions in human health *continued*

INTERVENTION	ROLE FOR EU	ROLE FOR MEMBER STATES	OPERATIONAL CONSIDERATIONS	FINANCIAL CONSIDERATIONS	REGULATORY CONSIDERATIONS
<p><b>Vaccination to prevent emergence and spread of certain pathogens</b></p>	<ul style="list-style-type: none"> <li>EMA assesses quality, safety and efficacy of vaccines; based on this assessment EC grants central market authorization</li> <li>EC coordinates joint procurement of certain vaccines (i.e. influenza) for Member States, and could invest in manufacturing capacity</li> <li>ECDC monitors vaccine schedules and coverage across Member States, hosts the 'European Vaccine Information Portal' (with the EC and EMA), and maintains the 'Vaccine Monitoring Platform' (with the EMA)</li> </ul>	<ul style="list-style-type: none"> <li>National health authorities develop vaccination schedules, procure and distribute vaccines, monitor coverage rates, and conduct public awareness and promotion campaigns</li> </ul>	<ul style="list-style-type: none"> <li>Essential to include vaccination as a strategic objective within AMR national action plans</li> <li>Crucial to address vaccine hesitancy and misinformation through public awareness campaigns</li> <li>Collaboration with social media influencers to enhance vaccination messages and counter misinformation</li> </ul>	<ul style="list-style-type: none"> <li>Member States frequently experience shortages of vaccines because of limited suppliers, supply-chain issues or poor stock management</li> <li>Reimbursement models can be adapted to ensure financial incentives exist for healthcare providers to comply with vaccination schedules</li> </ul>	<ul style="list-style-type: none"> <li>The benefits of vaccines in combating AMR should be routinely included within assessment and appraisal of vaccines by regulatory and health technology assessment bodies</li> </ul>

AMR – antimicrobial resistance, AMS – antimicrobial stewardship, AMU – antimicrobial usage, ASP – antimicrobial stewardship programme, CDSS – clinical decision support system, EC – European Commission, ECDC – European Centre for Disease Prevention and Control, EMA – European Medicines Agency, HAI – healthcare-associated infection, IPC – infection prevention and control, IT – information technology, JPIAMR – Joint Programming Initiative on Antimicrobial Resistance, R&D – research and development.

## 2.2. Animal health

### 2.2.1 Regulation and related supervision to promote the prudent use of antimicrobials

Several aspects of the pharmaceutical regulation are used to govern appropriate AMU in animal health in the EU. A significant development was banning the use of antibiotics as growth promoters in animal feed for all EU countries in 2006 (EUR-Lex, 2003a). Regulation 2019/6 on veterinary medicinal products (EUR-Lex, 2018a) includes a wide range of complementary measures to ensure prudent use of antimicrobials, most of which are applicable since January 2022 (Box 9). There has also been a multitude of other actions, and legislation with regard to AMR in bacteria and zoonoses, to prevention and control of diseases (e.g. Directive 2003/99/EC, Commission Implementing Decision (EU) 2020/1729, Regulation 2016/429, Regulation 2020/687 and Regulation 2020/689) (EUR-Lex, 2003b, 2016, 2019, 2020a,b) as well as prudent use (guidelines for the prudent use of antimicrobials in veterinary medicine 215/C, 299/04) (European Union, 2015) and restricted use of antimicrobials (Regulation 2019/4 and Regulation 2019/6), has been put in place at EU level (EUR-Lex, 2018b, 2022).

#### Box 9: The EU's veterinary regulation of 2019

Regulation 2019/6 on veterinary medicinal products, also known as the new veterinary regulation (NVR), sets out the rules for the authorization, use and monitoring of veterinary medicinal products in the EU. The legislation came into effect in January 2019, to be applied in all EU Member States from January 2022. Notable provisions on the prudent use of antibiotics include: ban on the preventive (prophylactic) use of antibiotics in groups of animals; ban on the use of antimicrobials to promote growth or increase yield (in addition to the ban of 2006); significant restriction of the use of antimicrobials in groups of animals ahead of expected disease outbreaks (metaphylactic use); clear framework imposing strict conditions for antimicrobial prescriptions; an obligation for Member States to collect data on the sales of veterinary antimicrobials, but also on the use of antimicrobials per animal species. This will allow national authorities and stakeholders to design more targeted measures per sector to reduce AMU in animals to what is strictly necessary.

The European Commission is responsible for introducing pharmaceutical regulation related to AMU in animals (which the European Parliament and Council of the EU subsequently adopt); and the EMA (and in some cases competent authorities from Member States) is responsible for assessment of quality, efficacy and safety of antimicrobials. National authorities in Member States are responsible for enforcing regulations within their territories, and enforcement measures include inspections, penalties for non-compliance and legal actions against those who violate the regulations. Member States are also required to report their data on the volume of sales and use of antimicrobial medicinal products in animals to the EMA (EMA, 2024a), in line with the Veterinary Medicinal Products Regulation (EUR-Lex, 2018a). The EMA then reports this data through the 'Antimicrobials Sales and Use Platform'

to support the mandatory collection and reporting of data on antimicrobial medicinal products in animals from across the EU (EMA, 2024b). The EFSA, EMA and ECDC also produce joint AMR surveillance reports taking a 'One Health' approach (ECDC, EFSA & EMA, 2024).

**Strengthened regulation of AMU in animal health could entail sector-specific targets and benchmarking; revenue models that alter direct profits from antimicrobial sales; enhanced conditions on usage of certain broad-spectrum antimicrobials; and aligning summary product characteristics for veterinary antimicrobials across the EU.**

A previous review of measures to reduce the need to use antimicrobials in animal husbandry concluded that setting targets and benchmarking could be an effective strategy to reduce AMU (Murphy et al., 2017). The EC will therefore take action to reduce overall EU sales of antimicrobials for farmed animals and in aquaculture by 50% by 2030 (European Commission, 2020a). However, sector-specific guidelines could improve implementation of these targets, reflecting the breadth of food-producing and companion animals. Veterinarians frequently feel obliged to prescribe antimicrobials as they are paid on a fee-for-service basis, and in many EU Member States they make a profit from selling antimicrobials. Payment mechanisms could be adjusted to remove incentives to prescribe antimicrobials and encourage preventative advice (see also below section on biosecurity). This has been used successfully in several Nordic countries to reduce AMU in the animal health sector (Sternberg-Lewerin et al., 2022). Introducing additional conditions on usage of broad-spectrum antibiotics may help promote prudent use, such as registration of usage and justification based on laboratory analysis. For example, legislation was introduced in Belgium in 2016 that imposes these conditions on the use of third- and fourth-generation cephalosporins and fluoroquinolones by veterinarians in food-producing animals and will be applicable to all other animals as of September 2024 (with the exception of intramammary therapy for mastitis) (AMCRA, 2024). This has led to a 75% reduction in the use of these critically important antibiotics (AMCRA, 2021).

Despite EU regulations stating that veterinary medicinal products can only be used in accordance with the terms of their marketing authorization<sup>1</sup>, deviations in prescribing practices across Member States and what is listed within Summary of Product Characteristic (SPC) certificates is a source of confusion, hampers efforts to develop national prescribing guidelines, and creates barriers for the circulation of antimicrobials within the EU. A review of SPCs for antimicrobials conducted by the EMA, with an emphasis on the optimal dose and duration to prevent risk of AMR, could be the first step to aligning SPCs for veterinary antimicrobials across the EU. Finally, beyond regulatory efforts, AMS efforts are just as crucial in the animal sector as they are in the human health sector (see Box 10 on page 25).

1 Regulation (EE) 2019/6 of the European Parliament and of the Council of 11 December 2018 on Veterinary Medicinal Products states that Veterinary Medicinal Products shall only be used in accordance with the terms of the marketing authorization.

**Box 10: Antimicrobial stewardship programmes and clinical decision support systems in veterinary medicine**

Antimicrobial stewardship is also a key component of promoting prudent AMU in veterinary medicine (Lloyd & Page, 2018). Implementation of ASPs in animal health shares many similar implementation enablers to ASPs in human health, including strong leadership commitment combined with clear roles, responsibilities and accountability mechanisms, behavioural science approaches (i.e. goal setting, behaviour monitoring, feedback, social support, social comparison, incentives and sanctions), improved diagnostic capacity, consistent access to antimicrobials, and integration with IPC programmes (Magalhães-Sant'Ana et al., 2017; Hardefeldt et al., 2018; Golding, Ogden & Higgins, 2019). Education and awareness campaigns are necessary to achieve sustained behaviour change (Vercelli et al., 2022). CDSSs for prescribers also have a role in animal health, as they can play an important role in the quality of the sales and use data for veterinary antimicrobials (Fox et al., 2021). Supporting implementation requires integration within prescriber software, user-friendly interfaces that minimize registration fatigue, and investment in strengthening veterinary IT infrastructure.

Importantly, veterinarians need to be included as an equal partner in the One Health approach. They play an important role in the battle against AMR and are rightly proud of what has already been achieved. Increased acknowledgment of their efforts and sustainable support are needed to ensure continued motivation and cooperation.

**2.2.2 Improved biosecurity to prevent emergence and spread of infection**

Improved biosecurity within animal health is listed as a key priority within the 2017 EU One Health Action Plan against AMR (European Commission, 2017) and the 2023 EU Council Recommendations on stepping up EU actions to combat AMR (General Secretariat of the Council, 2023). Two key examples of biosecurity systems include the Biocheck and Farmfit systems (Box 11). Components of biosecurity in animal health include controlled access to facilities, access to clear water, sanitation, quarantine procedures and the management of animal movements. Implementing biosecurity practices is a cost-effective strategy to reduce AMR by preventing disease outbreaks, thereby reducing the need for antimicrobial treatments and their associated expenses (Hofacre et al., 2002). The upfront costs of implementing biosecurity are justified by the long-term economic benefits, making it a crucial component of a comprehensive strategy to address AMR in animal agriculture (Jimenez et al., 2023).

The European Commission can introduce legislation on biosecurity, and produces policies and initiatives to improve it (EUR-Lex, 2016; European Commission, 2020a). One example is the mandatory requirements for biosecurity in aquaculture listed within EU regulation 2020/691 for aquaculture establishments and transporters of aquatic animals (European Commission, 2020b). At the same time, the EFSA provides technical advice on biosecurity measures to Member States. It is important to emphasize that biosecurity measures sit within a broad framework of EU actions that aim to make food systems fair, healthy and environmentally friendly. These actions are summarized within the Farm to Fork strategy, but also include regulations to prevent transmission of animal diseases (i.e. through the

**Box 11: Biocheck and FarmFit systems**

Biocheck.UGent is a risk-based scoring system, which quantifies the level of on-farm biosecurity (Gelaude et al., 2014). It is not focused on a specific disease, but facilitates an assessment of biosecurity levels in general and on those aspects that are common to the transmission of many different types of infectious disease. Biocheck surveys are divided into several subcategories for internal and external biosecurity, and encapsulate five principles: 1) Separation of high and low risk animals and environments; 2) Reduction of the general infection pressure; 3) Taking into account the risk of each transmission route, as not all are equally important; 4) Risk is a combination of probability of transmission and frequency of occurrence of transmission routes; and 5) Larger animal groups and thus larger farms pose, in general, higher risks for disease outbreaks and spread (Dewulf et al., 2018). Biocheck has been used in over 100 countries (Biocheck.UGent, undated), allowing benchmarking and progress tracking of biosecurity in multiple species globally.

FarmFit is a tool developed by the animal health associations DGZ (Animal Health Care Flanders) and ARSIA (Association Régionale de Santé et d'Identification Animales). It serves as a platform for both veterinarians and farmers to optimize herd health management and to register herd visits and action plans, covering essential aspects of animal health, disease prevention and biosecurity (FarmFit, undated). One of the elements integrated into FarmFit is a biosecurity evaluation, based on the Biocheck.UGent questionnaires. By using the biosecurity module in FarmFit, veterinarians can efficiently assess biosecurity on poultry and pig farms. The biosecurity evaluations facilitated by FarmFit also align with mandatory requirements for biosecurity outlined within the Belgian frameworks of avian influenza legislation (FASFC, 2021) and African Swine Fever legislation (FASFC, undated). Additionally, veterinarians and farmers receive tailored recommendations and actions through the tool, aimed at enhancing the biosecurity status of the farm. This highlights one of FarmFit's main objectives, which is to foster collaboration between farmers and veterinarians. While a comprehensive evaluation of the data is still in progress, initial unpublished findings from Belgium indicate an improvement of the biosecurity status of pig and poultry farms.

*Dr Nele Caekebeke, Professor Jeroen Dewulf and Mr Willem Van Praet kindly provided information on the Biocheck and FarmFit initiatives that was used to develop this box.*

EU Animal Health Law) (EUR-Lex, 2016), promote animal welfare (i.e. Council Directive 98/58/EC concerning the protection of animals kept for animal purposes) (EUR-Lex, 1998) and protect animal welfare. Member States are responsible for enforcing EU regulation through farm inspections, educational initiatives and surveillance of AMR. National authorities also develop their own policies and legislation on biosecurity and conduct risk assessments of potential threats.

**Payment mechanisms need to be designed to reward veterinarians for giving preventative and biosecurity advice, and the cost benefits of biosecurity need to be routinely reported and emphasized to farmers.**

Implementation of biosecurity measures is often perceived as costly for farmers. Therefore, the benefit-cost ratio of biosecurity needs to be routinely reported and emphasized to farmers to encourage implementation (Dewulf et al., 2020). Overcoming resistance to change also requires investment in education and training, capacity building, and coordination among stakeholders. As previously mentioned, veterinarians often feel they cannot charge for giving preventative advice in agricultural settings. Therefore,

contracts must be (re)designed to ensure that prophylactic advice from veterinarians is appropriately rewarded. One example of such contracts are the Veterinary Advisory Service Contracts (VASC) in Denmark, which focus on advice and prevention of disease rather than treatment, in order to optimize the use of antimicrobials (DVFA, 2024). In 2010, it became mandatory for owners of large herds of cattle and pigs, and for mink farm owners, to sign a VASC. On the other hand, from a regulatory perspective, sanctioning farms can be difficult, as defining the boundaries of 'acceptable' biosecurity standards is challenging even with the development of checklists such as BioCheck (Box 11, page 25). Therefore, greater clarity in this respect would help improve standards and compliance with biosecurity measures.

