# Environmental dimensions of Antimicrobial Resistance

## Consultation September 2022

CSA DESIGN OH AMR

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Joint Programming Initiative on Antimicrobial Resistance

# Contents

# Background and Objectives


## Summary

The role of the environment in the evolution, spread and transmission of antimicrobial resistance was discussed at the Environmental Dimensions of Antibiotic Resistance (EDAR) 6 meeting in Gothenburg, Sweden on the 22-27 September 2022. The following report provides an overview of the consultation that was undertaken during the EDAR6 conference to provide feedback on the draft Strategic Research and Innovation Objectives of the candidate One Health AMR partnership in the Horizon Europe Framework programme. The consultation was an in-kind activity funded by the Swedish Research Council and part of the activities conducted through the Coordination and Support Action (CSA) DESIGN One Health Antimicrobial Resistance (DESIGN OH AMR). The consultation was carried out by JPIAMR together with the Swedish Research Council and the French National Research Agency.

Within this consultation, the following activities were carried out:

- Presentation of the candidate One Health AMR partnership and the objectives of the consultation exercise.
- Assessment of the draft priorities Research and Innovation Objectives by conference participants
- Panel discussion and participant consultation


## Scientific rationale

The role of the environment in the development and spread of antibiotic resistance has become more and more recognized. This is true not only among academic researchers. The environment is also becoming an important component of both national and international AMR policies. This recognition stems from an increased appreciation that bacteria and their genes can move between the environment, human and animal microbiota (the One Health concept). EDAR attempts to embrace a broad set of topics, including e.g. pollution sources and fates in the environment, environmental selection and evolution of resistance, transmission of genes and bacteria between different environments/humans/animals, surveillance, risk assessment strategies, and both technical and policy-related means of mitigating risks.

The partnership on One Health AMR is an international initiative that is expected to be launched in 2025 which will support research and innovation to curb AMR for many years ahead. In order to properly define the research and innovation objectives of the partnership, a series of consultations are ongoing.

## Strategic rationale

The JPIAMR Strategic Research and Innovation Agenda contained six priority topic areas (Figure 1): Therapeutics, Diagnostics, Surveillance, Transmission, Environment and Interventions. The candidate One Health AMR partnership intends to incorporate environmental aspects into the prioritised research and innovation objectives in a cross-cutting manner, with One Health being an overarching topic in the One Health AMR partnership Strategic Research and Innovation Agenda (Figure 2).

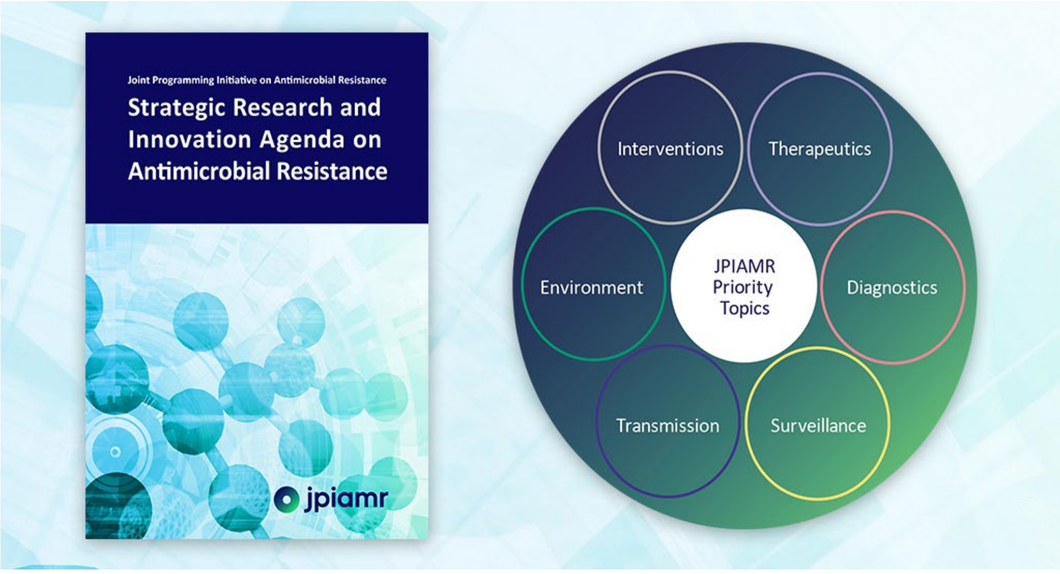



**Figure 1.** The Strategic Research and Innovation Agenda of the Joint Programming Initiative on Antimicrobial Resistance contains six priority topics, including Environment.


**Figure 2.** The priority topic areas of the One Health AMR partnership are Therapeutics, Diagnostics, Surveillance, Transmission and Evolution and Prevention and Intervention. One Health is the central focus of the partnership and encompasses all One Health compartments, putting the environment on an equal level with human and animal health. Cross-cutting issues include research, social sciences, diversity, innovation, implementation and international collaboration.

The integration of environmental dimensions into the One Health over-arching lens that will be applied to the One Health AMR partnership involves restructuring and incorporation of the existing, and newly emerging, research and innovation priorities in the environmental domain. The consultation held as part of the EDAR6 conference was a key element in assuring the appropriate consideration of these elements.

### The 6th International symposium on the Environmental Dimension of Antibiotic Resistance

The 6th International symposium on the Environmental Dimension of Antibiotic Resistance (EDAR6) was held in Gothenburg, Sweden from the 22-27 September 2022 (Figure 3). The conference was organised by the Centre for Antibiotic Resistance Research, CARe, at Gothenburg University. One of the sponsors for the event was the Swedish Research Council, as part of an in-kind activity within the framework of the DESIGN OH AMR Coordination and Support Action.


**Figure 3.** Communication of the EDAR6 conference.

The EDAR6 conference included a presentation of the One Health AMR partnership on Sunday the 25th of September, as well as an interactive workshop and panel discussion on the final day. The objectives of the round-table panel discussion were to identify and discuss environmental aspects of AMR to be addressed in the OH AMR partnership. A draft of a Strategic Research and Innovation Agenda (SRIA) is available for downloading by participants in order to provide insight into the existing text. Participants were strongly recommended to download and read the document ahead of the round-table session and take the opportunity to influence research directions and funding on AMR in the next decade.

