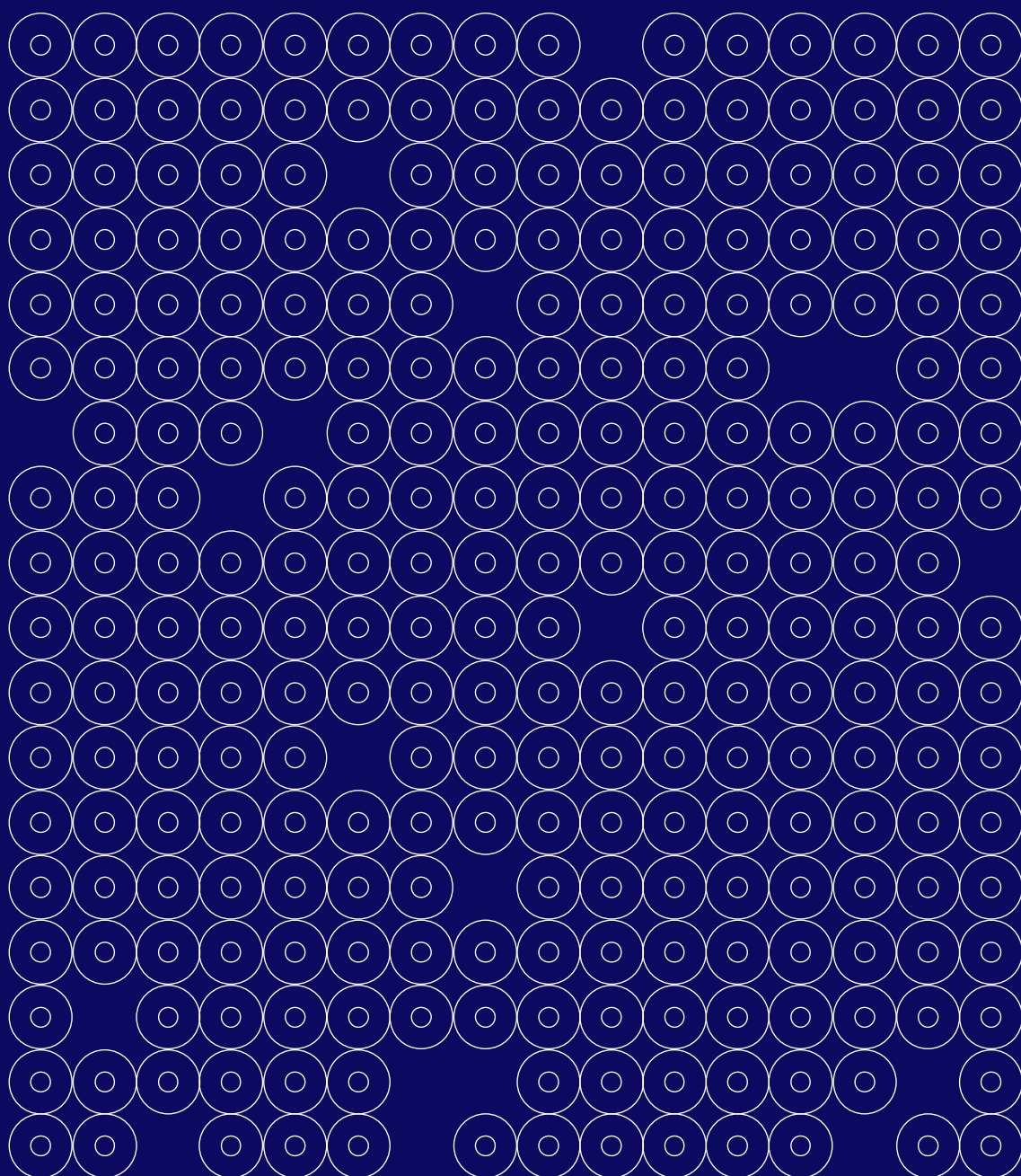


# JPIAMR Start Up Workshop for projects funded under the call: One Health interventions to prevent or reduce the development and transmission of AMR



# Contents

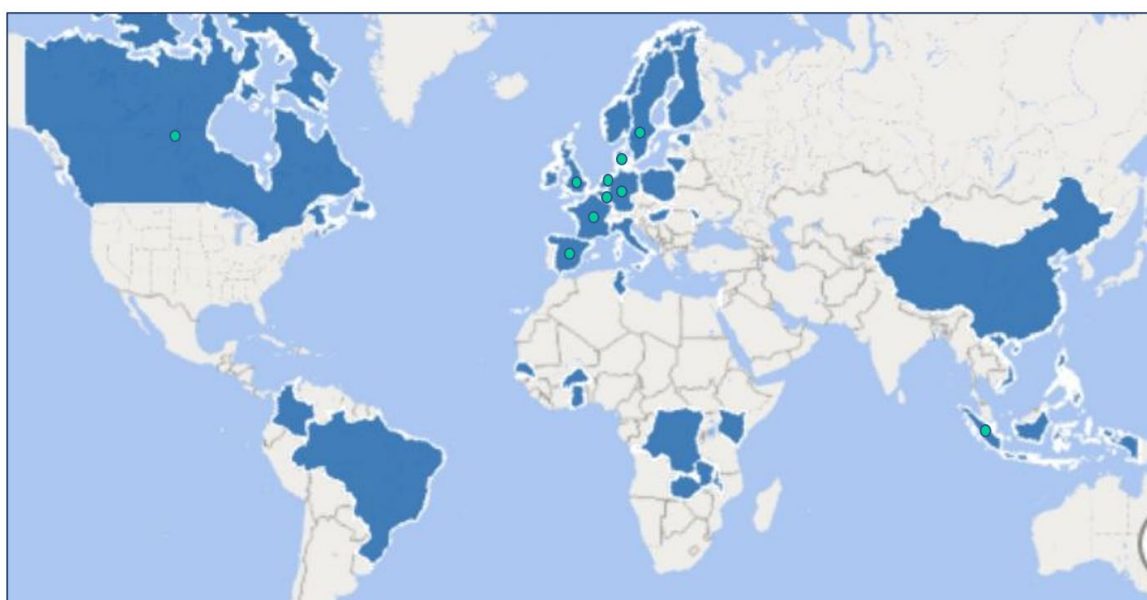
<b>Introduction .....</b>	<b>2</b>
Background .....	2
Workshop objectives .....	3
Workshop outcomes.....	4
Meeting organisation.....	4
<b>Funded projects within the JPIAMR HARISSA call .....</b>	<b>5</b>
STARS-TAP.....	6
I-CRECT .....	7
SEFASI.....	8
ICONIC.....	9
CABU-EICO .....	10
COINCIDE .....	11
FARM-CARE.....	12
SNAP ONE .....	13
DESIGN .....	14
MISTAR.....	15
MOB-TARGET .....	16
Phage-Stop-AMR.....	17
COMBAT.....	18
STRESST.....	19
PhageLand.....	20
ENVIRE .....	21
ARPHILAKE .....	22
HOTMATS.....	23
PHAGE-EX.....	24
<b>Annex A. Agenda HARISSA projects start up workshop.....</b>	<b>25</b>

# Introduction

## Background

The JPIAMR launched an international call for projects within JPIAMR and within the ERA-NET JPIAMR-ACTION framework. The 13<sup>th</sup> JPIAMR call 'One Health interventions to prevent or reduce the development and transmission of AMR', in short HARISSA, launched early 2021. The call included 30 funding organisations from 21 JPIAMR member countries and was co-funded by the European Commission. In total, 19 proposals were funded funding, with consortia members coming from 21 countries. A total funding of €25.8 million was awarded under this call.