### **2.2.3 Vaccination to prevent emergence and spread of certain pathogens**

Similar to human health, vaccines are used extensively in animal health for the prevention of infectious diseases and therefore to reduce the need for antimicrobials. Vaccines are often used in livestock as part of a broader strategy that includes good biosecurity practices and responsible AMU. Several studies have emphasized how vaccination is a cost-effective strategy to prevent infectious diseases, reduce AMU and improve livestock productivity (Longworth, Mourits & Saatkamp, 2014; Tang et al., 2022; da Silva Giacomini et al., 2023; Jimenez et al., 2023). However, the availability of veterinary vaccines varies significantly across Member States in the EU (Videnova & Mackay, 2012). Moreover, there are many diseases frequently occurring within animals for which there are no vaccines currently available (Videnova & Mackay, 2012). To address such needs, Regulation (EU) 2019/6 derogations allow, under some circumstances, the use of vaccines not authorized within the EU. It also includes regulatory incentives for the development of new vaccines (EUR-Lex, 2018a).

The competent authorities of the Member States and EMA are responsible for the evaluation of quality, effectiveness and safety of vaccines used in animals. The Directorate-General for Research and Innovation has the authority to finance the R&D of new vaccines. National authorities are responsible for developing vaccination guidelines, establishing educational standards, funding R&D, and surveillance of the sale and administration of vaccines.

### **Investment is needed to stimulate R&D of novel vaccines in animal health to reduce AMR and transmission to humans, with an emphasis on unmet need.**

There are many animal diseases for which no vaccine exists, or vaccines have limited efficacy. In particular, there is low availability of effective veterinary vaccines for use in aquatic animals (Du et al., 2022). There is also general low availability of effective vaccines for minor use or minor species (MUMS) with limited markets (EMA, 2017a). Driving

this issue is a lack of incentives to encourage the R&D of new vaccines for animal health. Market unattractiveness for veterinary vaccines in many species will mean that significant public subsidization of R&D will be required to supply more effective vaccines. However, a review of where the significant gaps are in terms of unmet need for vaccines to reduce AMR and transmission to humans would help target when and where public investment is needed the most. From a regulatory perspective, the industry has proposed recommendations to optimize regulatory requirements to improve availability of new vaccines, including simplifying mutual recognition procedure (MRP), utilizing serology data as surrogate markers, improving pharmacovigilance data utilization, and aligning regulatory requirements with those of the United States of America (USA) (EMA, 2017b). However, the implications of these recommendations for ensuring the quality and safety of vaccines for use in animals need to be considered.

### **2.2.4 Food safety compliance programmes**

Food safety compliance programmes refer to multicomponent frameworks developed by EU institutions and competent authorities in Member States to limit the presence and transmission of pathogens through food supply chains and to consumers. This is important as resistant bacteria have been detected in various food products, including meat, dairy and vegetables (Van Boeckel et al., 2015), and contaminated food can serve as a direct source of resistant strains for consumers. Food safety compliance programmes typically include regulations, guidelines, inspections and audits that aim to limit the infection or contamination of animals, plants and products during production, processing and distribution, and to foster adherence to recommended withdrawal periods<sup>2</sup> for antimicrobials to ensure that treated animals do not enter the food chain until the residues of the drugs have sufficiently cleared (EUR-Lex, 2003a).

The European Commission is responsible for introducing legislation on food safety across food supply chains and developing EU policies related to food safety (e.g. the Farm to Fork strategy and the EU hygiene package) (European Commission, 2020; Food Safety Authority of Ireland, undated). The EFSA provides technical advice and communicates risks to food safety to Member States; collects data on chemical (including antimicrobial) residues, zoonoses and food safety criteria parameters in food and process hygiene criteria parameters in food processing; and conducts risk assessments across the food supply chain. National food safety authorities enforce EU legislation through actions such as conducting inspections to monitor standards and compliance with regulations; undertaking risk assessment to identify hazards; providing education and training; and performing surveillance on chemical residues, zoonoses and food safety criteria parameters in food and on process hygiene criteria parameters in food processing.

<sup>2</sup> Withdrawal periods are the time that must elapse between the last administration of a veterinary medicine and the slaughter or production of food from that animal, to ensure that the food does not contain levels of the medicine that exceed the maximum residue limit. The withdrawal period is set during regulatory authorization of veterinary medicinal products.

**Food safety messages, such as thorough cooking and good hygiene practices, need to be integrated into AMR awareness campaigns, and surveillance of AMR in food needs to be strengthened.**

Several barriers exist to sustainable implementation of food safety programmes. The complexity of regulatory requirements can sometimes be challenging for food business operators (FBOs) to navigate, including differences between EU and non-EU regulations (Pederson & Hernandez, 2014). Compliance with food safety standards can be costly for FBOs (particularly SMEs), including investment in training, equipment and regulatory fees (Villamiel & Méndez-Albiñana, 2022). The large number of actors involved in food supply chains also creates challenges in traceability, transparency and accountability of food safety standards. Integrating a food safety component into public AMR awareness campaigns can be a useful opportunity to promote food safety. Key messages could include thorough cooking to destroy bacteria and applying good hygiene practices at all stages of the food chain to reduce the risk of contamination and spreading of bacteria potentially carrying AMR genes to other foods. While surveillance of AMR in fresh meat at the retail level is already included within EU regulations (EUR-Lex, 2020a), strengthened and more frequent surveillance of AMR in food in more downstream FBOs, such as retailers, may help build a more comprehensive understanding of AMR in food products, as the majority of surveillance currently takes place in large-scale FBOs, such as abattoirs (EFSA Panel on Biological Hazards (BIOHAZ) et al., 2022). Finally, more research is needed to address gaps in our understanding of how various interventions impact AMR and subsequent food safety, such as different cleaning and disinfection protocols, approaches to animal transportation, mechanical versus manual catching/loading of animals, and the effect of type and amount of bedding (EFSA Panel on Biological Hazards (BIOHAZ) et al., 2022).

Table 4: Selected implementation considerations for key AMR interventions in animal health

INTERVENTION	ROLE FOR EU	ROLE FOR MEMBER STATES	OPERATIONAL CONSIDERATIONS	FINANCIAL CONSIDERATIONS	REGULATORY CONSIDERATIONS
<b>Animal health</b>					
<b>Regulation and related supervision to promote prudent antimicrobial use</b>	<ul style="list-style-type: none"> <li>• EC introduces legislation for prudent AMU and surveillance</li> <li>• EC sets targets for AMU across Europe</li> <li>• EMA is responsible for assessment of quality, efficacy and safety of antimicrobials, and surveillance of AMU through the 'Antimicrobials Sales and Use Platform'</li> <li>• EFSA, EMA and ECDC produce joint AMR surveillance report</li> </ul>	<ul style="list-style-type: none"> <li>• National authorities enforce EU regulation on appropriate use, develop national guidelines on AMU, outline educational standards, conduct surveillance of AMU and AMR, and can set targets at regional and farm levels</li> <li>• National legislators are responsible for transposing EU legislation into national law</li> </ul>	<ul style="list-style-type: none"> <li>• Targets and benchmarking to reduce antimicrobials can be effective, but need to be sector- and animal-specific, and applicable to both internal consumption and exports</li> <li>• Enhanced conditions (i.e. mandatory registration and laboratory analysis of samples) can be introduced to reduce usage of broad-spectrum antibiotics</li> <li>• Improved availability of diagnostic tests, combined with strengthened surveillance and feedback, can help support implementation</li> </ul>	<ul style="list-style-type: none"> <li>• Revenue models that alter direct profits from antimicrobial sales can remove potential incentives for veterinarians to prescribe antimicrobials, i.e. by moving into service contracts that reward preventative advice</li> <li>• Supporting integration of ASPs within prescriber software, user-friendly interfaces and investment in strengthening veterinary IT infrastructure</li> </ul>	<ul style="list-style-type: none"> <li>• Despite regulation stating that veterinary medicinal products must be used within the terms of their marketing authorization, prescribing practices sometimes deviate from SPCs in violation of regulations, creating challenges when designing guidelines; therefore, SPCs could be reviewed by the EMA</li> </ul>
<b>Improved biosecurity to prevent emergence and spread of infection</b>	<ul style="list-style-type: none"> <li>• EC introduces legislation on animal welfare and biosecurity to prevent emergence and spread of infection</li> <li>• EC produces policies and initiatives to improve biosecurity (i.e. the Farm to Fork strategy)</li> <li>• EFSA provides technical advice on biosecurity measures to Member States</li> </ul>	<ul style="list-style-type: none"> <li>• National authorities develop policies and legislation on biosecurity, enforce EU regulation, undertake farm inspections, conduct risk assessments of potential threats, outline educational standards, and perform surveillance of AMR</li> </ul>	<ul style="list-style-type: none"> <li>• Effective biosecurity requires robust surveillance systems and access to biosecurity equipment</li> <li>• Overcoming resistance to change – requires education and training, capacity building and coordination among stakeholders</li> </ul>	<ul style="list-style-type: none"> <li>• Implementing biosecurity measures is often costly for farmers and they must be convinced of cost-benefits</li> <li>• Contracts must be designed to encourage advice on prevention and AMS from veterinarians</li> </ul>	<ul style="list-style-type: none"> <li>• Sanctioning farms can be difficult as defining boundaries of 'acceptable' biosecurity standards is challenging</li> </ul>

continued on next page

Table 4: Selected implementation considerations for key AMR interventions in animal health *continued*

INTERVENTION	ROLE FOR EU	ROLE FOR MEMBER STATES	OPERATIONAL CONSIDERATIONS	FINANCIAL CONSIDERATIONS	REGULATORY CONSIDERATIONS
<b>Vaccination to prevent emergence and spread of certain pathogens</b>	<ul style="list-style-type: none"> <li>EMA is responsible for assessment of quality, efficacy and safety of vaccines (although in some cases competent authorities in member states also undertake these functions)</li> <li>EC can fund research and development of new vaccines</li> </ul>	<ul style="list-style-type: none"> <li>National authorities, develop vaccination guidelines, outline educational standards, fund research and development, and conduct surveillance of vaccination sales and administration</li> </ul>	<ul style="list-style-type: none"> <li>Shortages of vaccines are commonplace, and hinder implementation</li> <li>Efficacy of vaccines is limited for certain indications or there are no vaccines for certain diseases</li> </ul>	<ul style="list-style-type: none"> <li>Lack of incentives to stimulate research and development of novel vaccines in animal health</li> <li>Vaccines are typically more expensive than antimicrobials</li> </ul>	<ul style="list-style-type: none"> <li>Industry has suggested recommendations to improve availability of new vaccines, such as simplification of MRPs, use of serology data as surrogate markers, better use of pharmacovigilance data, and alignment of regulatory requirements with USA regulators</li> </ul>
<b>Food safety compliance programmes</b>	<ul style="list-style-type: none"> <li>EC introduces legislation on managing food safety risks across supply chains</li> <li>EFSA provides technical advice to Member States on food safety, collects data on chemical (including antimicrobial) residues, zoonotic agents and food safety criteria in food, and conducts risk assessments across supply chains</li> </ul>	<ul style="list-style-type: none"> <li>National food safety authorities enforce legislation using sanctions, conduct risks assessment to identify hazards, conduct inspections to enforce standards, providing education and training, and perform surveillance on chemical residues, zoonoses and food safety criteria in food</li> </ul>	<ul style="list-style-type: none"> <li>Having multiple actors involved in food supply chains creates challenges in traceability, transparency and accountability</li> <li>Integrating food safety advice into AMR awareness campaigns can promote One Health approaches</li> </ul>	<ul style="list-style-type: none"> <li>Compliance with food safety standards can be costly for FBOs (particularly SMEs), including investment in training, equipment and regulatory fees</li> </ul>	<ul style="list-style-type: none"> <li>Complexity of regulatory requirements can sometimes be challenging for FBOs to navigate, including differences between EU and non-EU regulations</li> </ul>

AMR – antimicrobial resistance, AMU – antimicrobial usage, ASP – antimicrobial stewardship programme, EC – European Commission, ECDC – European Centre for Disease Prevention and Control, EFSA – European Food Safety Authority, EMA – European Medicines Agency, EU – European Union, FBO – food business operator, MRP – mutual recognition procedure, SME – small and medium-sized enterprise, SPC – summary of product characteristic, USA – United States of America.

## 2.3. Environmental health

### 2.3.1 Optimizing wastewater treatment to minimize spread of AMR

Wastewater treatment plants provide opportunities for bacteria, antibiotics and ARGs from a variety of different sources, such as hospitals, sewage, agriculture and industrial sites, to interact (Sambaza & Naicker, 2023). This can promote the development and further dissemination of AMR into waterways and the environment. However, there are also opportunities to implement improvements in wastewater treatment facilities that can limit the dissemination of AMR and ARGs. Approaches that have been explored to date include chlorination, ozonation, ferrate ultrasonic treatment, ultraviolet radiation, electrochemical technology and membrane technology (Amin, Hashemi & Bovini, 2013). Chlorination is a commonly used approach, but there is some evidence that disinfection by-products from this technique may further promote the development of ARGs (Li & Gu, 2019). Many of these techniques have been shown to be effective but there is no clear consensus regarding which is the most effective or sustainable approach to reducing resistant bacteria or ARGs in wastewater (Pandey et al., 2023).

The European Commission proposes legislation on wastewater treatment (to be adopted by the Parliament and the Council), and the European Environment Agency provides related scientific advice (Council of the EU and the European Council, 2024a). A revision of the EU's Urban Wastewater Treatment Directive is underway (political agreement was reached in March 2024) (Council of the EU and the European Council, 2024b). National environmental agencies enforce legislation on wastewater treatment, conduct inspections, monitor antimicrobial residues in water, and provide education and training. The EU has a relatively strong regulatory framework for wastewater treatment in relation to removal of organic matter and chemicals, although it is important to note that there is no legal obligation in the EU to monitor and remove antimicrobial residues or ARGs at present (EEA, 2022).

**Investment in research and consensus building is required to develop EU-wide regulations and standards on the improvements in wastewater treatment facilities necessary to reduce AMR.**

Further research is crucial to fully understand the role of the environment as a pool and driver of AMR (groundwaters and surface waters, wastewater, and agricultural soils), with several projects underway (Box 12). While some 'safe' concentration targets for antimicrobials have been identified in the scientific literature (Tell et al., 2019), there remains a lack of consensus among academics and policy-makers as to whether these targets should be implemented. While several countries are experimenting with different innovations in wastewater treatment to reduce AMR (Yu K-F et al., 2023; WISE-Freshwater, 2024), these need to be systematically evaluated and monitored. From a financial perspective,

compliance with additional wastewater regulations may require investment in treatment technologies, process modifications, or environmental monitoring programmes to meet standards. Depending upon how wastewater treatment facilities are financed in each Member State, the costs associated with these investments may be passed onto the public through increased utility bills. Therefore, a strong evidence base is necessary before new wastewater treatment requirements can be mandated and implemented.