A total of 250 people attended the conference in person, with 74 people attending digitally via Zoom. The attendees came from 41 countries.

## Aims

The aim of the consultation was to scope gaps and priorities for the prioritised research and innovation objectives outlined in the first draft of the Strategic Research and Innovations Agenda of the candidate One Health AMR Partnership.

Specific aims included:

- Identification of missing environmental issues in the proposed R&I priorities?
- Determination of whether certain research and innovation priorities require further development or redrafting
- Consideration of the appropriateness of the terminology used

## Introduction to the One Health AMR partnership and the consultation on the One Health AMR Strategic Research and Innovation Agenda

On Sunday the 25 September, a presentation of the candidate One Health AMR partnership and the development process for the One Health AMR SRIA was presented by Sophie Gay (ANR) and Laura Plant (SRC).

# Consultation outputs

On Tuesday 27 September, a two-hour panel discussion and interactive workshop were held on the existing draft of the One Health AMR partnership. The roundtable discussion was chaired by Joakim Larsson, with participation from the panellists Sophie Gay, Will Gaze, Ed Topp, Sabiha Essacks, Heike Schmitt and Christian Munthe

The working document was available for download on the EDAR6 meeting website.

The session was opened by the Chair, Joakim Larsson, who explained that the Strategic Research and Innovation Agenda is not an action plan and should explain what we need to know in order to support research to curb AMR. He highlighted that discussions should be bold and broad and valid for the coming decade. Not all thematic areas have strong environmental dimensions and there is not space for details in the chapters when considering their length.

For the session, the participants should focus on the needs within the area of environment since this is no longer a stand-alone topic and needs to be incorporated into other thematic areas. The alignment between the thematic areas is still to be conducted but the inputs from the discussion from the consultation could provide input into how environmental dimensions can be further supported in the future alignment.

Menti was used to provide input from the audience, including online participants. A total of 130 people submitted responses via mentimeter. Two questions were asked per thematic area:

- What are the most important environmental aspects to be included in each priority topic?
- What is missing from the current draft?

# Chair and Panellists

## Chair

**Professor Joakim Larsson**
*Department of Infectious Diseases, Institute of Biomedicine, University of Gothenburg, Sweden*

Joakim Larsson is a Professor in Environmental Pharmacology at the Department of Infectious Disease, University of Gothenburg, Sweden. He received his PhD in animal physiology in 2000 in Gothenburg, and after two years of guest research in Canada and USA, he decided to combine his interest for the environment with medicine. He became associate professor in human physiology in 2007 and full professor in 2013. From 2016 he is director for the multidisciplinary Centre for Antibiotic Resistance Research (CARe) at University of Gothenburg, involving +100 researches from six faculties. Larsson has (co)-authored more than 185 papers, and he is among the 1% most highly cited researchers on Web of Science according to Clarivate Analytics. His earlier work on environmental pollution from drug manufacturing, and his research on selective concentrations of antibiotics has contributed various management initiatives across the world. His current research focus on the environmental dimensions of antibiotic resistance. Ongoing projects include e.g. research on: the role of antibiotics and biocides in the evolution of antibiotic resistance; understanding the evolutionary history of antibiotic resistance acquisition in pathogens; exploration of the environmental resistome for novel resistance genes; surveillance of resistance in the human population using sewage bacteria; environmental transmission of resistant pathogens; as well as both technical and societal measures to reduce environmental pollution with antibiotics and antibiotic resistant bacteria.

## Panellists

**Professor Sabiha Essack**
*Pharmaceutical Sciences at the University of KwaZulu-Natal (UKZN)*

Sabiha Essack is the South African Research Chair (SARChI) in Antibiotic Resistance and One Health and Professor in Pharmaceutical Sciences at the University of KwaZulu-Natal (UKZN). She is also the Vice Chair of the WHO Strategic and Technical Advisory Group for Antimicrobial Resistance (STAG-AMR), Senior Implementation Research Advisor at the International Centre for Antimicrobial Resistance Solutions (ICARS) in Denmark, member of the Scientific Advisory Board of the Joint Programming Initiative on AMR (JPIAMR) and member of the International Pharmacy Federation (FIP) AMR Commission. Professor Essack is chairperson of the Global Respiratory Infection Partnership (GRIP), she serves on the Advisory Board of the Combating Antibiotic Resistant Bacteria Biopharmaceutical Accelerator (CARB-X), the Fleming Fund Expert

Advisory Group and is a member of the Wellcome Trust Surveillance and Epidemiology of Drug Resistant Infections Consortium (SEDRIC). Her research focuses on the molecular epidemiology of AMR using next generation sequencing and bioinformatics as well as One Health systems strengthening in the context of AMR.

**Professor Ed Topp**
*Principal Research Scientist, Environmental microbiology and chemistry, Agriculture and Agri-Food Canada*

Ed is a Principal Research Scientist with Agriculture and Agri-Food Canada, and has affiliations with the University of Western Ontario, the Ontario Veterinary College, and the University of Florida. A native of Montréal, Ed obtained his PhD from the Department of Microbiology at the University of Minnesota. Ed's research concerns the interface between agriculture and human and environmental health. In the last decade he has notably led several national studies concerning the fate and management in agro-ecosystems of pharmaceuticals and pathogenic and antibiotic-resistant bacteria. He is the project coordinator for the Genomics Research and Development Initiative project on antimicrobial resistance, a key component of the innovation pillar of the Canadian Federal Framework for Action on antimicrobial resistance. He is a Past-President [2011] of the Canadian Society of Microbiologists.