Figure 1 displays the geographic localisation of the partners of the funded projects. The most common countries where coordinators and partners within funded projects come from are the United Kingdom (20%), Germany (12%), France (10%), the Netherlands (9%), Spain (7%), and Belgium (7%).



**Figure 1.** Geographic localisation of the participants: funded proposals.

Since this call encouraged transdisciplinary research and the participation of partners from low- and middle-income countries (LMICs), 19 partners of funded projects come from LMICs. Figure 2 shows the geographic distribution of partners from LMICs requesting funding. Funded proposal are shown in black.

The consortia included six partners on average in the funded proposals. Among the consortia, 58.8% of the partners (including coordinators) are male compared to 41.2% who are female. Figure 3 shows the distribution of all partners and coordinators during the three proposal stages.

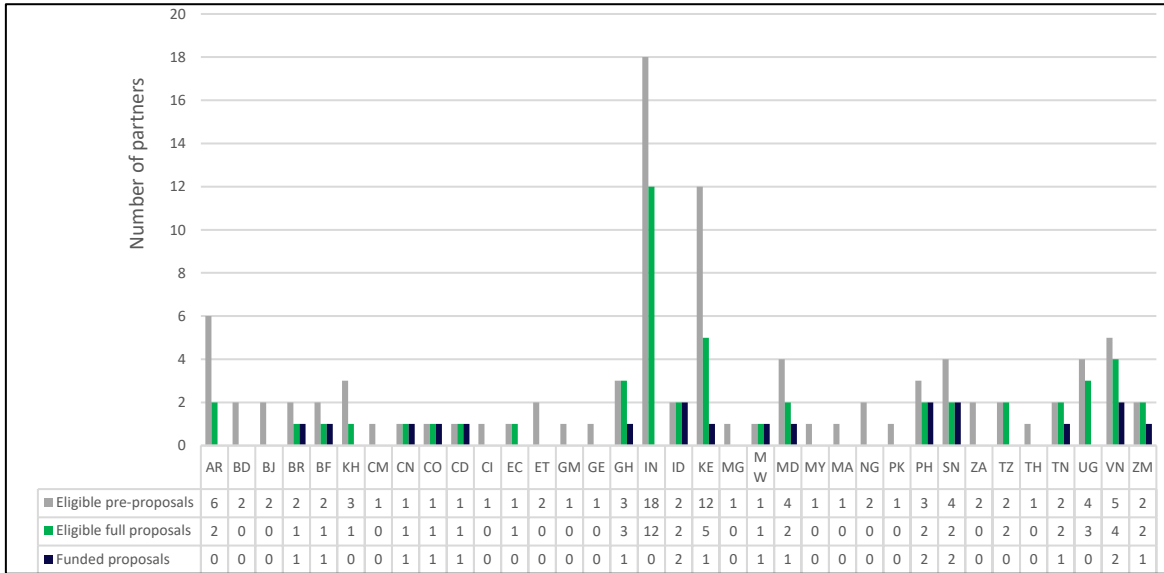


Figure 2. Geographic distribution of the partners from LMICs requesting funding.

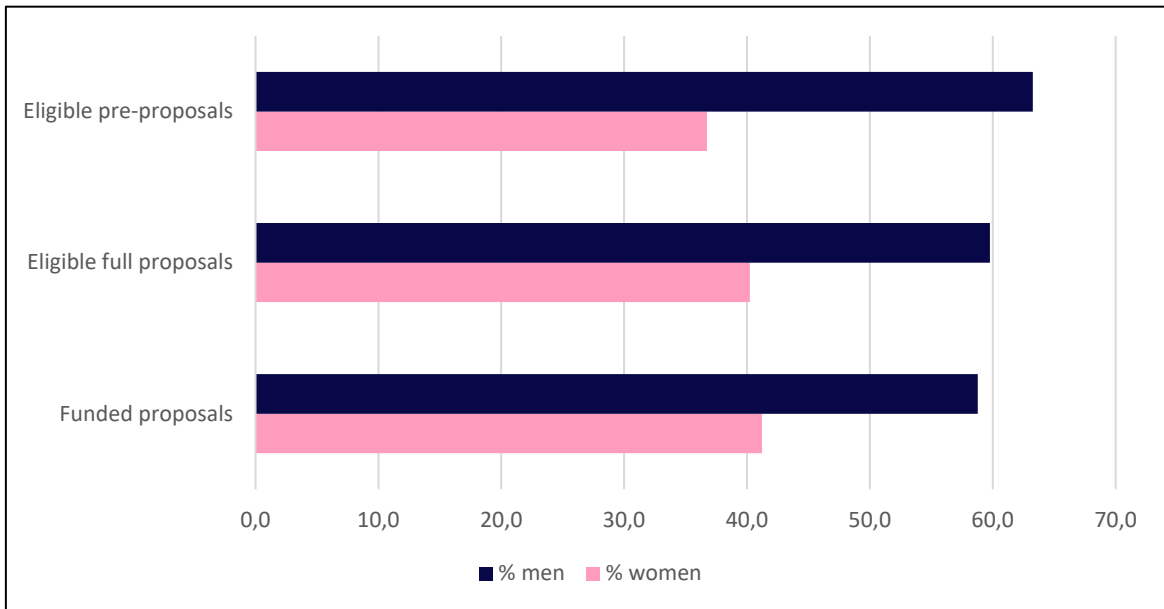


Figure 3. Gender distribution of all partners including the coordinators.

**Workshop objectives**

The start-up workshop for the 19 funded projects within the HARISSA call took place virtually on April 28 via Zoom. The aim of the workshop was to introduce the projects, exchange ideas and share experiences. Each project coordinator, or in some cases project partner, presented the project objectives and aims in a 10-minute presentation. The project presentations were scheduled over two sessions, each chaired by experts from the funding agencies participating in the call. The workshop promoted the facilitation of discussion and enabled the participants to interact and find synergies. Participants mainly consisted of project coordinators and partners, but funding agency representatives took part as well.