#### Box 12: Research projects to understand spread of AMR in the environment in Belgium

In addition to the routine or prospective monitoring of antimicrobials in surface and ground water, several research projects have been launched to study AMR in the environment. For instance, ISSeP, a Walloon research centre, has raised awareness on the role of surface water in spreading AMR in the environment. In 2019 and 2020, the AntibioBug 1 project revealed the presence of antimicrobial-resistant *E. coli* in all of its 24 sampling points in the Ourthe, Amblève and Meuse basins (Crettels et al., 2022). In 2021, a follow-up project (AntibioBug 2) was launched to assess the rates of AMR of *E. coli* in bathing waters (BELMAP, 2023).

Sciensano, a federal research institute that provides support for public health policy in Belgium, is also investigating how AMR can develop and spread in the environment, through pilot studies. These include gathering data on *Klebsiella pneumoniae* strains and their resistance via the screening of wastewater samples over time and space (Sciensano, undated), and taking samples from two wastewater treatment plants in Belgium twice a week to test for the presence of a selection of eight ARGs. There are also upcoming plans to monitor the prevalence of multidrug-resistant organisms (MDROs) in nursing homes, including examining wastewater from these facilities to evaluate if this can serve as a measure of the prevalence of MDROs among residents.

### 2.3.2 Limiting dissemination from the pharmaceutical industry

Discharge effluent from the pharmaceutical industry is responsible for dissemination of high concentrations of different antibiotics and ARGs (Xue et al., 2022) as well as active pharmaceutical ingredients that can promote the emergence and increase of AMR (Larsson, 2014). This has received significant attention internationally, and the AMR Industry Alliance has produced recommended predicted no-effect concentrations (PNECs) for discharge effluents from pharmaceutical manufacturers (Vestel et al., 2022). However, in the absence of any standardized monitoring, the implementation of these recommended PNECs has predominantly relied on voluntary agreements with the pharmaceutical industry to report data on their facilities and suppliers (Boston Consulting Group & Wellcome, 2022).

The EC introduces legislation on good manufacturing practice (GMP) for medicines and active substances<sup>3</sup>, including limiting dissemination of chemicals to the environment (EUR-Lex, 2018a; European Commission, 2024b). The EC's recently proposed revisions to EU pharmaceutical legislation include strengthening

<sup>3</sup> An 'active substance' means any substance or mixture of substances intended to be used in the manufacture of a medicinal product that, when used in its production, becomes an active ingredient of that product.



environmental risk assessments (ERA)<sup>4</sup> during pharmaceutical manufacturing processes (European Commission, 2024c). The EMA provides technical advice on GMPs and hosts the 'GMP Inspectors Working Group', which aims to harmonize GMP activities at EU level (EMA, 2024c). National inspectorates monitor compliance with GMP regulations in pharmaceutical companies through inspections, national guidelines, education and training, and certification.

**Current concentration targets for antimicrobials in waste effluent from the pharmaceutical industry are voluntary, and mandating maximum concentration targets at the EU-level may improve compliance and consistency of implementation.**

Mandating maximum concentration targets for antimicrobials in discharge effluent from the pharmaceutical industry could help improve compliance and consistency of implementation. This would require developing a regulatory framework with guidance on recommended monitoring processes and sanctions. Several implementation considerations need to be navigated to successfully design such a policy. There is potential that consumers and health systems may bear the cost burden of implementing stricter manufacturing standards, and this may create challenges in securing public support for such a policy. Even if requirements to comply with mandated concentration targets for antimicrobials in waste effluent are incorporated into procurement processes, it is also challenging to monitor and enforce these regulations in non-EU manufacturers. There is also the possibility that new EU regulations on pharmaceutical production may exacerbate shortages for generic medication if implementing these regulations is responsible for significant additional costs or delays in manufacturing processes. Despite these trade-offs, it is important that the EU institutions consider options to regulate antimicrobial concentrations in discharge effluents from the pharmaceutical industry to protect the environment and limit the potential for further spread of AMR.

**2.3.3 Improving waste management in agricultural production**

It is estimated that approximately 75% of antibiotics are not absorbed by animals and are excreted in waste (Chee-Sanford et al., 2009), and disposal of agricultural waste can contribute to the dissemination of antimicrobial residues and resistant bacteria into the environment. As a result, there has been increasing attention to improving waste management in agricultural settings as a strategy to reduce AMR. Interventions include controlling runoff from agricultural areas to water bodies (Chee-Sanford et al., 2009), composting and anaerobic digestion techniques for manure management that reduce antimicrobial residues (Katada et al., 2021; Zalewska et al., 2021), and proper disposal of antimicrobial-contaminated waste. Most importantly, sustainable farming approaches are needed that limit reliance on antimicrobials, and therefore excretion

in waste, including improved biosecurity and husbandry practices, rotational cropping and vaccination, as discussed in previous sections (Van Boeckel et al., 2015).

The EC introduces legislation on waste management and sustainable farming, and provides some funding for initiatives (e.g. through Common Agricultural Policy and Rural Development Programmes) (Duquennoi & Martinez, 2022). National authorities enforce regulations on waste management, conduct inspections and issue permits, provide technical assistance, and collect data on waste generation and environmental impacts.

**Improvements in agricultural waste management would have multiple benefits including reducing the dissemination of AMR in the environment and promoting sustainable soil management practices, although more evidence is needed on acceptable concentration levels of antimicrobials.**

Approaches to the treatment of manure (i.e. composting) vary across Member States because of diverse agricultural practices, limited monitoring and enforcement capacity, and lack of awareness and education (European Court of Auditors, 2023). Barriers to implementation of stricter regulations on agricultural waste management include the perception that this would increase costs for farmers, despite the fact that interventions such as treatment of manure that may reduce AMR can also promote sustainable soil management and would promote long-term food security in the EU and increase long-term yields for farmers (European Court of Auditors, 2023). This means that awareness raising discussed in previous sections could incorporate clear communication on these trade-offs as well. While it is known that several agricultural waste management approaches can limit the dissemination of antimicrobial residues and genes in the environment (Van Epps & Blaney, 2016; Keenum et al., 2021; Tang et al., 2023; Zalewska et al., 2023), there is currently no consensus from the scientific community on acceptable antimicrobial residue concentration levels in agriculture waste to minimize dissemination in the environment and potential transmission to humans and animals. Once established, this would help provide the rationale for stricter regulations on waste management in agricultural production.

<sup>4</sup> The 'environmental risk assessment (ERA)' means the evaluation of risks to the environment, or risks to public health, posed by the release of the medicinal product in the environment from the use and disposal of the medicinal product and the identification of risk prevention, limitation and mitigation measures. For medicinal products with an antimicrobial mode of action, the ERA also encompasses an evaluation of the risk for AMR selection in the environment due to the manufacturing, use and disposal of that medicinal product.

Table 5: Selected implementation considerations for key AMR interventions in environmental health

INTERVENTION	ROLE FOR EU	ROLE FOR MEMBER STATES	OPERATIONAL CONSIDERATIONS	FINANCIAL CONSIDERATIONS	REGULATORY CONSIDERATIONS
<b>Environmental health</b>					
<b>Optimizing wastewater treatment to minimize spread of AMR</b>	<ul style="list-style-type: none"> <li>EC introduces legislation on wastewater treatment (such as the Urban Wastewater Treatment Directive)</li> <li>EEA provides scientific advice on wastewater treatment</li> </ul>	<ul style="list-style-type: none"> <li>National environmental agencies are responsible for enforcing legislation on wastewater treatment, conducting inspections, monitoring antimicrobial residues in water, and providing education and training</li> </ul>	<ul style="list-style-type: none"> <li>Innovations in wastewater treatment to reduce AMR need to be evaluated and monitored</li> <li>More evidence is needed regarding which residues and concentration limits should be prioritized for wastewater treatment</li> </ul>	<ul style="list-style-type: none"> <li>Compliance with wastewater regulations may require investments in additional treatment technologies, process modifications, or environmental monitoring programmes to meet standards; these costs may increase utility bills</li> </ul>	<ul style="list-style-type: none"> <li>Lack of consensus regarding which residues and concentrations should be monitored to minimize dissemination of AMR in the environment creates challenges in defining standards and developing regulations</li> <li>As the existing EC regulation in this area is extensive, integrating AMR into existing regulations might be easier than creating parallel regulatory frameworks</li> </ul>
<b>Limiting dissemination from the pharmaceutical industry</b>	<ul style="list-style-type: none"> <li>EC introduces legislation on GMP, including limiting dissemination of chemicals to environment</li> <li>EMA provides technical advice on GMPs and hosts the 'GMP Inspectors Working Group', which aims to harmonize GMP activities at EU level</li> </ul>	<ul style="list-style-type: none"> <li>National inspectorates monitor compliance with GMP regulations in pharmaceutical companies through inspections, national guidelines, education and training, and certification</li> </ul>	<ul style="list-style-type: none"> <li>Challenges in regulating non-EU manufacturers and the global impact of potential new EU regulations on pharmaceutical production (including exacerbating shortages)</li> </ul>	<ul style="list-style-type: none"> <li>Consumers may bear the cost burden of implementing stricter manufacturing standards related to antimicrobial concentrations in waste effluent</li> </ul>	<ul style="list-style-type: none"> <li>The current concentration targets for antimicrobials in waste effluent have been developed by industry and are subject to voluntary agreements</li> </ul>
<b>Improving waste management in agricultural production</b>	<ul style="list-style-type: none"> <li>EC introduces legislation on waste management and sustainable farming, and provides some funding for initiatives (i.e. through Common Agricultural Policy and Rural Development Programmes)</li> </ul>	<ul style="list-style-type: none"> <li>National authorities enforce regulations on waste management, conduct inspections and issue permits, provide technical assistance, and collect data on waste generation and environmental impacts</li> </ul>	<ul style="list-style-type: none"> <li>Implementation of standards for treatment of manure (i.e. composting) varies across Member States because of diverse agricultural practices, limited monitoring and enforcement capacity, and lack of awareness and education</li> </ul>	<ul style="list-style-type: none"> <li>Perception that stricter regulations on agricultural waste management may increase costs for farmers</li> </ul>	<ul style="list-style-type: none"> <li>There is no consensus on acceptable antimicrobial residue concentration levels in waste to minimize dissemination in the environment and potential transmission to humans and animals</li> </ul>

AMR – antimicrobial resistance, EC – European Commission, EEA – European Economic Area, EMA – European Medicines Agency, EU – European Union, GMP – good manufacturing practice.

## 2.4 Antimicrobial innovation and access

Policy interventions to support sustainable innovation and access to effective antibiotics in the EU and relevant implementation considerations have been comprehensively reviewed within recent European Observatory on Health Systems and Policies publications produced during the 2023 Swedish Presidency of the Council of the EU (Anderson, Panteli & Mossialos, 2023; Anderson et al., 2023). Key findings from this work that complement the previous sections of this policy brief are summarized below.

### 2.4.1 Ensuring consistent access to essential antimicrobials

Several policy interventions are required to secure consistent access to essential antimicrobials (Table 6). Overcoming shortages of antimicrobials will require addressing financial unattractiveness, broadening suppliers, investment in manufacturing capacity, and maintaining consistent production. Employing innovative measures, such as group purchasing and subscription models, can ensure that contracts are commercially viable and promote market stability. However, challenges arise from the limited number of producers and unpredictable demand, with much production based outside the EU. Another solution entails developing a European pharmaceutical database, which would pinpoint all the players, optimizing risk management and offering alternative sourcing avenues during shortages. Coordination between EU and national strategies and diversifying stockpiles are also key. In conclusion, a multifaceted approach that includes regulatory reforms, production strategy shifts and robust data systems is crucial for a resilient antimicrobial supply chain.

### 2.4.2 Stimulating research and development of novel antimicrobials

To advance antimicrobial R&D, a comprehensive incentive framework is needed (Figure 3, page 34). This framework should prioritize public health by addressing pressing medical needs, promoting responsible AMU, enhancing patient access, and preserving environmental integrity (Anderson et al., 2023). On the commercial side, enhancing returns from innovative antimicrobials and ensuring that SMEs thrive in the market is essential. Successful deployment of these incentives also requires strategic considerations about their magnitude, timing and governance, and a commitment to international collaboration.

More investment in push incentives, such as direct grants, is crucial throughout all R&D stages, especially during the preclinical phase when many antimicrobial developers struggle to resource funding to continue research and development. This helps in navigating the difficult transitions from early discovery to preclinical research, and from preclinical to early clinical research. While some entities (such as the Combating Antibiotic Resistant Bacteria Biopharmaceutical Accelerator (CARB-X) and the Global Antibiotic Research and Development Partnership (GARDP)) already aid in various R&D stages, there is an urgent need for more financial backing from international and national donors to increase investment.

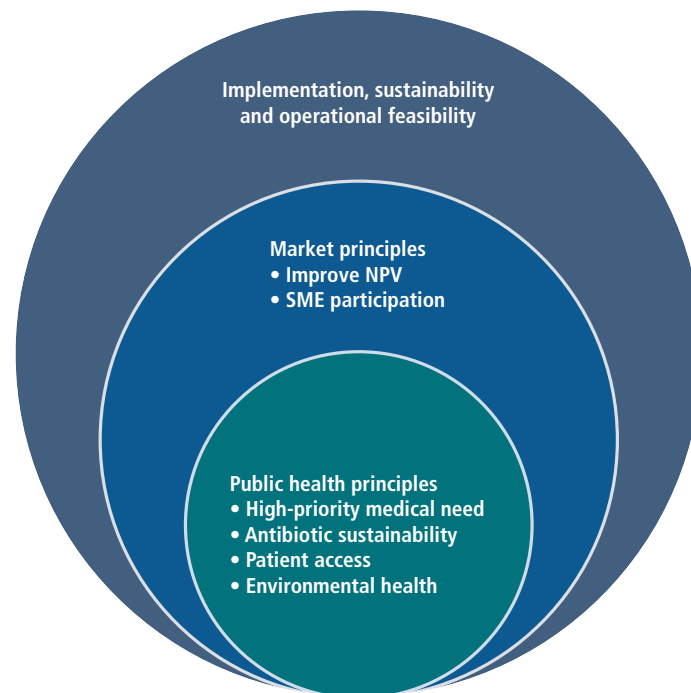
Pull incentives, such as financial rewards linked to R&D results, reimbursement reforms and regulatory changes, are also needed to create viable markets for antimicrobials. Several options are currently being proposed by different EU actors, including subscription payments, milestone

**Table 6: Policy actions to secure sustainable access to antimicrobials**

POLICY DOMAIN	POLICY ACTION	DEFINITION
<b>Procurement</b>	Joint procurement	The practice of multiple buyers (such as multiple countries) collaborating to collectively publish a single tender for a drug. This can have several advantages, including enhancing transparency through better information sharing, strengthening bargaining power, and mitigating overly high transaction costs by pooling skills, capacities and negotiations.
	Delinking revenues from sales volumes	Payments for antimicrobials based on an ongoing and guaranteed revenue, irrespective of sales volumes, which removes incentives to oversell antimicrobials (e.g. annual revenue guarantees).
<b>Mapping and stockpiling products</b>	Mapping of available products	Identifying distribution of available stockpiles of antimicrobials, e.g. across different countries.
	Physical stockpiling	Physical stockpiles of medications procured and stored using public funds.
	Virtual stockpiling	A virtual database on needs and deployable stocks of antimicrobials in each country, to facilitate the voluntary exchange of available supplies to meet surges in demand.
<b>Optimizing manufacturing</b>	Production capacity mapping	Identifying distribution of suppliers capable of producing antimicrobials or their precursors (such as active pharmaceutical ingredients (APIs), and their ability to increase output if required.
	Capital investment in manufacturing capacity	Investment in diversification of global manufacturing capacity, which is currently heavily concentrated in China and India.