**Professor Christian Munthe**
*Department of Philosophy, Linguistics, Theory of Science, University of Gothenburg, Sweden*

Christian Munthe is professor of practical philosophy and conducts research and expert consultation on ethics, value and policy issues arising in the intersection of health, science & technology, the environment and society. He is elected member of the Royal Society of Arts and Sciences in Gothenburg, and serves on several ethics' councils in Sweden and internationally. In 2016-18, he was faculty elected member of the board of the University of Gothenburg, and in 2019, a Nobel Week Dialogue Panellist. Munthe has developed a cross-disciplinary approach, collaborating with researchers and practitioners from, e.g., medicine and care, environmental-, natural and technological science, economics, law and politics. He is a frequently commissioned expert by public agencies in Sweden and abroad, and a source and participant in media reporting and debates within his area of expertise. He also engages with the public through the blog Philosophical Comment and Twitter.

**Professor William Gaze**
*Medical School, University of Exeter, United Kingdom*

Professor Will Gaze has over 15 years' experience of antimicrobial resistance research in farmed and natural environments, including major elements of environmental sampling and wide-ranging analytical methodologies. His research group consists of over 20 researchers funded by over £4 million in current and recent antimicrobial resistance (AMR) grants. Current activity within Prof Gaze's group covers fundamental issues of AMR evolution in the environment, using in situ and in vivo experiments, landscape scale dissemination of AMR and human exposure and transmission studies. Projects are divided into three main themes: ecology, evolution and public health perspectives. These map onto those identified in successive WHO, EU and UK AMR action plans facilitating interdisciplinary research approaches and joined up thinking.

**Professor Frank Møller Aarestrup**
*National Food Institute, Research Group for Genomic Epidemiology, DTU Microbes Initiative, Denmark*

Frank Møller Aarestrup research has primarily targeted the association between use of antimicrobial agents to farm animals and the emergence and spread of antimicrobial resistance including the human health consequences. It has become increasingly clear that bacteria do not respect traditional borders and with the increased globalisation a problem in one country has become a problem for all countries. Thus, the research has increasingly been directed towards global spread of initially foodborne, but now also other pathogenic bacteria. The research has contributed to the international standards for detection and monitoring of antimicrobial resistance in food borne pathogens and had major influence on the ways antimicrobial agents are used worldwide. The global focus is also documented by the fact that the research has been conducted with more than 400 co-authors, in more than 135 institutions in more than 35 countries. Furthermore, DTU-Food has partly based on the research been appointed WHO and EU reference laboratory for antimicrobial resistance in foodborne pathogens.

**Dr Heike Schmitt**

*National Institute for Public Health and the Environment (RIVM), Centre for Zoonoses and Environmental Microbiology*

Heike Schmitt works on the transmission of antimicrobial resistance (AMR) from the environment to humans and is combining fundamental and applied research with capacity building. At the National Institute for Public Health and the Environment (RIVM), she is principal investigator on AMR in the environment, and leads the environmental part of the Dutch National Action Plan on AMR. She has applied wastewater-based epidemiology (WBE) for several years, focusing on wastewater analysis to monitor circulation of WHO resistant priority pathogens in the general population. She works on capacity building for international One Health surveillance of antibiotic resistance, and on the relevance of inadequate WASH for exposure to AMR, within the WHO Collaborating Centre on Risk Assessment of Pathogens in Food and Water. She is coordinating several international research consortia and contributes to national and international advisory bodies. In addition, she serves as research advisor at the European centre of excellence for sustainable water technology (WETSUS), and as researcher at Utrecht University, where she focuses on wastewater treatment and its effects of antibiotic resistance.

**Dr Sophie Gay**

*French National Research Agency, France*

Sophie Gay is a scientific officer for transnational collaborations in the Biology & Health department of the French National Research Agency (ANR). After a PhD at the Sorbonne Université in Paris, she moved to Milan (Italy) to pursue her research activity at the IFOM Cancer Research Centre. She joined ANR in 2018 to manage national and multilateral programs. She is currently coordinating the drafting of the Scientific Research and Innovation Agenda of the candidate OH-AMR Partnership in the framework of the DESIGN CSA

# Discussions and Outcomes

## Therapeutics

The impact of manufacturing is covered in this chapter but are there more environmental aspects.

***What are the most important environmental aspects to be included in each priority topic?***

*Panel discussion*

The panel briefly discussed the feedback from the Menti session, including green prescribing and how the environment can be used as a source of novel antibiotic compounds including both therapeutics and novel resistance genes. It is not common practice to screen candidate therapeutics through screening for already existing resistance mechanism in commensals and environmental bacteria to determine whether they lead to high levels of resistance. There is a need for an environmental risk assessment for pharmaceuticals and biocides and improvement of this dimension in the regulations regarding antimicrobial use. Antibiotic production emission control and economic and other social science research that could drive change in this direction was also discussed.

It is important to consider gene editing of crops to reduce the need and use of fungicides in the farming sector.

*Menti*

- Discovery of new antibiotics and alternatives from the environment
  - Extreme environments (deep ocean, arctic etc) as a potential source
  - Herbal sources
- Probiotics and prebiotics
- Phage and bacterial/microbial predators
- Green chemistry and green prescribing for antimicrobials, alternatives and biocides
- New delivery systems to limit antibiotic action to site of infection and reduce within host evolution in commensals
- A developed risk assessment protocol
- Produce and use narrow spectrum antimicrobials
- Antibiotic production emission control and consideration of environmental impacts
- Regulation
  - Separating antimicrobial discovery from current economic system
  - Including a trade-off between health and environmental impact
  - Economic model to prevent discharge from drug producers
- Smaller packaging
- Economic studies into the possibility for public entities to develop new drugs including clinical trials

- Social science studies aimed at reducing public pressure for using therapeutics too frequently
- Co-selection and cross-selection with other drugs
- Understanding existing resistance to new drugs in the environment
- Biocides in cosmetics
- Possibility of intrinsic AMR of newly developed antibiotics
- Assess selection pressures of new antibiotics when coming to market

***What is missing from the current draft?***

*Panel discussion*

The panel highlighted that it was important to have a broad and open mind to possible alternative strategies and that the environment is a rich source for novel antimicrobials. Social science could also contribute to identify effective ultimate drivers for reduced emissions from manufacturing of therapeutics.