## **Workshop outcomes**

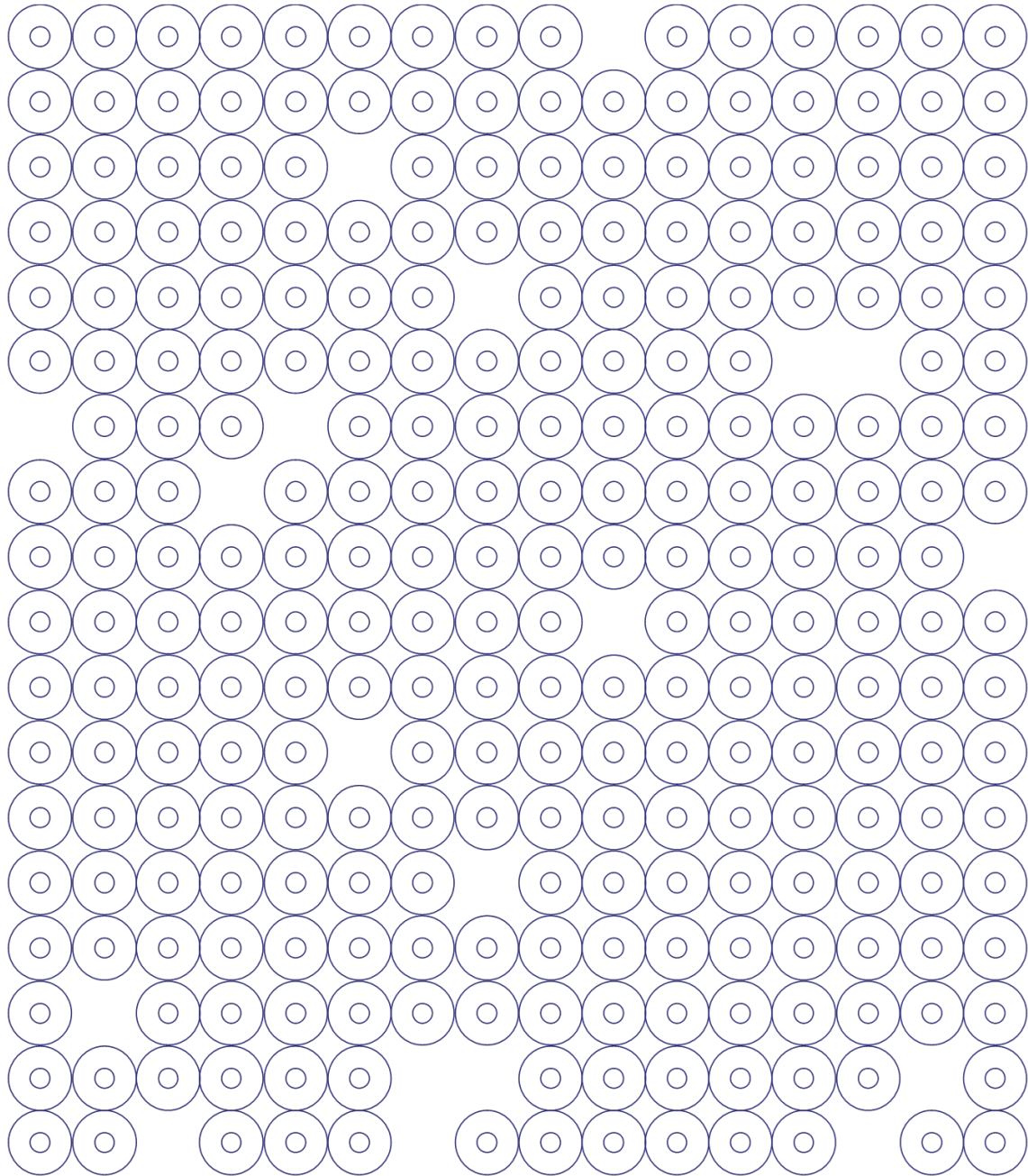
Interesting presentations and discussions were held and the major outcomes included:

- The workshop highlighted the importance of international calls and support for organisations such as JPIAMR that allow and facilitate international collaboration.
- A wide range of interventions were presented focussing on different topics – from testing and uptake of innovation to public health interventions to preventing and managing AMR transmission.
- Besides cost-effectiveness, the importance of interdisciplinary collaboration during the projects became clear.

## **Meeting organisation**

The HARISSA project start-up workshop was organised and planned by ZonMw, in collaboration with the JPIAMR, secretariat and the Joint Call Secretariat for the Call (ANR). During the meeting Kris Pelleboer (ZonMw) provided the opening and Sanne Kwakkelstein (ZonMw) and Anouk Warmerdam (ZonMw) took care of the background tasks, making sure the meeting ran smoothly. The first presentation session was chaired by Ghada Zoubiane (ICARS) and the second by Carolyn Johnson (MRC UK). Finally, Kris Pelleboer presented a wrap-up of the meeting, summarising the main discussion topics of the day. For a full overview, the agenda can be seen in Annex A.

# Funded projects within the JPIAMR HARISSA call



### **STARS-TAP: Specific Targeting of Antimicrobial Resistant Strains *in situ* using Targeted-Antibacterial-Plasmids**

The global spread of antimicrobial resistance (AMR) among pathogenic bacteria is recognised as one of the biggest concerns in public health and a research priority in microbiology. Drug-resistance increases exponentially for certain bacterial organisms and is becoming the main threat to human health worldwide. As a consequence, national and international authorities have emphasised the need to taking a broad, coordinated approach to develop new antimicrobial strategies to fight against drug-resistant bacteria across multiple sectors such as human health and animal health, agriculture and environment (i.e. 'One health' major challenge). The STARS-TAP research program aims at developing an innovative non-antibiotic antibacterial methodology to specifically target AMR strains from natural bacterial communities in several ecosystems *in situ*. The proposed methodology is based on Targeted-Antibacterial-Plasmids (TAPs) that use DNA conjugation to deliver CRISPR/Cas systems exerting a strain-specific antibacterial activity. If successful, our research would represent a real breakthrough for clinical and environmental microbiology, and open new options for the elimination of AMR strains from various ecosystems. This unexplored and versatile strategy complementary to antibiotic treatments holds the potential to be used for preventive decolonisation purposes, or even in agriculture to tackle AMR prevalence in amended soils.