Source: Adapted from Anderson, Panteli & Mossialos, 2023.

**Figure 3: Incentives developed to encourage antimicrobial research and development can be aligned by considering public health and market factors, as well as implementation and feasibility**



Source: Adapted from Simpkin et al., 2017, who developed the figure using principles from Renwick, Simpkin & Mossialos, 2016.

Note: NPV: net present value; SME: small and medium-sized enterprise.

payments, market entry rewards and transferable exclusivity extension vouchers. Subscription payments stand out as an effective means to maintain the sustainability of antimicrobials and secure improved access (Anderson & Mossialos, 2020). Moreover, these incentives can be integrated with others, including market entry rewards. However, challenges exist when coordinating the implementation of subscription payments for antimicrobials across Member States. Transferable exclusivity extensions may be relatively easier

to implement (Anderson, Wouters & Mossialos, 2023) but uncertainty regarding their financial impact and effectiveness has created concerns among Member States who have opposed their implementation (McDonnell, 2022; Årdal C et al., 2024). Lastly, for SMEs, milestone payments can be a particularly useful incentive, granting them the financial backing they need during pivotal moments in their R&D journey.

### 3. Conclusions

AMR is a significant public health threat, with multiple drivers in different sectors. However, while policy discussions about the need to address it have been ongoing for years, observed progress towards national and international targets is variable and generally lagging behind. This clearly shows that there needs to be a change of perspective in how the AMR response is approached, with concerted intersectoral and multilevel action that focuses on strategies that have been shown to be effective. Recent developments at the EU and Member State levels are encouraging, but their success greatly depends on how they are taken forward.

It is essential that policy-makers at different levels recognize the need to take strong action, prioritize strategies that work, and consider how best to implement them in each setting. Adopting a One Health approach is a prerequisite for addressing AMR, but given the many levels of necessary action, the multiple actors concerned and the siloed nature of many regulatory and operational provisions, incentives are difficult to align and the implementation of successful interventions is challenging. To support these objectives, this policy brief identified 12 key strategies spanning the human, animal and environmental sectors, along with enablers and barriers for their implementation.

A key common enabler that emerged across strategies and sectors is strong leadership commitment. This implies that understanding the political economy around AMR action is crucial for high-level policy-makers at the European and national levels. Those responsible for setting the framework for (joint) targets and standards, and drawing up implementation strategies (e.g. in the form of updated national action plans), should have a clear understanding of the stakeholders involved and how they need to be engaged in the process to ensure they are properly supported. This should increase the likelihood of sustained implementation and meaningful change. However, it also requires mobilization across various government departments to ensure that investment and support are really channeled where they are most needed, and that implemented measures are coherent and enable concerted action.

Another fundamental enabler for the successful implementation of effective strategies to address AMR is raising awareness and cultivating the overall understanding of how the drivers of resistance can be addressed. This can include targeted campaigns for different stakeholders around the drivers of AMR, and a more basic incorporation of AMR considerations in education, for the general public and for professionals in the human, animal and environmental sectors. Here too, stakeholder engagement in the development of such initiatives is key to ensure they are effective.

The findings of this brief reinforce the importance of both horizontal and vertical collaboration, across sectors and between the European, national, regional and local levels. Platforms such as the European Union's AMR One Health Network, and its envisioned interagency AMR working group can support these objectives. Linked to this is the

necessity for a clear definition of responsibilities and the establishment and/or reshaping of the corresponding accountability mechanisms to ensure action can be monitored and adapted as needed. This presupposes strong information systems that can enhance surveillance data towards evaluating policy effectiveness.

The EU has a key role to play, not least by setting a common regulatory framework, defining common standards, monitoring progress towards desired targets, and supporting Member State collaboration and exchange. Additional actions, such as the joint purchasing of antimicrobials or joint incentives for the development of innovative medicines, have been proposed and merit further attention. However, most of the recommended actions discussed in this brief remain within the remit of Member States. Even within Europe, different countries may need to pay particular attention to specific drivers, depending on which contributing factors are most pronounced in their settings. What is more, socioeconomic and sociocultural differences will influence the way strategies to address AMR, be it in terms of availability of diagnostics and medicines or the rollout of behavioural interventions, will impact different population groups within countries, and must be taken into account. Tools such as the WHO AMR Compass can support in identifying areas of particular focus.

Finally, keeping AMR high on international and national political agendas is a prerequisite for sustained support towards the implementation of successful strategies. The current momentum, created on the basis of strong international collaboration at different levels would need to be sustained, and the initiative shown by successive Presidencies of the Council of the European Union would need to be carried forward into the future, linked to the monitoring of progress towards joint targets and the evaluation of successes and failures.

## 4. References

- Aabenhus R et al. (2014). Biomarkers as point-of-care tests to guide prescription of antibiotics in patients with acute respiratory infections in primary care. *Cochrane Database of Systematic Reviews*, 11:CD010130.
- Agyeman WY et al. (2022). A systematic review of antibiotic resistance trends and treatment options for hospital-acquired multidrug-resistant infections. *Cureus*, 14(10):e29956.
- AMCRA (2021). *Activities and achievements regarding the reduction of antibiotics use and resistance in animals in Belgium 2016–2020*. Brussels, AMCRA (Knowledge Centre on Antibiotic Use and Resistance in Animals in Belgium) ([https://www.fasfc.be/sites/default/files/content/explorer/Animals/AMR2020\\_AMR\\_report\\_EN.pdf](https://www.fasfc.be/sites/default/files/content/explorer/Animals/AMR2020_AMR_report_EN.pdf), accessed Mar 14, 2024).
- AMCRA (2024). *Recommendations and legislation*. Brussels, AMCRA (Knowledge Centre on Antibiotic Use and Resistance in Animals in Belgium) (<https://www.amcra.be/en/recommendations-and-legislation>, accessed Mar 14, 2024).
- Amin MM, Hashemi H, Bovini AM (2013). A review on wastewater disinfection. *International Journal of Environmental Health Engineering*, 2(1):1–9.
- Anderson M, Mossialos E (2020). Incentivising antibiotic research and development: Is the UK's subscription payment model part of the solution? *The Lancet Infectious Diseases*, 20(2):162–163.
- Anderson M, Panteli D, Mossialos E (2023). *How can the EU support sustainable innovation and access to effective antibiotics? Policy options for existing and new medicines*. Copenhagen, World Health Organization (acting as the host organization for, and secretariat of, the European Observatory on Health Systems and Policies), Policy Brief No. 51 (<http://www.ncbi.nlm.nih.gov/books/NBK594073>, accessed Mar 13, 2024).
- Anderson M, Wouters OJ, Mossialos E (2023). Transferable exclusivity extensions to stimulate antibiotic research and development: What is at stake? *The Lancet Microbe*, 4(3):e127–128.
- Anderson M et al. (2019). *Averting the AMR crisis: What are the avenues for policy action for countries in Europe?* Copenhagen, World Health Organization (acting as the host organization for, and secretariat of, the European Observatory on Health Systems and Policies), Policy Brief No. 32 (<http://www.ncbi.nlm.nih.gov/books/NBK543406>, accessed Jan 24, 2024).
- Anderson M et al. (2023). Challenges and opportunities for incentivising antibiotic research and development in Europe. *The Lancet Regional Health Europe*, 33:100705.
- Årdal C et al. (2024). Transferable exclusivity voucher: A flawed incentive to stimulate antibiotic innovation. *The Lancet*, 403(10422):e2–4.
- Atkins KE et al. (2018). Use of mathematical modelling to assess the impact of vaccines on antibiotic resistance. *The Lancet Infectious Diseases*, 18(6):e204–213.
- BELMAP (2023). *BELMAP: One health report on antibiotic use and resistance in Belgium*. ([https://www.health.belgium.be/sites/default/files/belmap2022\\_report.pdf](https://www.health.belgium.be/sites/default/files/belmap2022_report.pdf), accessed Mar 14, 2024).
- Biocheck.UGent (undated). *My Biocheck* (home page) (<https://biocheckgent.com/en/worldwide>, accessed Mar 16, 2024).
- Borek AJ et al. (2020). Optimising antimicrobial stewardship interventions in English primary care: A behavioural analysis of qualitative and intervention studies. *BMJ Open*, 10:e039284.
- Borek AJ et al. (2022). How can behavioural science contribute to qualitative research on antimicrobial stewardship in primary care? *JAC Antimicrobial Resistance*, 4(1):dlac007.
- Boston Consulting Group & Wellcome (2022). *Understanding the antibiotic manufacturing ecosystem* (<https://cms.wellcome.org/sites/default/files/2022-04/understanding-the-antibiotic-manufacturing-ecosystem-2022.pdf>, accessed Dec 30, 2023).
- Brigadoi G et al. (2023). The impact of antimicrobial stewardship programmes in paediatric emergency departments and primary care: A systematic review. *Therapeutic Advances in Infectious Diseases*, 10:20499361221141771.
- British Society for Antimicrobial Chemotherapy (2023). *Global Antimicrobial Stewardship Scheme: First centres of excellence announced*. Birmingham, British Society for Antimicrobial Chemotherapy (<https://bsac.org.uk/global-antimicrobial-stewardship-scheme-first-centres-of-excellence-announced>, accessed Mar 14, 2024).
- Browne K, Mitchell BG (2023). Multimodal environmental cleaning strategies to prevent healthcare-associated infections. *Antimicrobial Resistance and Infection Control*, 12:83.
- Butler CC et al. (2012). Effectiveness of multifaceted educational programme to reduce antibiotic dispensing in primary care: Practice based randomised controlled trial. *BMJ*, 344:d8173.
- Chee-Sanford JC et al. (2009). Fate and transport of antibiotic residues and antibiotic resistance genes following land application of manure waste. *Journal of Environmental Quality*, 38(3):1086–1108.
- Council of the EU and the European Council (2024a). *Wastewater treatment*. Brussels, Council of the EU and the European Council (<https://www.consilium.europa.eu/en/policies/wastewater-treatment>, accessed Mar 14, 2024).

- Council of the EU and the European Council (2024b). *Urban wastewater: Council and Parliament reach a deal on new rules for more efficient treatment and monitoring*. Brussels, Council of the EU and the European Council (<https://www.consilium.europa.eu/en/press/press-releases/2024/01/29/urban-wastewater-council-and-parliament-reach-a-deal-on-new-rules-for-more-efficient-treatment-and-monitoring>, accessed Mar 30, 2024).
- Cox CM, Jones M (2001). Is it possible to decrease antibiotic prescribing in primary care? An analysis of outcomes in the management of patients with sore throats. *Family Practice*, 18(1):9–13.
- Crettels L et al. (2022). Antimicrobial resistance of *Escherichia coli* isolated from freshwaters and hospital effluents in Belgium. *Letters in Applied Microbiology*, 74(3):411–418.
- da Silva Giacomini L et al. (2023). Production performance and economic analysis of broiler chickens after vaccination with a live attenuated vaccine against avian coccidiosis. *Parasitology Research*, 122(7):1677–1683.
- Dancer SJ (2023). Hospital cleaning: Past, present, and future. *Antimicrobial Resistance & Infection Control*, 12:80.
- Davey P et al. (2017). Interventions to improve antibiotic prescribing practices for hospital inpatients. *Cochrane Database of Systematic Reviews*, 2(2):CD003543.
- Dewulf J et al. (2018). How to measure biosecurity and the hygiene status of farms. In: *Biosecurity in animal production and veterinary medicine: From principles to practice*. Leuven, Academische Coöperatieve Venootshchap (ACCO), 115–32.
- Dewulf J et al. (2020). Tackling antimicrobial resistance in the food and livestock sector. In: Anderson M, Cecchini M, Mossialos E, eds. *Challenges to tackling antimicrobial resistance: Economic and policy responses*. Cambridge, Cambridge University Press, 99–124.
- Diana A et al. (2020). Effect of welfare standards and biosecurity practices on antimicrobial use in beef cattle. *Scientific Reports*, 10(1):20939.
- Du Y et al. (2022). Current status and development prospects of aquatic vaccines. *Frontiers in Immunology*, 13:1040336.
- Duquennoi C, Martinez J (2022). European Union's policymaking on sustainable waste management and circularity in agroecosystems: The potential for innovative interactions between science and decision-making. *Frontiers in Sustainable Food Systems*, 6:doi:10.3389/fsufs.2022.937802.
- DVFA (2024). *Distribution and use of veterinary medicinal products*. Glostrup, Danish Veterinary Food Administration (<https://en.foedevarestyrelsen.dk/animals/animal-health/veterinary-medicine/distribution-and-use-of-veterinary-medicinal-products->, accessed Mar 14, 2024).
- ECDC (2022). *Assessing the health burden of infections with antibiotic-resistant bacteria in the EU/EEA, 2016–2020*. Stockholm, European Centre for Disease Prevention and Control (<https://www.ecdc.europa.eu/en/publications-data/health-burden-infections-antibiotic-resistant-bacteria-2016-2020>, accessed Mar 31, 2024).
- ECDC (2023a). *Amended ECDC Strategy 2021–2027*. Stockholm, European Centre for Disease Prevention and Control (<https://www.ecdc.europa.eu/en/publications-data/amended-ecdc-strategy-2021-2027>, accessed Jan 8, 2024).
- ECDC (2023b). *Vaccine Monitoring Platform*. Stockholm, European Centre for Disease Prevention and Control (<https://www.ecdc.europa.eu/en/about-ecdc/what-we-do/partners-and-networks/eu-institutions-and-agencies/vaccine-monitoring>, accessed Mar 14, 2024).
- ECDC, EFSA, EMA (2024). Antimicrobial consumption and resistance in bacteria from humans and food-producing animals. European Centre for Disease Prevention and Control, European Food Safety Authority and European Medicines Agency. *EFSA Journal*, 22:e8589.
- Edeghere O, Wilson J, Hyde C (2010). *Interventions to improve the prescribing of antibiotics by healthcare professionals in ambulatory care settings*. Birmingham, University of Birmingham, Unit of Public Health, Epidemiology and Biostatistics (<https://www.birmingham.ac.uk/Documents/college-mds/haps/projects/WMHTAC/REPreports/2010/Antibiotics.pdf>, accessed Apr 14, 2024).
- Edwards R et al. (2012). Optimisation of infection prevention and control in acute health care by use of behaviour change: A systematic review. *The Lancet Infectious Diseases*, 12(4):318–329.
- EEA (2022). *Water signals*. Copenhagen, European Environment Agency (<https://www.eea.europa.eu/publications/zero-pollution/health/signals/water>, accessed Mar 14, 2024).
- EFSA Panel on Biological Hazards (BIOHAZ) et al. (2022). Transmission of antimicrobial resistance (AMR) during animal transport. Parma, European Food Safety Authority. *EFSA Journal*, 20:e07586.
- EMA (2017a). *Data requirements for immunological veterinary medicinal products intended for minor use or minor species – Scientific guideline*. Amsterdam, European Medicines Agency (<https://www.ema.europa.eu/en/data-requirements-immunological-veterinary-medicinal-products-intended-minor-use-or-minor-species-scientific-guideline>, accessed Mar 14, 2024).
- EMA (2017b). *Joint EMA/HMA Veterinary Vaccine Availability Action Plan: Analysis of industry recommendations*. Amsterdam, European Medicines Agency ([https://www.ema.europa.eu/system/files/documents/other/wc500229116\\_en.pdf](https://www.ema.europa.eu/system/files/documents/other/wc500229116_en.pdf), accessed Mar 14, 2024).