*Menti*

- Identification of knowledge of what we need to do to reduce the need for therapeutics
- Ranking therapeutic options based on their environmental impact
- Libraries of environmental phage
- Increased public awareness of when treatment is needed
- Basic research on the complexity of incentives and possible value conflicts to ground optimal policy.
- Guidelines for controlling the use of antibiotics at the national level
- Identification of new targets
- Development of high-throughput screening techniques to identify new targets
- The environment as a source for novel antimicrobials
- Reserve the use of important antibiotics
- Increase the development of new antibiotics
- Restrict free availability of antibiotics
- Identify and curb selection pressures to prolong the use of newly developed antibiotics
- Green chemistry
- Natural sources of antimicrobials
- Therapeutic combinations
- Phage therapeutics
- Development of therapeutics and alternatives by public entities
- Antimicrobial peptides
- Fast and High throughput parallel micro culturomics to identify agents
- Membrane targeting antibiotics

**Diagnostics**

***What are the most important environmental aspects to be included in each priority topic?***

*Panel discussion*

The discussion on diagnostics was limited but the panel raised the need to include crop diagnostics, and possibly also expanding the classical definition of diagnostics to rapid tests/ways to get information on how to address AMR in a broader perspective, not just to inform the type of antimicrobial to use to treat a specific patient. An example of such use cold be to test different environments (e.g. bathing water) for high risks for AMR transmission, which could then inform immediate, local measures to reduce exposure risks.

*Menti*

- Diagnostics should be fast, cheap, available and used at point-of-care/point-of-need
- Use of diagnostics for early warning for faecal carriage of rare resistances or pathogens
- Harmonize diagnostics/methodology applied in all aspects of One Health to create comparable results from the clinic and the environment
- Link diagnostics to surveillance systems
- Investigate whether the use of a diagnostic tool would reduce emissions of antibiotic residues into the environment
- Identify decision-makers and develop decision trees for health professionals, veterinarians and farmers based on disease pressure and resistance prevalence in their region
- Rapid tests for assessing environmental transmission or evolution "risk" or probability
- Capture, share and compare data from clinical diagnosis to surveillance in real time
- Inclusion of ecologically relevant targets in diagnostics
- Validation of mobile sequencing technology and AI to support diagnostic results
- Use of farmer's own diagnostic skills (stockpersonship) over high-tech solutions which may not be always necessary
- Consider the matrix use when developing diagnostics for field (crop use)/water (aquaculture) use and optimize use
- Consider personalized medicine (dysbiosis)
- Link phenotype with genotype; identify pathogens and their resistance
- Translation of new tools/strategies developed from environmental side to clinical side
- Use community-based surveillance data to identify hotspots to support patient diagnosis
- Use AI to help improve the accuracy and speed of diagnostics - consider ethical issues with the use of AI
- Consider use in low resource settings, including LMIC
- Connections of ARGs and hosts

- Develop population-based diagnostics
- Economic impacts and challenges

***What is missing from the current draft?***

*Panel discussion*

Diagnostics are needed for AMR on crops and livestock.

*Menti*

- Linkage of clinical diagnostics with environment
  - Early warning of carriage in a community through wastewater-based epidemiology
  - Detect new emerging pathogens in the environment and connect this information with clinicians
  - Research showing the effects of using a rapid diagnostic tool on the antimicrobial residues released into the environment
- Diagnostics for AMR on crops and environmental compartments (soil, water, air)
- Evaluation must include ethical assessment re justifiability, besides feasibility.
- Diagnostic procedures for guiding empiric treatment
- Consolidation and validation of in field pathogen sequencing and determination so that the correct drugs can be used
- Develop easier and faster diagnostics
- Need more on livestock and arable diagnostics
- Personalised medicine
- Rapid test to determine a viral versus a bacterial pathogen
- Environmentally friendly diagnostics
- Sensitivity
- Need for site-specific/appropriate diagnostics
- Relationship between research, governance and industry

**Surveillance**

*Panel discussion*

The panellists discussed the topic of global surveillance and reasons for why it is not already in place. Surveillance has been conducted for many years but there continues to be discrepancy on the definition of surveillance, why it is done and being precise regarding the messaging and language used when discussing the topic. There is no political organization currently implementing surveillance on a global One Health scale and currently surveillance is conducted according to individual mandates, for example national, public health (ECDC), food (EFSA) etc. Research is needed into the barriers hindering integration. The Quadripartite was noted as one positive step forward for AMR integrative actions.

Surveillance research needs to include research on the implementation of surveillance – including cooperation between sectors and research can contribute to actions to understand how the different actors can implement this. There is a balance between collection of information and implementation. Informative targets are needed for Surveillance of AMR, including clear understanding of the purpose, gaps and actions needed. Systems should be designed to cover several elements, to remove issues related to implementation. Local and national issues should be linked with existing global systems, such as GLASS, and methods that are developed should consider resource constrained settings and the value of citizen science.

The different objectives of environmental surveillance were also brought up in the panel discussion, and during several talks at the meeting. It was stressed that it is important to distinguish surveillance with the intent to inform about the regional resistance situation (rather similar objective as for traditional, clinical surveillance) and objectives such as assessing the risks for transmission via specific environmental routes, or the objective of identifying particular risks environments for the evolution/emergence of resistance. Depending on the objective, one would be best informed by measuring different endpoints, in different matrices in different places and at different intervals. Hence, whenever environmental surveillance is discussed, it is critical to be clear on the objectives.

The invited presentation by Ramanan Laxminarayan was also discussed during the panel discussion. Prof Laxminarayan highlighted that for surveillance to have a value it should reduce an important uncertainty and be actionable (different outcomes should lead to different actions).

*Menti*

- Global surveillance
  - Standardisation
    - » Development and use of a uniform standard, associated guidelines and acceptable/unacceptable levels
    - » Where
      - Soil, water, wildlife, air, food
      - Local, national, global
    - » When
      - Active vs passive
      - Carriage vs zoonotic
      - Long term evaluations at representative sites
      - Real-time
    - » What
      - Comprehensive list of targets needed
      - Identify “normal” levels, including those for micropollutants
      - ARGs, plasmids, mixtures, latent genes, microbiome
      - Comprehensively investigating antimicrobial resistance (antibiotic, antiviral, antifungal and antiparasitic)
      - Who has the responsibility?