#### **Project consortium**

<b>Coordinator</b>	<b>Christian Lesterlin</b>	<b>Centre National de la Recherche Scientifique (CNRS)</b>	<b>France</b>
Partner	William Couet	French National Institute of Health and Medical Research	France
Partner	Gregory Jubelin	French National Research Institute for Agriculture, Food and Environment	France
Partner	Anna Marzec-Grzadziel	Institute of Soil Science and Plant Cultivation – State Research Institute	Poland
Partner	Pierre Bogaerts	UCL - Université Catholique de Louvain	Belgium

### **I-CRECT: Interventions to decrease CRE colonisation and transmission between hospitals, households, communities and domesticated animals**

In middle-income countries antibiotic resistance is increasing causing suffering and high mortality. In 12 Vietnamese hospitals half of patients were colonised with “superbugs” called carbapenem resistant *Enterobacteriaceae*, for short CRE, at admission 13% and after 2 weeks in hospital 89%. CRE colonisation cause hospital infections and high mortality. As many patients are CRE colonised at hospital discharge it can spread to the household members and out in community and environment. If CRE spreads in the community it will be very difficult to treat community infections as urinary tract infections and pneumonia, increasing treatment times, costs and mortality. It is hence important to stop the spread of CRE from hospitals to community. In our research we will follow patients that are CRE colonised at discharge out to their households. The households will be randomised to intervention and control group. An intervention to improve hygiene and decrease unnecessary antibiotic use will be evaluated on CRE transmission in the household and to domesticated. Colistin, a last resort antibiotic for very ill patients, is often used for animals in feed as growth promoter, selecting for antibiotic resistance that boomerang back into hospitals. We will assess colistin resistance in households and animals and to targeted interventions to reduce transmission. Wastewater from hospitals will be tested for antibiotics and resistant bacteria. The relatedness of bacteria in humans, animals and environment resistance genes will be investigated.

### **Project consortium**

<b>Coordinator</b>	<b>Håkan Hanberger</b>	<b>Linköping University</b>	<b>Sweden</b>
Partner	Flavie Goutard	Centre de coopération internationale en recherche agronomique pour le développement	France
Partner	Mattias Larsson	Karolinska Institutet	Sweden
Partner	P Velavan Thirumalaisamy	The Universitätsklinikum Tübingen	Germany
Partner	Yaovi Mahuton Gildas Hounmanou	University of Copenhagen	Denmark
Partner	Phuc Duc Pham	Hanoi University of Public Health	Viet Nam
Partner	Dien Minh Tran	Vietnam National Children's Hospital/ Research Institute of Childrens Health	Viet Nam



## **SEFASI: Selecting Efficient Farm-level Antimicrobial Stewardship Interventions from a one health perspective**

Antimicrobial resistance (AMR) links together people, plants, animals and their environments under the One Health umbrella. In this work we will similarly link interventions aimed at AMR by considering their impact not only in terms of impact on hospitals, communities or farmers, but across all of these groups. This is key to informing optimal intervention selection by governments in tackling AMR in the future. Our research will combine statistical analysis, mathematical simulations and economic-impact models within a single intervention assessment framework. We will bring together an interdisciplinary team of economists, mathematical modellers and veterinary scientists to apply this modelling framework to three country cases studies: England, Senegal and Denmark. All three countries are global leaders in terms of AMR data collection and intervention, providing ideal settings for intervention assessment. Our outcome will be a ranking of farm-level interventions for policymakers to assess their impact from a One Health perspective, and an insight into where more data in the future would be most beneficial, in terms of reducing uncertainty in such economic evaluations of interventions.

### **Project consortium**

<b>Coordinator</b>	<b>Gwenan Knight</b>	<b>London School of Hygiene and Tropical Medicine</b>	<b>United Kingdom</b>
Partner	Nichola Naylor	Public Health England	United Kingdom
Partner	Dagim Belay	University of Copenhagen	Denmark
Partner	Michel Dione	International Livestock Research Institute	Senegal
Partner	Ana Mateus	Royal Veterinary College	United Kingdom

### **ICONIC: Ionophore coccidiostats: risk of CO-selection of antimicrobial resistance - Clinical impact and intervention strategies**

Today's intensive broiler production is highly dependent on in-feed ionophore coccidiostats. Because these ionophores are not used in humans, it is widely assumed that their use in poultry is not a risk for human health. Recent evidence, however, suggests that they may cause co-selection of medically important antimicrobial resistance. This means that the use of ionophores can cause the spread of bacteria which, when they cause infections in humans, cannot be treated with certain antibiotics. The ICONIC project aims to gain more insight into the magnitude of this problem by analysing and comparing bacteria from poultry, environment and humans. The results will yield a better understanding of the human health impact of ionophore use in poultry industry. In parallel, the project will investigate the effects of alternatives to the use of ionophores, providing leads for reducing the risk of resistant bacteria transmitting from the poultry chain to humans.

#### **Project consortium**

<b>Coordinator</b>	<b>Mariel Pikkemaat</b>	<b>Stichting Wageningen Research</b>	<b>Netherlands</b>
Partner	Anne Margrete Urdahl	Norwegian Veterinary Institute	Norway
Partner	Roger Simm	University of Oslo	Norway
Partner	Daniela Maria Cirillo	San Raffaele Scientific Institute	Italy
Partner	Isabelle Kempf	Anses, laboratoire de Ploufragan	France
Partner	Jowita Niczyporuk	National Veterinary Research Institute PIWet	Poland

### **CABU-EICO: Optimising community antibiotic use and environmental infection control with behavioural interventions in rural Burkina Faso and DR Congo**

Incorrect use of antibiotics is a major cause of antibiotic resistance. In rural Africa, people often receive antibiotics without prescription from local pharmacy shops, increasing the risk of resistance. Sub-standard sanitation and hygiene practices result in frequent exchange of bacteria between humans' guts, and their environment. How important these different sources are for the acquisition of antimicrobial resistant (AMR) bacteria in humans is still unclear, but contacts between humans and animals, in particular rodents, are frequent in much of Africa. We will develop and evaluate a behavioural intervention for community pharmacy staff and their communities, to improve antibiotic use and hygiene practices, to ultimately reduce AMR. The intervention will be implemented over 12 months in Burkina Faso and DR Congo. We will measure as primary result changes in the use of specific AMR-prone and clinically vital antibiotics at community pharmacies throughout the intervention period. We will compare antibiotic use in pharmacies and surrounding communities where the intervention was implemented, and where the intervention did not take place. Also, we will assess changes in hygiene practices by surveying members of the surrounding communities. Then, we will determine how frequent AMR bacteria are transmitted by repeatedly analysing stool samples of those populations, and of rodents living in the surroundings, for bacteria and specific AMR genes. Through mathematical modelling we will quantify how changes in antibiotic use and hygiene practices will impact AMR transmission.