- EMA (2022). *Sales of veterinary antimicrobial agents in 31 European countries in 2021: Trends from 2010 to 2021 twelfth ESVAC report*. Luxembourg, Publications Office of the European Union ([https://www.ema.europa.eu/en/documents/report/sales-veterinary-antimicrobial-agents-31-european-countries-2021-trends-2010-2021-twelfth-esvac-report\\_en.pdf](https://www.ema.europa.eu/en/documents/report/sales-veterinary-antimicrobial-agents-31-european-countries-2021-trends-2010-2021-twelfth-esvac-report_en.pdf), accessed Mar 13, 2024).
- EMA (2023). *Sales of veterinary antimicrobial agents in 31 European countries in 2022: Trends from 2010 to 2022 thirteenth ESVAC report*. Luxembourg, Publications Office of the European Union ([https://www.ema.europa.eu/en/documents/report/sales-veterinary-antimicrobial-agents-31-european-countries-2022-trends-2010-2022-thirteenth-esvac-report\\_en.pdf](https://www.ema.europa.eu/en/documents/report/sales-veterinary-antimicrobial-agents-31-european-countries-2022-trends-2010-2022-thirteenth-esvac-report_en.pdf), accessed Apr 14, 2024).
- EMA (2024a). *European Surveillance of Veterinary Antimicrobial Consumption (ESVAC): 2009 – 2023*. Amsterdam, European Medicines Agency (<https://www.ema.europa.eu/en/veterinary-regulatory-overview/antimicrobial-resistance-veterinary-medicine/european-surveillance-veterinary-antimicrobial-consumption-esvac-2009-2023>, accessed Jan 25, 2024).
- EMA (2024b). *Antimicrobial Sales and Use Platform*. Amsterdam, European Medicines Agency (<https://www.ema.europa.eu/en/veterinary-regulatory-overview/antimicrobial-resistance-veterinary-medicine/antimicrobial-sales-use-platform>, accessed Mar 14, 2024).
- EMA (2024c). *Good manufacturing practice*. Amsterdam, European Medicines Agency (<https://www.ema.europa.eu/en/human-regulatory-overview/research-development/compliance-research-development/good-manufacturing-practice>, accessed Mar 14, 2024).
- EUR-Lex (1998). *Council Directive 98/58/EC of 20 July 1998 concerning the protection of animals kept for farming purposes*. Brussels, Council of the EU (<https://eur-lex.europa.eu/eli/dir/1998/58/oj>, accessed Mar 31, 2024).
- EUR-Lex (2001). *Community strategy against antimicrobial resistance*. Brussels, European Commission (<https://eur-lex.europa.eu/EN/legal-content/summary/community-strategy-against-antimicrobial-resistance.html>, accessed Apr 3, 2024).
- EUR-Lex (2002). *Council Recommendation of 15 November 2001 on the prudent use of antimicrobial agents in human medicine*. Brussels, Council of the EU (<http://data.europa.eu/eli/reco/2002/77/oj/eng>, accessed Apr 3, 2024).
- EUR-Lex (2003a). Regulation (EC) No 1831/2003 of the European Parliament and of the Council of 22 September 2003 on additives for use in animal nutrition. Brussels, European Parliament and Council (<https://eur-lex.europa.eu/eli/reg/2003/1831/oj>, accessed Jan 25, 2024).
- EUR-Lex (2003b). Directive 2003/99/EC of the European Parliament and of the Council of 17 November 2003 on the monitoring of zoonoses and zoonotic agents, amending Council Decision 90/424/EEC and repealing Council Directive 92/117/EEC. Brussels, European Parliament and Council (<http://data.europa.eu/eli/dir/2003/99/oj/eng>, accessed March 31, 2024).
- EUR-Lex (2011). Communication from the Commission to the European Parliament and the Council: Action plan against the rising threats from Antimicrobial Resistance. Brussels, European Commission (<https://eur-lex.europa.eu/legal-content/EN/TXT/?uri=CELEX%3A52011DC0748>, accessed Apr 14, 2024).
- EUR-Lex (2016). Regulation (EU) 2016/429 of the European Parliament and of the Council of 9 March 2016 on transmissible animal diseases and amending and repealing certain acts in the area of animal health (Animal Health Law). Brussels, European and Council (<https://eur-lex.europa.eu/eli/reg/2016/429/2019-12-14>, accessed Mar 14, 2024).
- EUR-Lex (2017). *Commission notice — EU Guidelines for the prudent use of antimicrobials in human health*. Brussels, European Commission ([https://eur-lex.europa.eu/legal-content/EN/TXT/?uri=uriserv:OJ.C\\_.2017.212.01.0001.01.ENG&toc=OJ:C:2017:212:TOC](https://eur-lex.europa.eu/legal-content/EN/TXT/?uri=uriserv:OJ.C_.2017.212.01.0001.01.ENG&toc=OJ:C:2017:212:TOC), accessed Feb 14, 2024).
- EUR-Lex (2018a). Regulation (EU) 2019/6 of the European Parliament and of the Council of 11 December 2018 on veterinary medicinal products and repealing Directive 2001/82/EC. Brussels, European Union (<https://eur-lex.europa.eu/eli/reg/2019/6/oj>, accessed Jan 25, 2024).
- EUR-Lex (2018b). Regulation (EU) 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. Brussels, European Parliament and Council (<https://eur-lex.europa.eu/eli/reg/2019/4/oj>, accessed Apr 14, 2024).
- EUR-Lex (2019). Commission Delegated Regulation (EU) 2020/689 of 17 December 2019 supplementing Regulation (EU) 2016/429 of the European Parliament and of the Council as regards rules for surveillance, eradication programmes, and disease-free status for certain listed and emerging diseases. Brussels, European Commission ([https://eur-lex.europa.eu/eli/reg\\_del/2020/689/oj](https://eur-lex.europa.eu/eli/reg_del/2020/689/oj), accessed Mar 31, 2024).
- EUR-Lex (2020a). Commission Implementing Decision (EU) 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. Brussels, European Commission ([http://data.europa.eu/eli/dec\\_impl/2020/1729/oj/eng](http://data.europa.eu/eli/dec_impl/2020/1729/oj/eng), accessed Jan 25, 2024).
- EUR-Lex (2020b). Commission Delegated Regulation (EU) 2020/687 of 17 December 2019 supplementing Regulation (EU) 2016/429 of the European Parliament and the Council, as regards rules for the prevention and control of certain listed diseases. Brussels, European Commission ([https://eur-lex.europa.eu/eli/reg\\_del/2020/687/oj](https://eur-lex.europa.eu/eli/reg_del/2020/687/oj), accessed Mar 31, 2024).



- EUR-Lex (2022). Regulation (EU) 2019/6 of the European Parliament and of the Council of 11 December 2018 on veterinary medicinal products and repealing Directive 2001/82/EC. Brussels, European Parliament and Council (<http://data.europa.eu/eli/reg/2019/6/2022-01-28/eng>, accessed Oct 5, 2023).
- EUR-Lex (2023). *Proposal for a COUNCIL RECOMMENDATION on stepping up EU actions to combat antimicrobial resistance in a One Health approach*. Brussels, European Commission (<https://eur-lex.europa.eu/legal-content/EN/TXT/?uri=CELEX%3A52023DC0191>, accessed Oct 5, 2023).
- European Commission (2017). *A European One Health Action Plan against Antimicrobial Resistance (AMR)*. Brussels, European Union ([https://health.ec.europa.eu/system/files/2020-01/amr\\_2017\\_action-plan\\_0.pdf](https://health.ec.europa.eu/system/files/2020-01/amr_2017_action-plan_0.pdf), accessed Apr 14, 2024).
- European Commission (2020a). *Farm to Fork Strategy: For a fair, healthy and environmentally-friendly food system*. Brussels, European Commission ([https://food.ec.europa.eu/system/files/2020-05/f2f\\_action-plan\\_2020\\_strategy-info\\_en.pdf](https://food.ec.europa.eu/system/files/2020-05/f2f_action-plan_2020_strategy-info_en.pdf), accessed Oct 5, 2023).
- European Commission (2020b). Commission Delegated Regulation (EU) 2020/691 of 30 January 2020 supplementing Regulation (EU) 2016/429 of the European Parliament and of Council as regards rules for aquaculture establishments and transporters of aquatic animals. Brussels, European Commission (<https://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:32020R0691>, accessed Mar 31, 2023).
- European Commission (2021a). *Future-proofing pharmaceutical legislation – study on medicine shortages. Final report (revised)*. Luxembourg, Publications Office of the European Union (<https://op.europa.eu/en/publication-detail/-/publication/1f8185d5-5325-11ec-91ac-01aa75ed71a1/language-en>, accessed Oct 5, 2023).
- European Commission (2021b). *Zero Pollution Action Plan*. Brussels, European Commission, Environment ([https://environment.ec.europa.eu/strategy/zero-pollution-action-plan\\_en](https://environment.ec.europa.eu/strategy/zero-pollution-action-plan_en), accessed Mar 13, 2024).
- European Commission (2022a). *HERA factsheet – HEALTH UNION: Identifying top 3 priority health threats*. Brussels, European Commission ([https://health.ec.europa.eu/publications/hera-factsheet-health-union-identifying-top-3-priority-health-threats\\_en](https://health.ec.europa.eu/publications/hera-factsheet-health-union-identifying-top-3-priority-health-threats_en), accessed Dec 5, 2023).
- European Commission (2022b). *Data-driven implementation of a behavioural Antimicrobial Stewardship approach and expert consultancy for a more appropriate use of antimicrobials in Europe*. Brussels, European Commission, EU Funding & Tenders Portal (<https://ec.europa.eu/info/funding-tenders/opportunities/portal/screen/opportunities/projects-details/43332642/101079985/EU4H>, accessed Mar 14, 2024).
- European Commission (2022c). *European Health Union: HERA signs Joint Procurement contract for Pandemic Influenza Vaccine*. Brussels, European Commission. ([https://ec.europa.eu/commission/presscorner/detail/en/ip\\_22\\_4363](https://ec.europa.eu/commission/presscorner/detail/en/ip_22_4363), accessed Mar 14, 2024).
- European Commission (2024a). *Falsified medicines*. Brussels, European Commission, Medicinal products ([https://health.ec.europa.eu/medicinal-products/falsified-medicines\\_en](https://health.ec.europa.eu/medicinal-products/falsified-medicines_en), accessed Jan 25, 2024).
- European Commission (2024b). *EudraLex – Volume 4 – Good Manufacturing Practice (GMP) guidelines*. Brussels, European Commission, Medicinal products ([https://health.ec.europa.eu/medicinal-products/eudralex/eudralex-volume-4\\_en](https://health.ec.europa.eu/medicinal-products/eudralex/eudralex-volume-4_en), accessed Mar 14, 2024).
- European Commission (2024c). *AMR One Health Network: Environmental risk assessment in the revision of the EU pharmaceutical legislation*. Brussels, European Commission, DG Santé ([https://ec.europa.eu/assets/sante/health/amr/docs/amr\\_20240229\\_co05\\_en.pdf](https://ec.europa.eu/assets/sante/health/amr/docs/amr_20240229_co05_en.pdf), accessed Mar 31, 2024).
- European Commission et al. (2023). *Study on the barriers to effective development and implementation of national policies on antimicrobial resistance – Final report*. Luxembourg, Publications Office of the European Union (<https://op.europa.eu/en/publication-detail/-/publication/8e6eeab8-4ba3-11ee-9220-01aa75ed71a1/language-en>, accessed Apr 14, 2024).
- European Court of Auditors (2023). *EU efforts for sustainable soil management: Unambitious standards and limited targeting*. Luxembourg, European Court of Auditors ([https://www.eca.europa.eu/ECAPublications/SR-2023-19/SR-2023-19\\_EN.pdf](https://www.eca.europa.eu/ECAPublications/SR-2023-19/SR-2023-19_EN.pdf), accessed Mar 14, 2023).
- European Union (2015). *Commission notice: Guidelines for the prudent use of antimicrobials in veterinary medicine (2015/C 299/04)*. Brussels, European Commission ([https://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:52015XC0911\(01\)](https://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:52015XC0911(01)), accessed Apr 14, 2024).
- European Vaccination Information Portal (2024). *European Vaccination Information Portal* (home page). Brussels, European Union (<https://vaccination-info.europa.eu/en>, accessed Mar 14, 2024).
- Falk G, Fahey T (2009). C-reactive protein and community-acquired pneumonia in ambulatory care: Systematic review of diagnostic accuracy studies. *Family Practice*, 26:10–21.
- FAO (2016). *The FAO Action Plan on Antimicrobial Resistance 2016–2020*. Rome, Food and Agriculture Organization of the United Nations (<https://www.fao.org/3/i5996e/i5996e.pdf>, accessed Apr 14, 2024).
- FAO (2021). *The FAO Action Plan on Antimicrobial Resistance 2021–2025*. Rome, Food and Agriculture Organization of the United Nations (<https://www.fao.org/documents/card/fr?details=CB5545EN#:~:text=The%20aim%20of%20this%20plan,of%20expertise%20for%20FAO%20support>, accessed Mar 13, 2024).