  - Integration
    - Building AMR surveillance into already existing environmental surveillance efforts
    - Human and animal health impact from environmental AMR
    - Risks that human and animal activities are having on the evolution and transmission of AMR in the environment
  - Data sharing – comprehensive metadata for genotypes and phenotypes
  - Sustainability
  - Citizen science
  - Monitoring AMR in low resource settings including LMICs
- Link surveillance to policy – what needs to be done to drive action?
- Promote public awareness
- Surveillance to predict:
  - Evolution of AMR
  - Transmission of AMR
  - Selection of AMR
  - Ecology and evolutionary trajectories for resistance including the role of the intrinsic resistome
  - Exposure risk to humans, including the development of appropriate endpoints
- Antifungal surveillance and associated databases
- Surveillance to study the effects of climate change
- Develop a quantitative risk assessment
- Studies on the role of conflicts between local values and regulation and practical surveillance
- Use surveillance to study the benefits/effects of interventions
- Ethical legal and social implications of surveillance
- Capacity building

***What is missing from the current draft?***

*Panel discussion*

Panellists discussed how to prioritise the different gaps, as well as best ways to compare surveillance within and between countries. It is important to recognize that there are different needs in different countries but that data needs to be comparable so benchmarking is needed.

The panellists raised the issue of standardisation vs harmonization and that this aspect should be further emphasized in the draft text.

Alternative mechanisms of surveillance or proxies in all sectors are needed. It is necessary to determine what should be measured for surveillance to indicate human health concern in particular situations such as following the use of antimicrobials in horticulture. Surveillance can be used to study contamination of the environment with different pollutants, to identify hotspots, and to determine the impact of pollutants on

AMR. Data can be examined retrospectively so it is important to ensure longevity and sharing of data and samples (biobanks).

Historically surveillance has been focused on pathogens and infection risk but it is important to use surveillance to study the resistome and emergence of resistance. It is important to use communication optimally to communicate with the public and policy makers to ensure that the topic of AMR is well understood. For example, that AMR is more complex than COVID and could be explained as thousands of potential individual pandemics based on the different risk genes.

*Menti*

- Definitions of surveillance and strategies for determining changes in long term trends, transmission risk, emergence/evolution
- Meaningful and economic targets to be measure
- Definition of the different surveillance objectives, desirable output for each and associated appropriate methodology
- Clear description of needs and goals
- Surveillance of environment surrounding landfills
- Quantitative estimates of the different AMR compartments
- Minimum quality standard in sampling
- A short summary of the goals of the current surveillance networks
- Too little about exploring the human, social and value aspects important for globally feasible environmental AMR surveillance
- It is important that environmental surveillance is not reduced to only sewage surveillance, which might need to be clearly pointed out
- Standard protocol for the surveillance
- Importance to know the bacterial host of ARGs (pathogen or not) to evaluate the risk they pose
- Clear separation between use of wastewater surveillance and environmental surveillance
- Innovative simple and cheap targets suitable for application in LMIC
- Sewage is a mirror of the society/ human population, and not necessarily in the remit of environment (except the effluent/biosolids) that are received
- Need to present AMR as a complex pandemic with environmental origins!
- Definition of real-time approaches that are available and the associated cost
- Need to include environmental surveillance as an early warning tool in the objectives, rather than only in the background
- Use of culture of specific pathogens in environmental samples as part of surveillance
- Sociological research on implementation hurdles
- Change over time should also consider the increase of humans to nature/loss of biodiversity (in line with a changing climate)
- A global map presenting the areas currently and actively doing surveillance (which type) and where would be useful

**Transmission and Evolution**

***What are the most important environmental aspects to be included in each priority topic?***

*Panel discussion*

It is important to identify environments for AMR evolution but if we are wrong in our assumption then what we do might be in vain. The scientific community is still lacking methodologies to show how significant gene transfer in the environment is and the issue is difficult to tackle. Some hotspots e.g. WWTP are currently know but more needs to be addressed by research.

The context specificity needs to be considered. There is currently a knowledge gap in how accurately derived Predicted No-Effect Concentrations (PNECs)can be applied to different matrixes (water, soil etc) and within mixtures. It is currently accepted that selection for resistance occurs in hotspots with high antimicrobial concentrations but the roles of mixtures of antimicrobials and synergistic effects could result in selection at concentrations below existing PNEC values. It is important to be open minded about the risks and the relevance of current knowledge on the compartments. Innovative ways to identify hotspots for evolution of AMR are needed.

The ecology of genes within the pan-genome across the One Health spectrum should be considered. The topic could be renamed to Transmission, Ecology and Evolution since ecology is missing in the chapter. It is important to understand resilience and biodiversity within a community.

The is a massive need for social science research within this topic. A mixture of both qualitative and quantitative methodologies and descriptive research are needed. These methodologies should include institutional systems, politics and drivers of politics.

Robust models are needed to predict transmission and evolution and an iterative discussion needs to include the different sectors involved.

The current text already includes the LMIC perspective.

*Menti*

- Intrinsic resistome of environmental bacteria exposed to pollutant mixture
- Role of the mobilome
- Transmission and selection
  - Linkage with clinical relevance
  - Quantitate transmission rates
  - Hot spots
  - Wildlife
  - Urban settings
- Ecology
  - Biodiversity