#### **Project consortium**

<b>Coordinator</b>	<b>Marianne van der Sande</b>	<b>Institute of Tropical Medicine</b>	<b>Belgium</b>
Partner	Halidou Tinto	Institut de Recherche en Science de la Santé - Direction Régionale du Centre-Ouest	Burkina Faso
Partner	Delphin Phanzu Mavinga	Institut Médical Evangélique de Kimpese	Congo, The Democratic Republic Of The
Partner	Edwin Wouters	University of Antwerp	Belgium
Partner	Tamara Giles-Vernick	Institut Pasteur	France
Partner	Stephen Baker	University of Cambridge	United Kingdom
Partner	Ben Cooper	University of Oxford	United Kingdom

## **COINCIDE: Impact of reducing colistin use on colistin resistance in humans and poultry in Indonesia**

Antimicrobials are drugs that help cure people and animals from infections with bacteria. The slogan: 'the more you use, the faster you lose' is definitely applicable for antimicrobials. When you use antimicrobials, more bacteria become resistant, meaning that an infection can no longer be treated. This is a worldwide challenge for the treatment of diseases in animals and humans. The World Health Organization (WHO), like many other organizations, are advocating for reduction of use of antimicrobials when they are not needed. The COINCIDE-project explores what will happen when the use of colistin in animals is banned in Indonesia. Colistin is a specific antimicrobial that is used as last resort in humans if nothing else works, resistance against this antimicrobial means that resistant disease causing bacteria will have free reign. In animals, colistin has been banned since 2020 and a group of human doctors, veterinarians, anthropologists and DNA researchers will look if less bacteria become resistant. We also want to reduce the colistin use in humans, as it is suspected to be used in humans without good reasons. We will work with farmers and their veterinarians, but also with people in the community and doctors and pharmacies to find out why they are still using colistin and if they can do without. The outcome of the project will help governments, farmers, veterinarians, human doctors, and everybody who really needs colistin, to safeguard this antimicrobial for use only when we cannot do without.

### **Project consortium**

<b>Coordinator</b>	<b>Anis Karuniawati</b>	<b>Faculty of Medicine, Universitas Indonesia</b>	<b>Indonesia</b>
Partner	Juliëtte Severin	Erasmus MC University Medical Center Rotterdam	Netherlands
Partner	Jaap Wagenaar	Utrecht University, Faculty of Veterinary Medicine	Netherlands
Partner	Sunandar Sunandar	Center for Indonesian Veterinary Analytical Studies	Indonesia
Partner	Herman Barkema	University of Calgary	Canada
Partner	Koen Peeters	Institute of Tropical Medicine	Belgium
Partner	Imron Suandy	Directorate of Veterinary Public Health, DG of Livestock and Animal Health Services, MoA-Indonesia	Indonesia

## **FARM-CARE: FARM interventions to Control Antimicrobial Resistance**

The aim of FARM-CARE is to control development and spread of antibiotic resistance in pig farming through four complementary interventions that reduce antibiotic use in pigs and prevent transfer of resistant bacteria to people. The four interventions include a farm practice that reduces stress and antibiotic use in pigs (intervention A); a strategy based on hygiene and disinfection that minimises the risk of transfer of resistant bacteria to farm workers and their families (intervention B); and two sophisticated computer programs enabling farmers and veterinarians to identify stressed piglets predisposed to disease and antibiotic treatment based on their behaviour and bacterial content in faeces, respectively (interventions C and D). We will evaluate the efficacy of these interventions using DNA sequencing methods that allow quantification of antibiotic resistance genes in pig faeces, human faeces, and slurry intended for agricultural use. Additionally, costs and benefits to the farmers and to the society as a whole will be assessed for each intervention. FARM-CARE is a project that requires knowledge and expertise from different disciplines and sectors. This is why the consortium brings together scientists and professionals with different backgrounds. Altogether the consortium comprises 3 universities, 3 public organisations (1 hospital, 1 research institute and 1 national agriculture and food authority) and 1 large non-profit company in representation of 5 countries (Denmark, Germany, Ireland, United Kingdom and Colombia).

### **Project consortium**

<b>Coordinator</b>	<b>Luca Guardabassi</b>	<b>University of Copenhagen</b>	<b>Denmark</b>
Partner	Melvyn Smith	University of the West England	United Kingdom
Partner	Emma Baxter	Scotland's Rural College	United Kingdom
Partner	Chantal Morel	University Hospital Bonn	Germany
Partner	Jesper Larsen	Statens Serum Institut	Denmark
Partner	Edgar Garcia Manzanilla	The Irish Agriculture and Food Development	Ireland
Partner	Corina Zambrano	Colombian Association of Pork Farmers	Colombia

## **SNAP ONE: Strengthening implementation of National Action Plans through a One Health AMR full economic costing exercise**

Antibiotic resistance costs lives and money. Yet if we don't have a good grasp of the numbers we will never know where it lies in terms of our other national priorities. In Africa we have especially little evidence on how people, animals, and the environment are affected by it. So those who make decisions do not see it as a particular problem - and, as a consequence, those who hold the purse strings in government do not fund the necessary efforts to combat antibiotic resistance. This project will estimate the full economic burden imposed by antibiotic resistance (epidemiological and financial) in Malawi and Zambia in order to fill this evidence gap. Findings from this work should help enhance political will to take greater action. It will also allow more informed decisions to be made about how best to tackle antibiotic resistance locally by calculating the important cost-related numbers that allow different strategies to be compared. Crucially this project will bring together the key people needed to make real and further progress on this issue each of these two countries. And, if successful, Malawi and Zambia will be setting the example for how to combat antibiotic resistance in other parts of Africa.

### **Project consortium**

<b>Coordinator</b>	<b>Chantal Morel</b>	<b>University Hospital Bonn</b>	<b>Germany</b>
Partner	Herman Goosens	University of Antwerp	Belgium
Partner	Finola Leonard	University College Dublin	Ireland
Partner	Chisomo Msefula	University of Malawi, College of Medicine	Malawi
Partner	Luigia Scudeller	Azienda Ospedaliero-Universitaria di Bologna	Italy
Partner	Lloyd Matowe	Eden University	Zambia

## **DESIGN: Designing One Health Governance for Antimicrobial Stewardship Interventions**

AMR is a problem of the global commons, whose resolution depends on coordination of collective global strategy. Addressing the challenges posed by AMR through a One Health approach relies on inter-sectoral policy coordination - across public health, agricultural, and environmental sectors - internationally, making stewardship complex, necessitating new approaches to policy development. Our research seeks to address these issues through a comparative analysis that will identify innovative international policy, legal and regulatory approaches in high-, medium- and low-income case study countries. We will apply systems analysis to understand the complex contingencies inherent in local and international contexts in order to clarify the manner in which national systems could better support the coordinated efforts of public health, agricultural, environmental sectors, professional groups, public and private sectors, and civil society to secure their cooperation. Design thinking workshops will leverage evidence emerging from the systems analysis by engaging governments and local stakeholders. Workshops will identify the incentives that foster a One Health approach to the governance of antibiotic stewardship, including innovative governance approaches that support the development of regional and national policies, regulations and laws to improve the global commons. The findings will be used to advise government, industry, public health and environmental agencies on solutions that foster implementation of a One Health approach to reduce AMR.