- FAO, UNEP, WHO, WOAHA (2022). *One Health Joint Plan of Action, 2022–2026: Working together for the health of humans, animals, plants and the environment*. Food and Agriculture Organization of the United Nations, United Nations Environment Programme, World Health Organization, World Organisation for Animal Health (<https://www.fao.org/3/cc2289en/cc2289en.pdf>, accessed Apr 14, 2024).
- FarmFit (undated). *Biosafety audit*. Torhout, FarmFit (<https://farmfit.be/bioveiligheidsaudit>, accessed March 16, 2024).
- FASFC (2021). *Legislation on avian influenza*. Brussels, Federation Agency for the Safety of the Food Chain (<https://www.fasfc.be/animals/animal-health/animal-diseases/avian-diseases/avian-influenza/legislation>, accessed Mar 16, 2024).
- FASFC (undated). *African swine fever*. Brussels, Federation Agency for the Safety of the Food Chain (<https://www.fasfc.be/african-swine-fever/situation-in-belgium>, accessed Mar 16, 2024).
- Filia A et al. (2022). Are vaccine shortages a relevant public health issue in Europe? Results from a survey conducted in the framework of the EU Joint Action on Vaccination. *Vaccine*, 40(13):1987–1995.
- Filippitzi ME et al. (2018). Review of transmission routes of 24 infectious diseases preventable by biosecurity measures and comparison of the implementation of these measures in pig herds in six European countries. *Transboundary and Emerging Diseases*, 65(2):381–398.
- Food Safety Authority of Ireland (undated). *General provisions of the hygiene package*. Dublin, Food Safety Authority of Ireland (<https://www.fsai.ie/Enforcement-and-Legislation/Legislation/Food-Legislation/Game/General-Provisions-of-the-Hygiene-Package>, accessed Mar 31, 2024).
- Fox K et al. (2021). Computerised decision support in veterinary medicine, exemplified in a canine idiopathic epilepsy care pathway. *Journal of Small Animal Practice*, 62:911–917.
- Francis NA et al. (2009). Effect of using an interactive booklet about childhood respiratory tract infections in primary care consultations on reconsulting and antibiotic prescribing: A cluster randomised controlled trial. *BMJ*, 339:b2885.
- Frost I et al. (2023). The role of bacterial vaccines in the fight against antimicrobial resistance: An analysis of the preclinical and clinical development pipeline. *The Lancet Microbe*, 4(2):e113–125.
- Gelaude P et al. (2014). Biocheck.UGent: A quantitative tool to measure biosecurity at broiler farms and the relationship with technical performances and antimicrobial use. *Poultry Science*, 93(11):2740–2751.
- General Secretariat of the Council (2023). Council Recommendation on stepping up EU actions to combat antimicrobial resistance in a One Health approach (legal basis proposed by the Commission: Article 168(6)TFEU) – Adoption. Brussels, Council of the European Union (<https://data.consilium.europa.eu/doc/document/ST-9581-2023-INIT/en/pdf>, accessed Oct 5, 2023).
- Gibbs EPJ (2014). The evolution of One Health: A decade of progress and challenges for the future. *Veterinary Record*, 174(4):85–91.
- Golding SE, Ogden J, Higgins HM (2019). Shared goals, different barriers: A qualitative study of UK veterinarians' and farmers' beliefs about antimicrobial resistance and stewardship. *Frontiers in Veterinary Science*, 6 (<https://doi.org/10.3389/fvets.2019.00132>).
- HAI (2023). *Antimicrobial resistance in the Netherlands: An analysis of the 2015 National Action Plan and Recommendations for the Future*. Amsterdam, Health Action International ([https://haiweb.org/wp-content/uploads/2023/10/AMR-in-the-Netherlands\\_NAP-Recommendations.pdf](https://haiweb.org/wp-content/uploads/2023/10/AMR-in-the-Netherlands_NAP-Recommendations.pdf), accessed Mar 14, 2024).
- Hallsworth M et al. (2016). Provision of social norm feedback to high prescribers of antibiotics in general practice: A pragmatic national randomised controlled trial. *The Lancet*, 387(10029):1743–1752.
- Hardefeldt LY et al. (2018). Barriers to and enablers of implementing antimicrobial stewardship programs in veterinary practices. *Journal of Veterinary Internal Medicine*, 32(3):1092–1099.
- Haustein T et al. (2011). Use of benchmarking and public reporting for infection control in four high-income countries. *The Lancet Infectious Diseases*, 11(6):471–481.
- Hofacre CL et al. (2002). Effect of a commercial competitive exclusion culture on reduction of colonization of an antibiotic-resistant pathogenic *Escherichia coli* in day-old broiler chickens. *Avian Diseases*, 46(1):198–202.
- Hojat LS et al. (2022). Can electronic clinical decision support systems improve the diagnosis of urinary tract infections? A systematic review and meta-analysis. *Open Forum Infectious Diseases*, 10(1):ofac691.
- Jimenez CEP et al. (2023). Biosecurity and water, sanitation, and hygiene (WASH) interventions in animal agricultural settings for reducing infection burden, antibiotic use, and antibiotic resistance: A One Health systematic review. *The Lancet Planetary Health*, 7(5):e418–434.
- Jit M, Anderson M, Cooper B (2020). Quantifying the benefits of vaccines in combating antimicrobial resistance. *Eurohealth*, 26(1):16–19.
- Jones C, Thornton J, Wyatt JC (2021). Enhancing trust in clinical decision support systems: A framework for developers. *BMJ Health & Care Informatics*, 28(1):e100247.

- Katada S et al. (2021). Aerobic composting and anaerobic digestion decrease the copy numbers of antibiotic-resistant genes and the levels of lactose-degrading Enterobacteriaceae in dairy farms in Hokkaido, Japan. *Frontiers in Microbiology*, 12:737420.
- Keenum I et al. (2021). Combined effects of composting and antibiotic administration on cattle manure-borne antibiotic resistance genes. *Microbiome*, 9(1):81.
- Kim KM et al. (2020). Do penalty-based pay-for-performance programs improve surgical care more effectively than other payment strategies? A systematic review. *Annals of Medicine and Surgery (London)*, 60:623–630.
- Knobloch MJ et al. (2021). Integrating antibiotic stewardship and infection prevention and control programs using a team science approach. *American Journal of Infection Control*, 49(8):1072–1074.
- Kooda K, Canterbury E, Bellolio F (2022). Impact of pharmacist-led antimicrobial stewardship on appropriate antibiotic prescribing in the emergency department: A systematic review and meta-analysis. *Annals of Emergency Medicine*, 79(4):374–387.
- Larsson DGJ (2014). Pollution from drug manufacturing: Review and perspectives. *Philosophical Transactions of the Royal Society B: Biological Sciences*, 369(1656):20130571.
- Lee SY, An SH (2022). Impact of pharmacist intervention in antibiotic stewardship programmes for critically ill neonates: A systematic review and meta-analysis. *Journal of Clinical Pharmacy and Therapeutics*, 47(4):430–444.
- Li D, Gu AZ (2019). Antimicrobial resistance: A new threat from disinfection byproducts and disinfection of drinking water? *Current Opinion in Environmental Science & Health*, 7:83–91.
- Lipsitch M, Siber GR (2016). How can vaccines contribute to solving the antimicrobial resistance problem? *mBio*, 7:e00428-16.
- Little P et al. (2013). Effects of internet-based training on antibiotic prescribing rates for acute respiratory-tract infections: A multinational, cluster, randomised, factorial, controlled trial. *The Lancet*, 382(9899):1175–1182.
- Lloyd DH, Page SW (2018). Antimicrobial stewardship in veterinary medicine. *Microbiology Spectrum*, 6(3).
- Longworth N, Mourits MCM, Saatkamp HW (2014). Economic analysis of HPAI control in the Netherlands II: Comparison of control strategies. *Transboundary and Emerging Diseases*, 61(3):217–232.
- Magalhães-Sant’Ana M et al. (2017). Challenges facing the veterinary profession in Ireland: 2. On-farm use of veterinary antimicrobials. *Irish Veterinary Journal*, 70:28.
- Martínez-González NA et al (2020). Point-of-care C-reactive protein testing to reduce antibiotic prescribing for respiratory tract infections in primary care: Systematic review and meta-analysis of randomised controlled trials. *Antibiotics*, 9(9):610.
- McDonnell A (2022). *The EU wants to transfer the costs of new antibiotics to its member states – they are right to revolt*. London, Center For Global Development. (<https://www.cgdev.org/blog/transferring-costs-its-member-states-eus-proposed-voucher-scheme-incentivising-antibiotics>, accessed Mar 13, 2024).
- McNulty C et al. (2018). Effects of primary care antimicrobial stewardship outreach on antibiotic use by general practice staff: Pragmatic randomized controlled trial of the TARGET antibiotics workshop. *Journal of Antimicrobial Chemotherapy*, 73(5):1423–1432.
- Mestrovic T et al. (2022). The burden of bacterial antimicrobial resistance in the WHO European region in 2019: A cross-country systematic analysis. *The Lancet Public Health*, 7(11):e897–913.
- Mettenleiter TC et al. (2023). The One Health High-Level Expert Panel (OHHLEP). *One Health Outlook*, 5:18.
- Mitchell AP et al. (2021). Are financial payments from the pharmaceutical industry associated with physician prescribing? A systematic review. *Annals of Internal Medicine*, 174(3):353–361.
- Monmaturapoj T et al. (2021). Pharmacist-led education-based antimicrobial stewardship interventions and their effect on antimicrobial use in hospital inpatients: A systematic review and narrative synthesis. *Journal of Hospital Infection*, 115:93–116.
- Murphy D et al. (2017). EMA and EFSA Joint Scientific Opinion on measures to reduce the need to use antimicrobial agents in animal husbandry in the European Union, and the resulting impacts on food safety (RONAFA). *EFSA Journal*, 15:e04666.
- NICE (2022). Vaccine uptake in the general population: Evidence review for interventions to increase the uptake of routine vaccines by improving infrastructure. London, National Institute for Health and Care Excellence (<https://www.nice.org.uk/guidance/ng218/evidence/g-interventions-to-increase-the-uptake-of-routine-vaccines-by-improving-infrastructure-pdf-11072221748>, accessed Mar 14, 2024).
- Niegowska M (2021). Knowledge gaps in the assessment of antimicrobial resistance in surface waters. *FEMS Microbiology Ecology*, 97(11):fiab140.
- Norman G (2021). *Rapid evidence synthesis: Behaviour change techniques for guideline compliance in infection prevention and control*. Manchester, University of Manchester, NIHR ARC ([https://arc-gm.nihr.ac.uk/media/Resources/ARC/Evaluation/RES/Behaviour%20Change%20in%20IPC/Behaviour%20change%20techniques%20in%20IPC\\_RES\\_new%20template.pdf](https://arc-gm.nihr.ac.uk/media/Resources/ARC/Evaluation/RES/Behaviour%20Change%20in%20IPC/Behaviour%20change%20techniques%20in%20IPC_RES_new%20template.pdf), accessed Mar 4, 2024).
- Norwegian Institute of Public Health (2023). *ATC/DDD Index 2023*. Oslo, Norwegian Institute of Public Health WHO Collaborating Centre for Drug Statistics Methodology ([https://www.whocc.no/atc\\_ddd\\_index](https://www.whocc.no/atc_ddd_index), accessed Oct 18, 2023).

- OECD (2023a). Fig 2.8: Trends in antimicrobial resistance in selected regions and country groups among priority antibiotic-bacterium combinations, by line of antimicrobial treatment. In: *Embracing a One Health Framework to Fight Antimicrobial Resistance – 2. Trends and patterns in antibiotic use and antimicrobial resistance*. Paris, Organisation for Economic Co-operation and Development (<https://www.oecd-ilibrary.org/sites/6b530230-en/index.html?itemId=/content/component/6b530230-en#:~:text=It%20is%20estimated%20that%2C%20in,and%2030%25%20in%20the%20G20,> accessed Mar 13, 2024).
- OECD (2023b). *Embracing a One Health Framework to Fight Antimicrobial Resistance*. Paris, Organisation for Economic Co-operation and Development (<https://doi.org/10.1787/ce44c755-en>, accessed Mar 13, 2024).
- OECD, ECDC, EFSA, EMA (2022). *Antimicrobial resistance in the EU/EEA: A One Health response*. Organisation for Economic Co-operation and Development, European Centre for Disease Prevention and Control, European Food Safety Authority and European Medicines Agency (<https://www.oecd.org/health/Antimicrobial-Resistance-in-the-EU-EEA-A-One-Health-Response-March-2022.pdf>, accessed Mar 13, 2024).
- OECD, EUIPO (2020). *Trade in counterfeit pharmaceutical products*. Paris, OECD Publishing, Illicit Trade ([https://www.oecd-ilibrary.org/governance/trade-in-counterfeit-pharmaceutical-products\\_a7c7e054-en](https://www.oecd-ilibrary.org/governance/trade-in-counterfeit-pharmaceutical-products_a7c7e054-en), accessed Apr 14, 2024).
- OIE (2016). *The OIE Strategy on Antimicrobial Resistance and the Prudent Use of Antimicrobials*. Paris, World Organisation for Animal Health (founded as OIE) ([https://www.woah.org/fileadmin/Home/eng/Media\\_Center/docs/pdf/PortailAMR/EN\\_OIE-AMRstrategy.pdf](https://www.woah.org/fileadmin/Home/eng/Media_Center/docs/pdf/PortailAMR/EN_OIE-AMRstrategy.pdf), accessed Mar 13, 2024).
- Pandey RP et al. (2023). Surveillance, distribution, and treatment methods of antimicrobial resistance in water: a review. *Science of the Total Environment*, 890:164360.
- Pauwels I et al. (2021). Assessing the impact of the Global Point Prevalence Survey of Antimicrobial Consumption and Resistance (Global-PPS) on hospital antimicrobial stewardship programmes: Results of a worldwide survey. *Antimicrobial Resistance & Infection Control*, 10(1):138.
- Pederson R, Hernandez G (2014). *Food safety: State-of-play, current and future challenges*. Brussels, European Parliament, Directorate-General for Internal Policies ([https://www.europarl.europa.eu/RegData/etudes/IDAN/2014/536287/IPOL\\_IDA%282014%29536287\\_EN.pdf](https://www.europarl.europa.eu/RegData/etudes/IDAN/2014/536287/IPOL_IDA%282014%29536287_EN.pdf), accessed Mar 14, 2024).
- Peters A et al. (2022). Impact of environmental hygiene interventions on healthcare-associated infections and patient colonization: A systematic review. *Antimicrobial Resistance & Infection Control*, 11:38.
- Postma M et al. (2016). Evaluation of the relationship between the biosecurity status, production parameters, herd characteristics and antimicrobial usage in farrow-to-finish pig production in four EU countries. *Porcine Health Management*, 2:9.
- Postma M et al. (2022). Capturing the value of vaccination within health technology assessment and health economics: Country analysis and priority value concepts. *Vaccine*, 40(30):3999–4007.
- Renwick MJ, Brogan DM, Mossialos E (2016). A systematic review and critical assessment of incentive strategies for discovery and development of novel antibiotics. *Journal of Antibiotics*, 69(2):73–88.
- Review on Antimicrobial Resistance (2016). *Tackling drug-resistant infections globally: Final report and recommendations*. London, The Review on Antimicrobial Resistance (<https://amr-review.org>, accessed Feb 27, 2024).
- Rice S et al. (2023). Economic evaluations of interventions to prevent and control health-care-associated infections: A systematic review. *The Lancet Infectious Diseases*, 23(7):e228–239.
- Rittmann B, Stevens MP (2019). Clinical decision support systems and their role in antibiotic stewardship: A systematic review. *Current Infectious Disease Reports*, 21(8):29.
- Roos L et al. (2019). *Proposals for a more effective antibiotic policy in Belgium*. Brussels, Belgian Health Care Knowledge Centre (KCE) ([https://kce.fgov.be/sites/default/files/2021-11/KCE\\_311R\\_Antibiotics\\_politics\\_Report.pdf](https://kce.fgov.be/sites/default/files/2021-11/KCE_311R_Antibiotics_politics_Report.pdf), accessed Apr 14, 2024).
- Saha SK, Hawes L, Mazza D (2019). Effectiveness of interventions involving pharmacists on antibiotic prescribing by general practitioners: A systematic review and meta-analysis. *Journal of Antimicrobial Chemotherapy*, 74(5):1173–1181.
- Sambaza SS, Naicker N (2023). Contribution of wastewater to antimicrobial resistance: A review article. *Journal of Global Antimicrobial Resistance*, 34:23–29.
- Samreen AI, Malak HA, Abulreesh HH (2021). Environmental antimicrobial resistance and its drivers: A potential threat to public health. *Journal of Global Antimicrobial Resistance*, 27:101–111.
- Sanders S et al. (2008). Systematic review of the diagnostic accuracy of C-reactive protein to detect bacterial infection in nonhospitalized infants and children with fever. *Journal of Pediatrics*, 153(4):570–574.
- Sciensano (undated). *Investigation of resistance mechanisms in emerging pathogens with the 'OneHealth' concept as missing link*. Brussels, Belgian Institute for Health, sciensano.be (<https://www.sciensano.be/en/projects/investigation-resistance-mechanisms-emerging-pathogens-onehealth-concept-missing-link>, accessed Mar 21, 2024).