  - Role of wastewater
  - Temperature
- Reservoirs of resistance (bacteria, MGE, ARG, unculturable bacteria) and their role on emergence of AMR
- Linking Human Health, Animal Health and the Environment
- Quantifying the role of human health on development of AMR
- Biosecurity
- Where ARGs come from and how/why
- Importance of ‘rare’ evolutionary events relative to more common events
- Proper assessment of public health consequences
- What is the relative contribution of the environment in relation to other transmission routes to human exposure to AMR - both quantitatively and qualitatively
- Dedicated studies on transmission in specific locations/matrices
- Selectors and the concentrations that have an effect
  - Role of microplastics
  - Combinations/mixtures
  - Concentrations of selectors
  - Metals
- Climate change
- Important matrices for transmission – water, air, soil
- Link with other disciplines e.g. physics
- Intersectoral collaboration
- Link with policy
- Data sharing
- Transmission and evolution in resource poor settings e.g. LMICs
- Selective pressures - quantifying them and risk
- Risk of transmission
- Link of planetary boundaries framework (novel entities) to AMR?
- Improve PEC predictions/more MEC collection
- PNECs for resistance
- Societal impact –stronger environmental regulation
- AMR and virulence should not be considered separate entities. Commensal to pathogen continuum
- Linking community ecology of AMR to the single-cell level
- Transmission of AMR from antimicrobial contain in herbal natural resources
- Resilience in different environments differ when it comes to WWTP effluent, biocide pollution etc.
- Implications for new drug discovery since most bacterial pathogens have retained resistance to older antibiotics that no longer are used clinically Stress response as possible risk to AMR evolution
- Vaccines to lower antibiotic selection pressure especially in animal production

***What is missing from the current draft?***

*Panel discussion*

The draft objectives were shown. Ecology was mentioned to be missing. Also, it was discussed that changes in e.g. relative levels of antibiotic resistance genes could sometimes simply reflect taxonomic changes within a complex community rather than selection within species, which is more critical for resistance evolution.

The chapter was complimented for the few gaps and the nice writing.

*Menti*

- Transmission via imported produce
- Public health and environmental risk assessments
- Sociological / cultural aspects of interventions
- Mixtures
- Potential or existing resistance to new drugs
- Mechanistic studies on a molecular level
- Plasmid curing as a valid option or potential option for preventing the spread of AMR
- Interdisciplinary approach
- Modelling (small and large scale) and AI
- Value- and norm-conflicts for justification and feasibility
- Scale (national, regional, continental) at which transmission of AMR occur
- Low resource settings including LMICs
- Ecology – should be central to understand AMR evolution, as ecology and evolution happens on the same timescale
- Drivers for emergence and drivers maintaining high resistance high or resilience
- Selection
  - Mixtures, chemistry, bioavailability and transformation products
  - Hotspots countries/sites
  - Heavy metals
- Abiotic and biotic factors influencing transmission
  - Temperature
  - pH
  - Conductivity
  - $O_2$ content
  - Chemicals
- Processes that limit the development of AMR in different environments (improve WWTPs, use digestate instead of manure etc.)
- Climate change
- Biodiversity
- Link between emerging opportunistic pathogens and the detected ARGs in environmental matrices.
- Understanding the existing resistance in the environment
- Broaden transmission context to include plant-human

- Risk assessments
- Use of synthetic ecology approaches to study eco-evolutionary dynamics of AMR
- Bacterial community assembly processes
- Role of bacteriophages
- Global guidelines to support studies
- Connection between research and policy makers
- Connection among research, governance and industrial sector

**Prevention and Intervention**

***What are the most important environmental aspects to be included in each priority topic?***

*Panel discussion*

A number of interventions have been developed in certain countries and this chapter also includes implementation science. This includes the 'how to' in terms of implementation in LMICs and HICs. The research on the design of interventions needs to consider the social science aspects early.

A cost-benefit analysis is needed for interventions when considering the transmission of AMR. Rare events that are difficult to monitor and predict and should be a subject for research. Predictive modelling is needed to develop and implement viable interventions and examine their effect. This is difficult but the model can be refined and the impact will likely be great.

Surveillance is not an intervention but is used to inform intervention so it should be removed from the chapter. The chapter mentions One Health settings but without specifically including the environment. There is a need to define One Health but the health of the environment is misconceived in the AMR field as the environment is not there because of concerns for "environmental health" but rather because microorganisms and their genes tend to move between humans, animals and the environment. The use of the term One Health intervention is often poorly used and should cross all three compartments. It is important to use the correct language in order to communicate effectively with policy makers and the public.

*Menti*

- Remove the source of release of antimicrobials
- Cost benefit analysis
- Where should interventions be implemented
- Cultural hurdles to implement WASH
- Sharing of information and honestly reporting data
- Identify priority populations or settings in which interventions are urgently needed
- Public education on antibiotic use
- Critical evaluation of interventions
- Standard approaches for testing impact of prevention technologies
- Interdisciplinary research

- Link interventions with the origins of AMR
- Risk evaluation
- Adaptation to specific settings, including resource poor settings
- Identification of barriers to human exposure to AMR from the environment
- Adequate and steady regulation to the use of antibiotics
- Economic drivers
- Effects of pesticides on ARG development!
- Economics and policy assessment and impact
- Model AMR in the environment to allow effective interventions
- Climate change - heat, flooding, displacement of species
- Public awareness of appropriate disposal of antimicrobials and biocides
- Studies on the effectivity of small, decentralized WWTP
- Improved monitoring methods for transmission, selection and evolution
- Improve methods for implementation research
- Guidelines that can be applied in different countries
- Investigation of sewers as intervention areas
- Paths and exposure routes
- The impact on human health by reducing AMR outflow from WWTP
- Methods to evaluate the success of interventions
- Microbial source tracking to identify and localize the source of the infection caused by environmental ARBs.
- Rigorous (quantitative) assessment of ARG/ARM mitigation of current and innovative residual stream technologies
- Strengthen multisectoral coordination mechanism
- Identify natural ecological barriers that can be utilized
- Standards for ARB removal in wastewater treatment
- Social media to bring awareness
- Barriers to stakeholder acceptance
- Modelling CC
- Dose response data
- Citizen science
- Social science/behavioural studies
- Increase the awareness of AMR on stakeholder level
- Impact of intensive farming practices
- Barriers to implementing interventions
- Define relevant targets and outcomes
- Integrated studies, cross-border studies
- Identification of transmission routes to inform interventions
- Macro/national economic, political, societal perspective
- Local sanitation
- Discharge limits based on biocide activity for manufacturing / industry
- Using models of predictions based on metagenomics data available
- Circular economy
- Sharing of effective interventions
- Participatory design
- Public engagement
- Define one health

- Proper system analysis/cost vs benefit
- Develop relevant legislation
- Research on efficiency of interventions
- Low cost sanitation strategies
- Supporting industry to self-regulate
- Evidence-based interventions
- Investment in animal health and alternatives to antibiotics
- Study interventions from ongoing outbreaks e.g. COVID on the prevention or enhancement in the AMR issue

***What is missing from the current draft?***

*Panel discussion*

The panel highlighted that a large number of social science issues were brought up via the participants.