### **Project consortium**

<b>Coordinator</b>	<b>Mary E. Wiktorowicz</b>	<b>York University</b>	<b>Canada</b>
Partner	Ria Benko	University of Szeged	Hungary
Partner	John Paget	Netherlands Institute for Health Care Research	Netherlands
Partner	Marion Bordier	Agricultural Research for Development	France
Partner	Alpha Amadou Diallo	Institut Sénégalais de Recherches Agricoles	Senegal
Partner	Marilen Balolong	University of the Philippines	Philippines

### **MISTAR: Microbiota Intervention Strategies Limiting Selection and Transmission of Antibiotic Resistance burden in the One Health domain**

The central aim of MISTAR is to implement and quantify the effect of novel intervention strategies based on the preservation of the “healthy microbiota” to eradicate and control the spread of antimicrobial resistance (AMR). We will do this using a One Health approach that involves hospitalised patients, healthy humans, pets, farm animals and the environment. In MISTAR we will follow three main approaches to control the spread of AMR. (i) Intervene with the gut microbiota either by prioritising potential interventions based of microbiota composition indices/diagnostic tools or by using faecal microbiota transplantation (FMT) to modulate the gut microbiota to reduce and possibly avoid the colonisation of and further infections by multidrug resistance pathogens. (ii) Intervene with airborne dust-bound spread of antibiotic resistant bacteria (ARB) between pets and humans in households, farm animals and hospitalised patients by applying air purifiers to remove these microorganisms from the air. Finally, we will (iii) develop novel innovative intervention approaches aimed at specifically targeting ARB in complex microbial communities, like the intestinal tract and sewage. MISTAR will bring perspectives on novel interventions to reduce the emergence of antibiotic resistance that can readily be integrated into existing organisational structures that are also applicable in low-and-middle income countries, and innovative technologies, which needs investment.

#### **Project consortium**

<b>Coordinator</b>	<b>Fernanda Paganelli</b>	<b>University Medical Centre Utrecht</b>	<b>Netherlands</b>
Partner	Teresa M. Coque	Instituto Ramón y Cajal de Investigación Sanitaria	Spain
Partner	Surbhi Malhotra-Kumar	University of Antwerp	Belgium
Partner	Stineke van Houte	University of Exeter	United Kingdom
Partner	Willem van Schaik	University of Birmingham	United Kingdom
Partner	Alex Bossers	Utrecht University	Netherlands
Partner	Ilana Lopes Baratella da Cunha Camargo	University of São Paulo	Brazil



## **MOB-TARGET: Novel interventions for eliminating one-health mobile antimicrobial resistance genes from human and animal microbiomes**

Many of the most important One Health AMR genes are carried on mobile genetic elements that move between bacterial strains through the process of conjugation. The genetic mobility of these AMR genes allows them to become widely disseminated across species of bacteria, including harmless commensal strains and dangerous pathogen strains, and ecological niches, including humans, farms and the environment. In our project, we will develop a series of novel interventions to combat these mobile resistance genes. First, we will develop novel genetic tools that will destroy plasmids carrying resistance genes and selectively kill AMR bacteria. In many regions of the world, infants are commonly colonised with AMR bacteria, complicating the treatment of dangerous infections, such as neonatal sepsis. We will test the ability of our genetic tools to eradicate AMR from the neonatal microbiome using experiments in mice containing a microbiome that is typical of human infants. Some phage (viruses that infect bacteria) infect and kill bacteria that carry conjugative plasmids. We will test the ability of both phage and novel genetic tools to eliminate AMR from the gut microbiome of chickens. Chickens provide a key source of animal protein (global production is about 120 million tonnes per year), but chickens act as an important source of AMR bacteria that can transfer to humans through food and through the use of chicken manure as a fertiliser. This two pronged approach will allow us to reduce the transmission of AMR to humans and to eliminate AMR from a high risk human population.

### **Project consortium**

<b>Coordinator</b>	<b>Craig MacLean</b>	<b>University of Oxford</b>	<b>United Kingdom</b>
Partner	Michael Brockhurst	University of Manchester	United Kingdom
Partner	Alvaro San Millan	Centro Nacional de Biotecnología	Spain
Partner	Jose Antonio Escudero	Universidad Complutense	Spain
Partner	Bärbel Stecher-Letsch	Max von Pettenkofer-Institute, LMU Munich	Germany
Partner	Didier Mazel	Institut Pasteur	France
Partner	Tao He	Jiangsu Academy of Agricultural Sciences	China

### **Phage-Stop-AMR: Phage Therapy to Reduce AMR *Enterobacteria* Spread from a One Health Perspective**

The spread of multi-drug resistant (MDR) bacteria in food-producing animals including broilers is a global public health concern. Controlling growth of MDR bacteria and limiting the transmission of antimicrobial resistance genes in broilers could be an effective mitigation strategy. To counteract the spread of MDR bacteria among zoonotic pathogens in food-producing animals and reduce the risk of their transmission to humans or the environment, antibiotic use in animal husbandry has to be reduced. Bacteriophage therapy is increasingly accepted as an environmentally-friendly antimicrobial intervention strategy, effective at specifically targeting bacterial pathogens, to prevent the transmission of resistant bacteria from foods to humans and vice versa. We use MDR *Salmonella* and *E. coli* in broilers as a model and will first select the most efficient phage combinations to specifically reduce these bacteria and MDR plasmids in broilers. Using an experimental chicken gut model and farm-level experiments, we will then establish the efficacy of phage formulations as feed additives within a commercial farming context to reduce bacterial numbers and progressively reduce MDR plasmid carriage in broilers. We will test the effect of phage therapy on intestinal parameters of the treated broilers and also on the broiler intestinal microbiome and resistome composition. We will investigate the transmission of AMR plasmids between different *Enterobacteria* in the broiler gut and improve on-site detection of MDR foodborne pathogens as an early warning system at farm level.