- Sharland M et al. (2018). Classifying antibiotics in the WHO Essential Medicines List for optimal use – be AWaRe. *The Lancet Infectious Diseases*, 18(1):18–20.
- Sharland M, et al. (2022). The WHO AWaRe antibiotic book: Providing guidance on optimal use and informing policy. *The Lancet Infectious Diseases*, 22(11):1528–1530.
- Simpkin V et al. (2017). Incentivising innovation in antibiotic drug discovery and development: Progress, challenges and next steps. *Journal of Antibiotics*, 70:1087–1096.
- Souillard R et al. (2024). Biosecurity implementation on large-scale poultry farms in Europe: A qualitative interview study with farmers. *Preventive Veterinary Medicine*, 224:106119.
- Sternberg-Lewerin S et al. (2022). Nordic vets against AMR – an initiative to share and promote good practices in the Nordic–Baltic region. *Antibiotics*, 11(8):1050.
- Storr J et al. (2017). Core components for effective infection prevention and control programmes: New WHO evidence-based recommendations. *Antimicrobial Resistance and Infection Control*, 6:6.
- Tacconelli E et al. (2014). ESCMID guidelines for the management of the infection control measures to reduce transmission of multidrug-resistant Gram-negative bacteria in hospitalized patients. *Clinical Microbiology and Infection*, 20(Suppl 1):1–55.
- Tang H et al. (2022). Benefit-cost analysis of a H7N9 vaccination program in poultry in Guangxi, China. *Preventive Veterinary Medicine*, 200:105580.
- Tang M et al. (2023). Effects of different composting methods on antibiotic-resistant bacteria, antibiotic resistance genes, and microbial diversity in dairy cattle manures. *Journal of Dairy Science*, 106(1):257–273.
- Tell J et al. (2019). Science-based targets for antibiotics in receiving waters from pharmaceutical manufacturing operations. *Integrated Environmental Assessment and Management*, 15(3):312–319.
- Tiseo K et al. (2020). Global trends in antimicrobial use in food animals from 2017 to 2030. *Antibiotics (Basel)*, 9(12):918.
- UN (2016). Political Declaration of the High-Level Meeting of the General Assembly on Antimicrobial Resistance: draft resolution / submitted by the President of the General Assembly. New York, United Nations, High-Level Plenary Meeting on Antimicrobial Resistance. (<https://digitallibrary.un.org/record/842813?ln=en>, accessed Feb 6, 2024).
- UNEP (2023). *Bracing for Superbugs: Strengthening environmental action in the One Health response to antimicrobial resistance*. Geneva, United Nations Environment Programme (<http://www.unep.org/resources/superbugs/environmental-action>, accessed Mar 13, 2024).
- Van Boeckel TP et al. (2015). Global trends in antimicrobial use in food animals. *Proceedings of the National Academy of Sciences*, 112(18):5649–5654.
- Van Epps A, Blaney LM (2016). Antibiotic residues in animal waste: Occurrence and degradation in conventional agricultural waste management practices. *Current Pollution Reports*, 2(3):135–155.
- van Heuvel L et al. (2022). Assessment of the inclusion of vaccination as an intervention to reduce antimicrobial resistance in AMR national action plans: A global review. *Globalization and Health*, 18:85.
- Vercelli C et al. (2022). Implications of veterinary medicine in the comprehension and stewardship of antimicrobial resistance phenomenon: From the origin till nowadays. *Veterinary and Animal Science*, 16:100249.
- Verhaegen M et al. (2023). On the use of antibiotics to control plant pathogenic bacteria: A genetic and genomic perspective. *Frontiers in Microbiology*, 14(1221478).
- Verhaegen M et al. (2024). Data collection on antibiotics for control of plant pathogenic bacteria. Louvain-la-Neuve, UCLouvain. *EFSA Supporting Publications*, 21:8522E.
- Vestel J et al. (2022). Default predicted no-effect target concentrations for antibiotics in the absence of data for the protection against antibiotic resistance and environmental toxicity. *Integrated Environmental Assessment and Management*, 18(4):863–867.
- Vicentini C et al. (2022). Antimicrobial stewardship strategies including point-of-care testing (POCT) for pediatric patients with upper-respiratory-tract infections in primary care: A systematic review of economic evaluations. *Antibiotics*, 11(8):1139.
- Videnova K, Mackay DKJ (2012). Availability of vaccines against major animal diseases in the European Union. *Revue Scientifique et Technique*, 31(3):971–978.
- Villamiel M, Méndez-Albiñana P (2022). Update of challenges for food quality and safety management. *Journal of Agriculture and Food Research*, 20(10):100393.
- Vokes RA, Bearman G, Bazzoli GJ (2018). Hospital-acquired infections under pay-for-performance systems: An administrative perspective on management and change. *Current Infectious Disease Reports*, 20(9):35.
- WHO (2015). *Global Action Plan on Antimicrobial Resistance*. Geneva, World Health Organization ([http://apps.who.int/iris/bitstream/handle/10665/193736/9789241509763\\_eng.pdf?sequence=](http://apps.who.int/iris/bitstream/handle/10665/193736/9789241509763_eng.pdf?sequence=), accessed Dec 7, 2018).
- WHO (2016). *Guidelines on core components of infection prevention and control programmes at the national and acute health care facility level*. Geneva, World Health Organization (<https://iris.who.int/bitstream/handle/10665/251730/9789241549929-eng.pdf?sequence=1>, accessed Apr 1, 2024).

- WHO (2017). *WHO Global Surveillance and Monitoring System for Substandard and Falsified Medical Products*. Geneva, World Health Organization (<https://www.who.int/publications-detail-redirect/9789241513425>, accessed Jan 25, 2024).
- WHO (2019a). *Ten threats to global health in 2019*. Geneva, World Health Organization (<https://www.who.int/news-room/spotlight/ten-threats-to-global-health-in-2019>, accessed Dec 5, 2023).
- WHO (2019b). *Thirteenth General Programme of Work 2019–2023*. Geneva, World Health Organization (<https://www.who.int/about/general-programme-of-work/thirteenth#:~:text=The%20Thirteenth%20General%20Programme%20of,health%20at%20the%20country%20level.>, accessed Oct 5, 2023).
- WHO (2019c). *Antimicrobial stewardship programmes in health-care facilities in low- and middle-income countries: A WHO practical toolkit*. Geneva, World Health Organization (<https://apps.who.int/iris/handle/10665/329404>, accessed Aug 2, 2023).
- WHO (2022a). *Global report on infection prevention and control*. Geneva, World Health Organization (<https://www.who.int/publications-detail-redirect/9789240051164>, accessed Mar 1, 2024).
- WHO (2022b). *The WHO AWaRe (Access, Watch, Reserve) antibiotic book*. Geneva, World Health Organization (<https://www.who.int/publications-detail-redirect/9789240062382>, accessed Oct 11, 2023).
- WHO (2022c). *2021 antibacterial agents in clinical and preclinical development: An overview and analysis*. Geneva, World Health Organization (<https://www.who.int/publications-detail-redirect/9789240047655>, accessed Oct 5, 2023).
- WHO (2023). *Global strategy on infection prevention and control*. Geneva, World Health Organization (<https://www.who.int/publications/m/item/global-strategy-on-infection-prevention-and-control>, accessed Apr 3, 2024).
- WHO Regional Office for Europe (2023). *Seventy-third Regional Committee for Europe: Astana, 24–26 October 2023: Roadmap on Antimicrobial Resistance for the WHO European Region 2023–2030*. World Health Organization, Institutional Repository for Information Sharing (IRIS) (<https://iris.who.int/handle/10665/372503>, accessed Apr 11, 2024).
- WISE-Freshwater (2024). *Country profiles on urban waste water treatment*. Water Information System for Europe (WISE) (<https://water.europa.eu/freshwater/countries/wwwt>, accessed Mar 14, 2024).
- WOAH (2022). *Strategy on Antimicrobial Resistance and the Prudent Use of Antimicrobials: Preserving the efficacy of antimicrobials*. Paris, World Organisation for Animal Health (founded as OIE) (<https://www.woah.org/app/uploads/2021/03/en-amr-strategy-2022-final-single-pages.pdf>, accessed Mar 13, 2024).
- Xue JJ et al. (2022). Antibiotic residue and toxicity assessment of wastewater during the pharmaceutical production processes. *Chemosphere*, 291(Pt 2):132837.
- Yu K-F et al. (2023). Technologies to tackle antimicrobial resistance during treated wastewater reuse: Current advances and future prospects. *Current Opinion in Chemical Engineering*, 42:100951.
- Zalewska M et al. (2021). Antibiotics and antibiotic resistance genes in animal manure – consequences of its application in agriculture. *Frontiers in Microbiology*, 12:610656.
- Zalewska M et al. (2023). Pig manure treatment strategies for mitigating the spread of antibiotic resistance. *Scientific Reports*, 13(1):11999.
- Zanichelli V, et al. (2023). The WHO AWaRe (Access, Watch, Reserve) antibiotic book and prevention of antimicrobial resistance. *Bulletin of the World Health Organization*, 101(4):290–296.
- Zarei E et al. (2023). Interaction between physicians and the pharmaceutical industry: A scoping review for developing a policy brief. *Frontiers in Public Health*, 10:1072708.
- Zingg W et al. (2015). Hospital organisation, management, and structure for prevention of health-care-associated infection: A systematic review and expert consensus. *The Lancet Infectious Diseases*, 15(2):212–224.

## 5. Annex

### List of attendees during workshop to discuss implementation challenges for AMR policy

#### EU Member States

COUNTRY REPRESENTED	ORGANIZATION REPRESENTED	NAME
Austria	Federal Ministry for Labour, Social Affairs, Health and Consumer Protection	Reinhild Strauss
Austria	Federal Ministry for Labour, Social Affairs, Health and Consumer Protection	Julia Weber
Belgium	Federal Public Service Public Health, Food Chain Safety and Environment	Katie Vermeersch
Belgium	Federal Public Service Public Health, Food Chain Safety and Environment	Ivo Deckers
Belgium	Federal Public Service Public Health, Food Chain Safety and Environment	Florine Croquet (Reporter)
Belgium	Federal Public Service Public Health, Food Chain Safety and Environment	Zeynep Darici (Reporter)
Belgium	Federal Public Service Public Health, Food Chain Safety and Environment	Pascaline Debie (Reporter)
Croatia	Department of Medical Microbiology at the University Hospital for Infectious Diseases, Zagreb, Croatia	Arjana Tambić Andrašević
Cyprus	Ministry of Health	Linos Hadjihannas
Cyprus	Archbishop Makarios III Hospital	Markella Marcou
Czechia	National Health Institute of Czechia	Helena Zemlickova
Denmark	Danish Health Authority	Gideon Ertner
Denmark	Danish Veterinary and Food Administration	Pia Holm Jul
Estonia	Estonian Health Board	Liidia Dotsenko
Estonia	Ministry of Regional Affairs and Agriculture	Piret Aasmäe
France	Ministry of Labour, Health, and Solidarity	Agathe Claud
France	Ministry of Agriculture and Food Sovereignty	Elisa Bohin
France	Ministry of Labour, Health, and Solidarity	Chantal Guilhaume
Germany	Environment and Consumer Protection Ministry	Ines Rönnefahrt
Germany	Health Ministry	Muna Abu Sin
Germany	Health Ministry	Alexandra Clarici
Germany	Health Ministry	Ralf Halfmann
Greece	The National Public Health Organization (NPHO)	Dimitrios Chatzigeorgiou
Greece	Greek Ministry of Rural Development and Food	Katerina Marinou
Hungary	Ministry of Human Resources	Krisztina Biró
Hungary	National Public Health Center Hungary	Ágnes Galgóczi
Hungary	Ministry of Agriculture	Eszter Kollár-Nagy
Ireland	National Patient Safety Office	Sharon O'Keeffe