*Menti*

- Knowledge, awareness and understanding fate and effects of anthropogenically used antibiotics
- Definition of One Health interventions
- Non-antimicrobial options for preventing disease (not just WASH) - stress, interactions with animals, lack of natural spaces etc.
- How to assess preventions and preventions - standard methodologies
- Policymakers want interventions based on ranked cost benefit
- Multidisciplinary PhD programs
- Identification of exposure routes
- Standardized methods to assess efficacy
- Predictive modelling
- Citizen science
- Global collaboration and implementation in appropriate locations
- Sharing effective interventions
- Adapting awareness campaigns to the culture of community/country
- Regulation of agrochemicals
- Critical Control Points estimation
- Data on selective concentrations to inform interventions
- Development of new technologies are not emphasized (wastewater, built environment)
- Develop integrated database containing information about preventions and interventions of many countries as case studies
- Economic and social science research
- Think long term – interventions may take time to have an effect
- Cross sectoral collaboration
- Implementation science
- Data sharing

# General feedback on JPIAMR calls and for future actions in the candidate One Health AMR partnership

The participants were asked to give feedback on more general aspects, including JPIAMR calls and future OH AMR partnership calls and activities.

**Based on previous experience of JPIAMR calls, what has been good?**

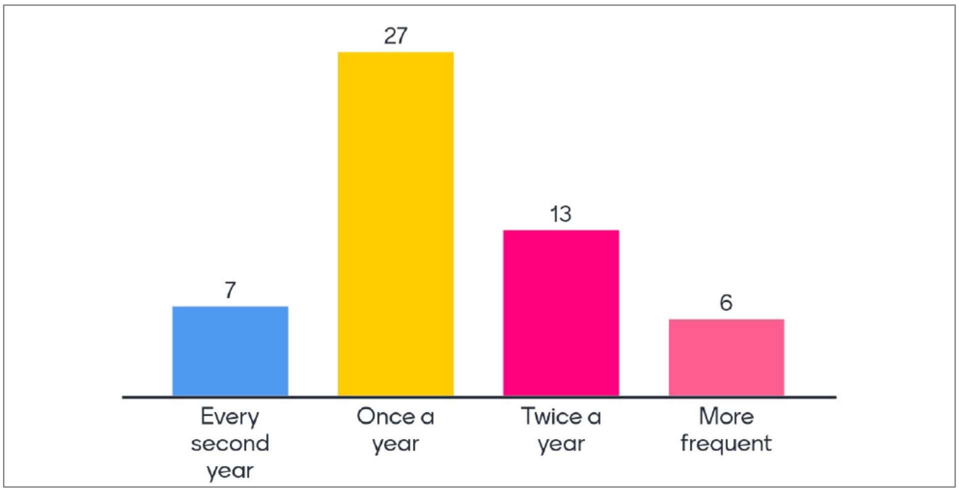
- Evaluation of the JPIAMR projects very fair but composition of panels biased towards medical experts
- LMIC inclusion
- International collaboration
- Networks are great collaborative exercises and value reaches beyond immediate outputs.
- Relatively wide freedom to design and address research questions within the research topics. Not too much directed research.
- The shared knowledge and opportunity to connect in a smaller group with people thinking of specific challenges of relevance to one health
- Good incentive to collaborate across countries and disciplines
- As a reviewer I can tell that the process has been fair and transparent. The process has been well organized.
- Collaboration with regulators/industry
- Ability for international and multidisciplinary collaboration
- Reporting
- Good size of consortia (not too big, not too small) that creates good synergies
- Involvement of multiple countries
- Promotes strong international and interdisciplinary cooperation but with own funding
- The emphasis of having partners from LMIC
- Limited formal requirements during proposal preparation
- A wide variety of calls
- Encourages international collaboration
- Inclusion of LMIC partners
- The opportunity to meet and support international conversation
- Two stages proposal evaluation
- Pre-announcements
- Good and well managed review process (from the reviewer perspective)
- quite flexible in terms of criteria for consortium building
- Review process seems to be as fair as possible
- One Health focus
- The number of groups supported
- Smooth (not too much) administration and reporting
- Efforts by JPIAMR (not fully successful - but nice) at bring different JPIAMR projects together for knowledge exchange
- no TRL expectations - i.e. can address problems without need for technology development
- Rather have high selection for the first step proposal

- Inclusion of environmental aspects in calls

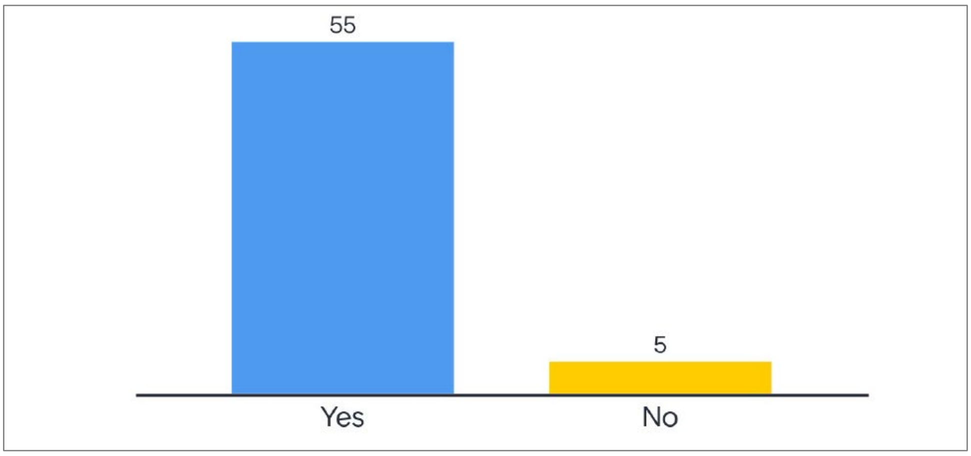
**Based on previous experience of JPIAMR calls, what has been bad?**