#### **Project consortium**

<b>Coordinator</b>	<b>Ulrich Dobrindt</b>	<b>Westfälische Wilhelms-Universität Münster, Universitätsklinikum Münster</b>	<b>Germany</b>
Partner	Danish Malik	Loughborough University	United Kingdom
Partner	Annamária Szmolka	Veterinary Medical Research Institute	Hungary
Partner	Eliora Ron	Tel Aviv University	Israel
Partner	Clara Marín-Orenga	Universidad Cardenal Herrera - CEU	Spain
Partner	Muna Anjum	Animal and Plant Health Agency	United Kingdom
Partner	Raul Fernandez Lopez	Universidad de Cantabria	Spain

## **COMBAT: COMplex Biofilms and AMR Transmission**

Antimicrobial resistant microorganisms are difficult to treat and lead to increased death and treatment costs. Antibiotic resistance is recognised as a critical threat in both human and animal medicine. Addressing this threat can be challenging when bacteria exist in complicated communities called biofilms. Biofilms form naturally and allow bacteria to survive and persist in diverse environments. Surviving bacteria facilitate the spread of antibiotic resistance genes contributing to the spread of antimicrobial resistance. The COMBAT (COMplex Biofilms and AMR Transmission) project will identify interventions that can actually control complex biofilms in three different environments, thereby decreasing the threat of antimicrobial resistance spreading. COMBAT's approach is based on solid novel laboratory-based biofilm study but also on the application of interventions in the domestic, healthcare and animal environments, providing a direct application to control real "One Health" antibiotic resistance problem.

### **Project consortium**

<b>Coordinator</b>	<b>Jean-Yves Maillard</b>	<b>Cardiff University</b>	<b>United Kingdom</b>
Partner	Mark Fielder	Kingston University London	United Kingdom
Partner	Noora Perkola	Finnish Environment Institute SYKE	Finland
Partner	Dirk Bockmühl	Rhein-Waal-University of Applied Sciences	Germany
Partner	Veljo Kisand	University of Tartu	Estonia
Partner	Seamus Fanning	University College Dublin	Ireland

### **STRESST: Antimicrobial Stewardship in Hospitals, Resistance Selection and Transfer in a One Health Context**

The transfer of antibiotic residues and antibiotic resistant bacteria into the environment and subsequently into animal drinking water may have an effect on the transmission of resistant bacteria and their resistance genes back into the human population. This holistic One Health view of antibiotic resistance is at the heart of our project. We want to determine if hospital-wide antimicrobial stewardship implementation will reduce antibiotics and antibiotic resistant bacteria from entering the environment and if the reduction of antibiotic concentrations will lower the transfer of resistance genes within and between bacteria in the environment and in animals. We will show that hospital wastewater is a hotspot for selection of resistance and pave the way for future, targeted interventions aimed at reducing the amounts of antibiotics released into the environment even further.

#### **Project consortium**

<b>Coordinator</b>	<b>Adam Roberts</b>	<b>Liverpool School of Tropical Medicine</b>	<b>United Kingdom</b>
Partner	Andrew Singer	UK Centre for Ecology and Hydrology	United Kingdom
Partner	Nina Langeland	University of Bergen	Norway
Partner	Michael Brouwer	Wageningen Bioveterinary Research	Netherlands

### **PhageLand: Phage treatment and wetland technology as intervention strategy to prevent dissemination of antibiotic resistance in surface waters**

PhageLand is aimed to develop a novel intervention strategy combining the low-cost and eco-friendly capacity of constructed wetlands with the specificity of bacteriophages (i.e., viruses killing bacteria) to prevent the dissemination of antibiotic resistance from wastewater into surface waters. PhageLand will investigate the prevalence of antibiotic resistant bacterial pathogens (ARB) in low-middle income countries (LMICs) in Eastern Europe, which will be then used as targets for the development of a dedicated phage-based treatment for their specific removal from communal wastes. In parallel, PhageLand will assess: a) the purification capacity of two reference, full-scale constructed wetlands operating in Spain and Moldova in the removal of antibiotic residues, ARB and antibiotic resistance genes; and b) the potential risk associated with the dissemination of these biological pollutants within indigenous bacterial communities and among animals inhabiting constructed wetlands. Finally, PhageLand will develop a pilot plant to scale-up the phage-wetland combined technology to assess its performance under real environmental conditions. This proof-of-concept will be used to demonstrate the efficacy of this nature-based technology for the removal of multidrug-resistant pathogens from communal wastes and to encourage stakeholders for its implementation in wastewater treatment to prevent the dissemination of antimicrobial resistance. The PhageLand technology will be particularly useful in LMICs, where costly and power-demanding treatment plants are difficult to set up.

#### **Project consortium**

<b>Coordinator</b>	<b>Carles Borrego</b>	<b>Catalan Institute for Water Research</b>	<b>Spain</b>
Partner	Lukasz Dziewit	University of Warsaw	Poland
Partner	Malgorzata Grzesiuk-Bieniek	Warsaw University of Life Sciences	Poland
Partner	Rob Lavigne	KU Leuven	Belgium
Partner	Evelien Adriaenssens	Quadram Institute Bioscience	United Kingdom
Partner	David Weissbrodt	Delft University of Technology	Netherlands
Partner	Alina Ferdohleb	Nicolae Testemitanu State University of Medicine and Pharmacy	Moldova

### **ENVIRE: Interventions to control the dynamics of antimicrobial resistance from chickens through the environment**

The overall objective of the project ENVIRE is to contribute to the reduction of antimicrobial resistance in broiler chickens and of the spread from chicken farms to the environment, and ultimately to humans. We will carry out intervention studies, either as an experiment or in chicken farms. We will test, which interventions are most effective and feasible: i) Antibiotic-free raising of chickens, ii) Treatment with medicinal plants as alternative for antibiotics, iii) Vaccination against the bacterium *Escherichia coli*, iv) Application of bacteriophages that infiltrate and destroy bacteria, v) Treatment or long storage of manure, vi) Treatment of farm effluents to remove antibiotics and their residues. Focus will be laid on certain bacteria that are widely distributed, and on certain resistances that can harm human health (e.g. so-called ESBL). A mathematical risk assessment model will be developed and used to assess the effectiveness as well as potential synergistic effects of the interventions, to reduce human exposure via the foodborne, occupational and environmental pathways. Data already available for the participating countries will be included in the model, and new, essential data will be generated within the studies. As a result, specific as well as general interventions will be identified that have the potential to reduce AMR in chicken and in the environment of chicken farms for Europe and Tunisia. To achieve this, six working groups from Germany, France, Lithuania, Poland, and Tunisia, bundle their leading expertise for the respective issue.