*continued on next page*

EU Member States *continued*

COUNTRY REPRESENTED	ORGANIZATION REPRESENTED	NAME
Ireland	Department of Agriculture, Food and the Marine	Julie Bolton
Italy	Ministry of Health	Michela Sabbatucci
Malta	National AMR Committee	Michael Borg
Malta	Veterinary Regulation Directorate (VRD) within the Animal Health and Welfare Department (AHWD)	Stephen Spiteri
Netherlands, Kingdom of the	Netherlands Ministry of Health, Welfare and Sport	Rosa Peran Sala
Portugal	Member of the National Programme for Prevention of Infection and Antimicrobial Resistance	Inés Leonor Leitão
Portugal	The General Directorate of Food and Veterinary Affairs	Inés Martins De Almeida
Romania	Ministry of Health Romania	Roxana Șerban
Romania	National Sanitary Veterinary and Food Safety Authority	Mirela Nicola
Slovakia	National Reference Centre	Martin Sojka
Slovakia	Ministry of Health	Andrej Vyskoč
Slovenia	Ministry of Health	Andreja Ljubič
Slovenia	Ministry of Health	Doroteja Novak Gosarič
Slovenia	National Institute of Public Health	Zoran Simonovič
Slovenia	National Institute of Public Health	Maja Šubelj
Slovenia	Administration of the Republic of Slovenia for Food Safety, Veterinary Sector and Plant Protection	Anton Svetlin
Spain	Spanish Agency for Medicines and Health Products	Antonio López Navas
Spain	Spanish Agency for Medicines and Health Products	Reyes Castillo
Spain	Spanish Agency for Medicines and Health Products	Ricardo Carapeto García
Sweden	Public Health Agency of Sweden	Olov Aspevall
Sweden	Swedish Veterinary Agency	Christina Greko



**EU institutions**

INSTITUTION	NAME
DG AGRI	Jean-Charles Cavitte
DG SANTE	Erba Pietro
DG SANTE	Pendolovska Velina
DG SANTE	Sigrid Weiland
ECDC	Dominique Monnet
EFSA	Ernesto Liebana
EMA	Steffen Thirstrup
EMA	Botgros Radu
European Commission	Hannah Sievers
HERA	Jean-Baptiste Perrin

**International institutions**

INSTITUTION	NAME
World Health Organization (WHO) Regional Office for Europe	Danilo Lo Fo Wong

## The Policy Brief Series

1. How can European health systems support investment in and the implementation of population health strategies? *David McDaid, Michael Drummond, Marc Suhrcke*
2. How can the impact of health technology assessments be enhanced? *Corinna Sorenson, Michael Drummond, Finn Børlum Kristensen, Reinhard Busse*
3. Where are the patients in decision-making about their own care? *Angela Coulter, Suzanne Parsons, Janet Askham*
4. How can the settings used to provide care to older people be balanced? *Peter C. Coyte, Nick Goodwin, Audrey Laporte*
5. When do vertical (stand-alone) programmes have a place in health systems? *Rifat A. Atun, Sara Bennett, Antonio Duran*
6. How can chronic disease management programmes operate across care settings and providers? *Debbie Singh*
7. How can the migration of health service professionals be managed so as to reduce any negative effects on supply? *James Buchan*
8. How can optimal skill mix be effectively implemented and why? *Ivy Lynn Bourgeault, Ellen Kuhlmann, Elena Neiterman, Sirpa Wrede*
9. Do lifelong learning and revalidation ensure that physicians are fit to practise? *Sherry Merkur, Philipa Mladovsky, Elias Mossialos, Martin McKee*
10. How can health systems respond to population ageing? *Bernd Rechel, Yvonne Doyle, Emily Grundy, Martin McKee*
11. How can European states design efficient, equitable and sustainable funding systems for long-term care for older people? *José-Luis Fernández, Julien Forder, Birgit Trukeschitz, Martina Rokosová, David McDaid*
12. How can gender equity be addressed through health systems? *Sarah Payne*
13. How can telehealth help in the provision of integrated care? *Karl A. Stroetmann, Lutz Kubitschke, Simon Robinson, Veli Stroetmann, Kevin Cullen, David McDaid*
14. How to create conditions for adapting physicians' skills to new needs and lifelong learning *Tanya Horsley, Jeremy Grimshaw, Craig Campbell*
15. How to create an attractive and supportive working environment for health professionals *Christiane Wiskow, Tit Albrecht, Carlo de Pietro*
16. How can knowledge brokering be better supported across European health systems? *John N. Lavis, Govin Permanand, Cristina Catalo, BRIDGE Study Team*
17. How can knowledge brokering be advanced in a country's health system? *John N. Lavis, Govin Permanand, Cristina Catalo, BRIDGE Study Team*
18. How can countries address the efficiency and equity implications of health professional mobility in Europe? Adapting policies in the context of the WHO Code and EU freedom of movement *Irene A. Glinos, Matthias Wismar, James Buchan, Ivo Rakovac*
19. Investing in health literacy: What do we know about the co-benefits to the education sector of actions targeted at children and young people? *David McDaid*
20. How can structured cooperation between countries address health workforce challenges related to highly specialized health care? Improving access to services through voluntary cooperation in the EU *Marieke Kroezen, James Buchan, Gilles Dussault, Irene Glinos, Matthias Wismar*
21. How can voluntary cross-border collaboration in public procurement improve access to health technologies in Europe? *Jaime Espin, Joan Rovira, Antoinette Calleja, Natasha Azzopardi-Muscat, Erica Richardson, Willy Palm, Dimitra Panteli*
22. How to strengthen patient-centredness in caring for people with multimorbidity in Europe? *Iris van der Heide, Sanne P. Snoeijis, Wienke GW Boerma, François GW Schellevis, Mieke P. Rijken. On behalf of the ICARE4EU consortium*
23. How to improve care for people with multimorbidity in Europe? *Mieke Rijken, Verena Struckmann, Iris van der Heide, Anneli Hujala, Francesco Barbabella, Ewout van Ginneken, François Schellevis. On behalf of the ICARE4EU consortium*
24. How to strengthen financing mechanisms to promote care for people with multimorbidity in Europe? *Verena Struckmann, Wilm Quentin, Reinhard Busse, Ewout van Ginneken. On behalf of the ICARE4EU consortium*
25. How can eHealth improve care for people with multimorbidity in Europe? *Francesco Barbabella, Maria Gabriella Melchiorre, Sabrina Quattrini, Roberta Papa, Giovanni Lamura. On behalf of the ICARE4EU consortium*
26. How to support integration to promote care for people with multimorbidity in Europe? *Anneli Hujala, Helena Taskinen, Sari Rissanen. On behalf of the ICARE4EU consortium*
27. How to make sense of health system efficiency comparisons? *Jonathan Cylus, Irene Papanicolas, Peter C. Smith*
28. What is the experience of decentralized hospital governance in Europe? *Bernd Rechel, Antonio Duran, Richard Saltman*
29. Ensuring access to medicines: How to stimulate innovation to meet patients' needs? *Dimitra Panteli, Suzanne Edwards*
30. Ensuring access to medicines: How to redesign pricing, reimbursement and procurement? *Sabine Vogler, Valérie Paris, Dimitra Panteli*
31. Connecting food systems for co-benefits: How can food systems combine diet-related health with environmental and economic policy goals? *Kelly Parsons, Corinna Hawkes*
32. Averting the AMR crisis: What are the avenues for policy action for countries in Europe? *Michael Anderson, Charles Clift, Kai Schulze, Anna Sagan, Saskia Nahrgang, Driss Ait Ouakrim, Elias Mossialos*
33. It's the governance, stupid! TAPIC: a governance framework to strengthen decision making and implementation *Scott L. Greer, Nikolai Vasev, Holly Jarman, Matthias Wismar, Josep Figueras*
34. How to enhance the integration of primary care and public health? Approaches, facilitating factors and policy options *Bernd Rechel*
35. Screening. When is it appropriate and how can we get it right? *Anna Sagan, David McDaid, Selina Rajan, Jill Farrington, Martin McKee*
36. Strengthening health systems resilience: key concepts and strategies *Steve Thomas, Anna Sagan, James Larkin, Jonathan Cylus, Josep Figueras, Marina Karanikolos*
37. Building on value-based health care *Peter C. Smith, Anna Sagan, Luigi Siciliani, Dimitra Panteli, Martin McKee, Agnès Soucat, Josep Figueras*
38. Regulating the unknown: A guide to regulating genomics for health policy-makers *Gemma A Williams, Sandra Liede, Nick Fahy, Kristiina Aittomaki, Markus Perola, Tuula Helander, Martin McKee, Anna Sagan*
39. In the wake of the pandemic: Preparing for Long COVID *Selina Rajan, Kamlesh Khunti, Nisreen Alwan, Claire Steves, Trish Greenhalgh, Nathalie MacDermott, Anna Sagan, Martin McKee*
40. How can we transfer service and policy innovations between health systems? *Ellen Nolte, Peter Groenewegen*
41. What are the key priority areas where European health systems can learn from each other? *Johan Hansen, Alexander Haarmann, Peter Groenewegen, Natasha Azzopardi Muscat, Gianpaolo Tomaselli, Mircha Poldrugovac*
42. Use of digital health tools in Europe: Before, during and after COVID-19 *Nick Fahy, Gemma A Williams, COVID-19 Health System Response Monitor Network*
43. European support for improving health and care systems *Nick Fahy, Nicole Mauer, Dimitra Panteli*
44. What are patient navigators and how can they improve integration of care? *Hannah Budde, Gemma A Williams, Giada Scarpetti, Marieke Kroezen, Claudia B Maier*
45. What are the implications of policies increasing transparency of prices paid for pharmaceuticals? *Erin Webb, Erica Richardson, Sabine Vogler, Dimitra Panteli*
46. How can skill-mix innovations support the implementation of integrated care for people with chronic conditions and multimorbidity? *Juliane Winkelmann, Giada Scarpetti, Gemma A Williams, Claudia B Maier*
47. Addressing backlogs and managing waiting lists during and beyond the COVID-19 pandemic *Ewout van Ginneken, Sarah Reed, Luigi Siciliani, Astrid Eriksen, Laura Schlepper, Florian Tille, Tomas Zapata*
48. Does provider competition improve health care quality and efficiency? *Luigi Siciliani, Martin Chalkley, Hugh Gravelle*
49. Health system performance assessment: A primer for policy-makers *Dheepa Rajan, Irene Papanicolas, Marina Karanikolos, Kira Koch, Katja Rohrer-Herold, Josep Figueras*
50. Making Health for All Policies: Harnessing the co-benefits of health *Scott L. Greer, Michelle Falkenbach, Luigi Siciliani, Martin McKee, Matthias Wismar, Praneetha Vissapragada, Marie C. Montás, Janamarie Perroud, Olivia Rockwell, Josep Figueras*
51. How can the EU support sustainable innovation and access to effective antibiotics? *Michael Anderson, Dimitra Panteli, Elias Mossialos*
52. Global Health Workforce responses to address the COVID-19 pandemic *Margaret Ziemann, Candice Chen, Rebecca Forman, Anna Sagan, Patricia Pittman*
53. What can intersectoral governance do to strengthen the health and care workforce? *Margaret Caffrey, Tara Tancred, Joanna Raven*
54. What steps can improve and promote investment in the health and care workforce? *Barbara McPake, Prarthna Dayal, Julia Zimmermann, Gemma A Williams*
55. Strengthening primary care in Europe: How to increase the attractiveness of primary care for medical students and primary care physicians? *Marieke Kroezen, Dheepa Rajan, Erica Richardson*
56. Engaging the private sector in delivering health care and goods: governance lessons from the COVID-19 pandemic *Anna Maresso, Ruth Waitzberg, Florian Tille, Yulia Litvinova, Gabriele Pastorino, Naomi Nathan, David Clarke*
57. European support for improving global health systems and policies *Scott L. Greer, Nicole Mauer, Holly Jarman, Michelle Falkenbach, Ilona Kickbusch, Dimitra Panteli, Matthias Wismar*
58. Transforming health service delivery: What can policy-makers do to drive change? *Dimitra Panteli, Nicole Mauer, Juliane Winkelmann, Nick Fahy*
59. Health system performance assessment: a renewed global framework for policy-making *Dheepa Rajan, Irene Papanicolas, Marina Karanikolos, Kira Koch, Katja Rohrer-Herold, Bernd Rechel, Rachel Greenley, Suszy Lessofo, Josep Figueras*
60. Assessing health system performance: Proof of concept for a HSPA dashboard of key indicators *Josep Figueras, Marina Karanikolos, Frederico Guanais, Suszy Lessofo, Guillaume Dedet, Natasha Azzopardi Muscat, Govin Permanand, Francesca Colombo*
61. Financing for health system transformation: spending more or spending better (or both)? *Rebecca Forman, Govin Permanand, Jonathan Cylus*
62. How to implement integrated care? A framework with 12 overall strategies to transform care delivery *Verena Struckmann, Nathan Shuftan, Giada Scarpetti, Willemijn Looman, Roland Bal, Maureen Rutten-van Mölken, Ewout van Ginneken*

The European Observatory has an independent programme of policy briefs and summaries which are available here: <https://eurohealthobservatory.who.int/publications/policy-briefs>

World Health Organization  
Regional Office for Europe  
UN City, Marmorvej 51,  
DK-2100 Copenhagen Ø,  
Denmark  
E-mail: [eurocontact@who.int](mailto:eurocontact@who.int)  
Website: [www.who.int/europe](http://www.who.int/europe)

The **European Observatory on Health Systems and Policies** is a partnership that supports and promotes evidence-based health policy-making through comprehensive and rigorous analysis of health systems in the European Region. It brings together a wide range of policy-makers, academics and practitioners to analyse trends in health reform, drawing on experience from across Europe to illuminate policy issues. The Observatory's products are available on its website ([www.healthobservatory.eu](http://www.healthobservatory.eu)).



The Observatory is a partnership, hosted by the WHO Regional Office for Europe, which includes other international organizations (the European Commission); national and regional governments (Austria, Belgium, Finland, Ireland, Netherlands (Kingdom of the), Norway, Slovenia, Spain, Sweden, Switzerland, the United Kingdom and the Veneto Region of Italy (with AGENAS)); other health system organizations (the French National Union of Health Insurance Funds (UNCAM), the Health Foundation); and academia (the London School of Economics and Political Science (LSE) and the London School of Hygiene & Tropical Medicine (LSHTM)). The Observatory has a secretariat in Brussels and it has hubs in London (at LSE and LSHTM) and at the Berlin University of Technology.

Print ISSN  
1997-8065

Web ISSN  
1997-8073