- Unclear national regulations
- Too few countries are involved
- Not possible to use funds after the project officially ends but when a vast amount of the work has been unfortunately not been completed for external reasons
- Too little recognition of the broad human and social science aspects: qualitative, quantitative, descriptive and evaluative
- The selection of partners is too political, i.e. they are mostly selected on what countries provided funding for the call rather than excellence and relevance for the proposal
- The possibility to still include countries that aren't participating - that comes down to the researchers being inclusive perhaps as well
- JPI general system where the countries are providing most of the funding. You must form the consortium according to the country where the PI comes rather than expertise.
- Hard to collaborate with LMICs if most of the money sits with HICs
- Countries missing you would like to collaborate with
- No databases appeared that will be generally available
- Seems it only for well-established researchers already with connections limiting ECR participating
- Imbalance between countries contribution sometimes has quite a strong effect on the composition of the consortia and thus the research questions.
- Funding for LMICs
- No or lack of Industry involvement
- First step proposal should be selected hard so that second one has high probability of being funded
- Not well advertised in non-Western countries
- Network calls just a little too limited to generate output
- Being out of remit due to local funder priorities which differed by national funder
- Too short project calls - three years is barely enough to get going. With five-year calls I think more goals could be achieved and created stability be obtained.
- Networks of one year is too short
- More flexibility with project lengths
- Duration of projects could be longer (e.g. measure effects of interventions)
- That one has to submit the application to (1) JPIAMR and (2) National funder
- Spent lots of time writing a proposal with one LMIC (who led) -- ended up not getting funded -- maybe adjust 'ranking' *assessments' 'when LMICs are included?
- Very important for the coming calls to make sure enough non-clinicians are in the panel
- The funding is too limited in some cases (country dependent)

**How often would you like to see calls from the One Health AMR Partnership for AMR?**




**Would you like to see some open calls within the field of AMR?**




An open call would allow can bottom up research that could be really risky and really novel. Directed calls are always purpose specific.

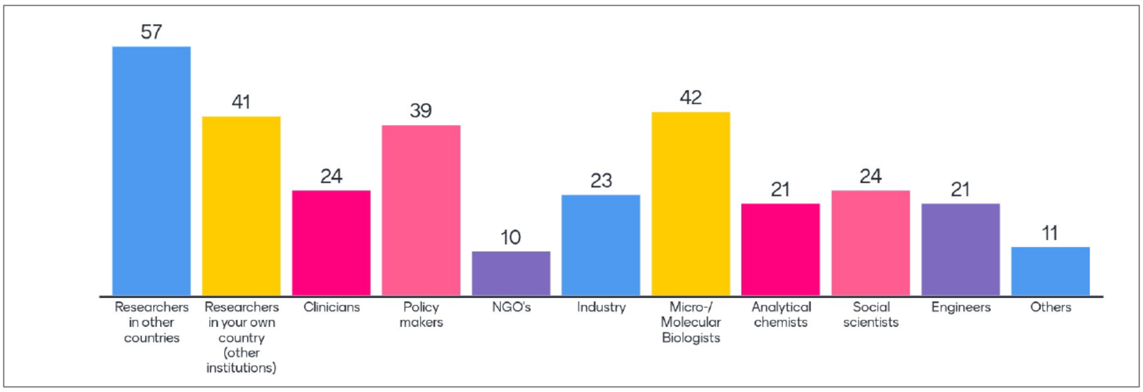
The ERC type of format for call was discussed - high risk, high gain research. However, if this was implemented in a programme like OH AMR it would be only a couple of times in the whole programme. The funders involved in the One Health AMR Partnership will soon discuss if "high risk, high gain" call for projects need to be implemented, and if yes, how.

The European Commission will likely support only the top-down directed approach, while the participants of the meeting apparently wanted to see more bottom-up. The One Health AMR Partnership will explore how call topics could be broaden, even in a top-down approach, by breaking the silos between the different thematic pillars (Transmission, Therapeutics…), and between the domains of One Health.

**What types of support (in addition to regular research calls) would you like to see in the candidate OH AMR partnership?**

- Support for young researcher mobility
- Funding exclusive for Early Career Researcher) (ECRs)
- ECR and LMIC researcher mentorship and networking
- Workshops in LMIC countries
- Early career fellowships
- SRA meetings
- Postdoc mobility
- Mobility and network building
- Fellowships
- Integrated data structures for e.g. surveillance data
- Infrastructures: databases, informatic tools etc.
- Training on techniques, could help with standardisation of research methods
- Joint calls with other partnerships
- Scholarship for PhD conference participate, research stays abroad, new cooperation
- Funding for those on fixed term contracts
- Internship among AMR laboratories
- Collaboration with industry
- Support best methodology used for certain approaches (standards, guidelines), would help to harmonize methods widely
- Building (not maintaining) new infrastructures
- Scholarships
- Interdisciplinary support for One Health collaborations
- Computer clusters
- Mental health and medical service support for researchers. And more on surveillance and data analysis.
- Workshops
- Faculty visits (sabbatical) and trainee visits
- Data management
- LMIC exchange fellowships
- Training workshops
- Translation services
- Start up support in the field of AMR
- Small grants (<5,000 euro). Can go long way in LMICs
- Collaboration between groups
- LMIC activities
- Education
- Conference funding
- Mentoring program
- Data management assistance
- Working with stakeholders
- Computer support HPC
- Dissemination e.g. one-year extension for a funded project for that
- Training opportunities for researchers from LMICs

**Which types of partners are most important for you?**




One reflection of this was that collaborators from within your own country received many votes, but given the current funding rules as applied through the JPIAMR, including partners from within the same country as yourself is discouraging as the maximum sum allowed is often set per country or per funding agency. The panellists also noted the relatively high numbers of votes for involving policy makers.