#### **Project consortium**

<b>Coordinator</b>	<b>Roswitha Merle</b>	<b>Freie Universität Berlin</b>	<b>Germany</b>
Partner	Lucie Collineau	French Agency for Food, Environmental and Occupational Health & Safety	France
Partner	Mindaugas Malakauskas	Veterinary Academy of Lithuanian University of Health Sciences	Lithuania
Partner	Marta Kuzminska-Bajor	Wroclaw University of Environmental and Life Sciences	Poland
Partner	Wejdene Mansour	University of Sousse	Tunisia
Partner	Tina Kabelitz	Leibniz Institute for Agricultural Engineering and Bioeconomy	Germany

## **ARPHILAKE: Combating Antibiotic Resistance in Philippine Lakes: One Health upstream interventions to reduce the burden**

Antimicrobial resistance (AMR) may lead to more deaths than cancer by 2050. Action is required now to avert this disaster. This study aims to implement key interventions in greater Manila, the Philippines to reduce AMR. Interventions will focus on hospitals, small farms, and the Laguna Lake, one of the largest freshwater lakes in Asia. Better antibiotic use, point of care testing in hospitals and farms, and novel solar-powered wastewater cleaning technologies will be implemented. Their impact will be assessed by state-of-the-art molecular surveillance for antibiotic resistance genes and bacteria in the water before and after interventions. The study will be the most comprehensive and systematic interventions to be introduced in Asia to reduce AMR in lakes.

### **Project consortium**

<b>Coordinator</b>	<b>Dylan Pillai</b>	<b>University of Calgary</b>	<b>Canada</b>
Partner	Maria Pythias Espino	University of the Philippines Diliman	Philippines
Partner	Stefanos Giannakis	Polytechnic University of Madrid	Spain
Partner	Ana Pereira do Vale	University College Dublin	Ireland
Partner	Paul Wigley	University of Liverpool	United Kingdom

**HOTMATS: Targeted removal of ARGs and facultative pathogenic bacteria (FPB) in wastewater from AMR hotspots using modular advanced treatment solutions**

The objective of the project HOTMATS is to design and demonstrate effective and compact solutions for the source-treatment of wastewater emitted from AMR hotspots. The goal is to stop the spread of antimicrobial resistant bacteria (ARB), antibiotic resistance genes (ARG), and other health-critical microorganisms from hotspots to the public sewage network, which currently is one of the major AMR transmission links between the three pillars of One Health. This intervention will unburden the sewage network including wastewater treatment plants from the load of AMR, and hence reduce their release to the environment. The capability of five different treatment principles, including, ozonation (O3), advanced oxidation (AOP), UV-C irradiation, membrane filtration (MF), and antimicrobial Blue light (aBL) will be investigated. A novel treatment unit based on aBL will be designed, and the destruction of ARB/ARGs in contaminated wastewater will be demonstrated. O3, AOP, MF, and UV-C based pilot-reactors will be developed and their effectiveness to destroy ARB/ARGs in concentrated wastewater streams will be assessed at a hospital, nursery homes, and animal facilities. Compared to existing methods, the investigated treatment solutions are more effective, have a lower footprint, and consume less energy and resources, making them attractive options for treatment at AMR hotspots, as retrofits at old building infrastructures, and where space is limited. The socio-economy assessment including the transfer from HIC to LMIC is part of the HOTMATS project by integration partners from LMICs.

**Project consortium**

<b>Coordinator</b>	<b>Thomas Schwartz</b>	<b>Karlsruhe Institute of Technology</b>	<b>Germany</b>
Partner	Carsten Schwermer	Norwegian Institute for Water Research	Norway
Partner	Jaqphet Opintan	University of Ghana	Ghana
Partner	Richard Wulwa	University of Nairobi	Kenya



**PHAGE-EX: Use of phage applications to combat MRSA at the sow-piglet interface to reduce exposure of staff and contamination of the environment**

This project addresses the issue of occupational and environmental exposure to livestock-associated MRSA in pig farms. Using bacterial phages, we will try to reduce the transmission of MRSA from sows to their piglets during the nursing phase. Specific phage cocktails will be designed using several phages to control MRSA on the skin of sows and in their environment. This is done to produce MRSA negative piglets in herds despite having positive sows. A reduction of MRSA in the piglets is expected to contribute to the reduction of MRSA in the whole pig production pyramid. This in turn will reduce the exposure of people working on pig farms and at slaughterhouses to this kind of MRSA. In regions with intensive pig husbandry, livestock associated MRSA may contribute substantially to the overall burden of MRSA in the hospital sector. We aim to reduce this burden. At the same time we will study potential side effects of the use of phages in pigs on the bacterial community living on pigs, in their environment and in aerosols found in pig stables. We will study changes to this community and will also study the persistence of the bacterial phages in the bacterial community and the environment. Finally we will model the effect of the use of the phages on the transmission of the resistant bacteria within the herds, between herds and to the public health system.

**Project consortium**

<b>Coordinator</b>	<b>Bernd-Alois Tenhagen</b>	<b>German Federal Institute for Risk Assessment</b>	<b>Germany</b>
Partner	Udo Jäckel	Federal Institute for Occupational Safety and Health	Germany
Partner	Thomas Rosendal	National Veterinary Institute, Sweden	Sweden
Partner	Kyrre Kausrud	Norwegian Veterinary Institute	Norway
Partner	Annemarie Käsbohrer	University of Veterinary Medicine	Austria

# Annex A. Agenda HARISSA projects start up workshop

**Date:** April 28<sup>th</sup>, 2022

**Time:** 9:30 – 17:10 CET

**Location:** online – Zoom

Time	Topic	Speaker	Supporting document
9:15 – 9:30	Opening of the meeting		
9:30 – 9:35	Welcome	Kris Pelleboer, ZonMw	
9:35 – 9:40	JPIAMR introduction	Anouk Warmerdam, ZonMw	
9:40 – 9:55	Presentation of the Call	Séverine Olivier, ANR	
9:55 – 10:10	Reporting timeline and responsibilities	Laura Plant, JPIAMR	
<b>Session 1</b>			
Chaired by Ghada Zoubiane (ICARS)			
10:10 – 11:00	Presentations of projects, 10' each 1. STARS-TAP 2. I-CRECT 3. SEFASI 4. ICONIC	Project coordinators	Booklet
11:00 – 11:20	Discussion	All	
11:20 – 11:40	Coffee break		
11:40 – 12:40	Presentations of projects, 10' each 5. CABU-EICO 6. COINCIDE 7. FARM-CARE 8. SNAP ONE 9. DESIGN	Project coordinators	Booklet
12:40 – 13:00	Discussion	All	
13:00 – 14:00	Lunch break		
<b>Session 2</b>			
Chaired by Carolyn Johnson (MRC)			
14:00– 15:00	Presentations of projects, 10' each 10. MISTAR 11. MOB-TARGET 12. Phage-Stop-AMR 13. COMBAT 14. STRESST	Project coordinators	Booklet
15:00 – 15:20	Discussion	All	
15:20 – 15:40	Coffee break		
15:40 – 16:40	Presentations of projects, 10' each 15. PhageLand 16. ENVIRE 17. ARPHILAKE 18. HOTMATS 19. PHAGE-EX	Project coordinators	Booklet
16:40 – 17:00	Opportunity for discussion	All	
17:00 – 17:10	Wrap up and ending	Kris Pelleboer, ZonMw	