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Executive Summary

Know where you come from to understand where you are going: a leap into the past for a plunge into the future." Arnaud Callegari

One Health EJP Project Coordinator

Anses

The foundations for the One Health European Joint Programme began in 2004 with the Med-Vet-Net (MVN) project receiving 5 years of funding via the EU Sixth Framework Programme Network of Excellence for the Integrated Research on the Prevention and Control of Zoonoses: the beginning of collaborations between 16 public health, animal health, and food safety institutes in 10 European member states.

Having demonstrated notable success as a Network of Excellence, the legal entity Med-Vet-Net Association was formed under French law in September 2009 on the conclusion of the 2004 project, with the aim of continuing to provide an environment for food safety scientists to share their knowledge and skills, develop collaborative projects and present joint research in and outside the Network.

In 2017, in recognition of the growing need for continuity of cross-sector collaborations in the same area, it was agreed that the Med-Vet-Net Association (MVNA) was mature enough to successfully turn into a large co-funded European project. Seizing the opportunity presented by the Horizon 2020 fund, members of the Association, led by André Jestin from the French Agency for Food, Environment and Occupational Health & Safety, submitted a proposal.

The successful outcome was that, in January 2018, the One Health European Joint Programme (OHEJP) was launched, a unique European network of 43 public institutions and the MVNA, spanning 22 European countries, with involvement by nearly 1600 scientists in the domains of foodborne zoonoses, antimicrobial resistance and emerging threats. At the time, Horizon 2020 was the biggest ever EU Research and Innovation Programme with ambitions to make world-first discoveries and take great ideas born in the laboratory to the market.

As the <u>One Health EJP</u> landmark partnership comes to an end in September 2023, our legacy is clear, having collectively generated scientific results in the field of surveillance, laboratory methods, risk assessment and risk management related to food safety and practical outcomes that can be taken up by stakeholders and other interested parties. The OHEJP created a credible impact via research and educational activities, engaging stakeholders and students alike, addressing the ambitions set out by the Horizon 2020 fund.

With a growing awareness that human health is tightly connected to the health of animals and the environment, the OHEJP is a prime example of a successful Med-Vet collaborative initiative. Historically, disease control has been hampered by divisions between medical and veterinary sciences: this European Joint Programme has made considerable inroads into

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breaking down these silos, building on commonalities, and encouraging transdisciplinary and sustainable collaboration between different health actors, thus strengthening the One Health approach.

The research activities - 24 Joint Research Projects, 6 Joint Integrative Projects, a simulation exercise and 17 PhD projects, short term missions, continuing professional development modules, Summer Schools, webinars and workshops - were proposed by partners in the participating member states to address key concerns with a One Health view. These activities have created numerous, tangible outcomes for exploitation by stakeholders, and, by enabling open access to the considerable knowledge base, surveillance data, and delivered tools, we envisage the uptake by the wider scientific audience and policy makers too.

The OHEJP is a ground-breaking foundation project leading the way for activities and outcomes related to food safety to be continued to be built upon for the <u>sustainability</u> and legacy of our work. This is an important asset for society as a whole, with the potential to make a substantial difference to the quality of life for citizens across Europe and beyond with our outcomes adding to the preparedness of countries for future threats.

With a five-year programme come opportunities and challenges. One big challenge was to disseminate the outcomes in the given timeframe and to fully measure these <u>results</u>. Communication and effective dissemination have been a strong thread throughout the programme and underpinned the OHEJP purpose. With an interpersonal approach of networking and getting to know each other - embracing technology to overcome the challenges of a global pandemic, communicating using a common language, we have created common understanding and built trust. This commonality has enabled a combined effort to highlight our work and, in turn, created a global presence to spread the message about the One Health approach to benefit the health of people, animals, and the environment.

One of the main aims was to continue to bring people together – researchers and policy makers alike – to further strengthen and grow the network initiated by the Med-Vet-Net Network of Excellence, with cross-sector activities linked to the process of prevent-detect-respond, or 'preparedness'. We have addressed common challenges where a combined approach has increased efficiencies and reduced overlaps of research, therefore boosting impacts. Dialogue has also been actively encouraged by our <u>Science to Policy</u> team between scientists, key <u>European agencies</u> and international policy makers.

Complementing the scientific research has been an extensive education and training programme, leveraging the expertise held within the Consortium, and providing PhD students and early career researchers with access to networking and learning from experts within their fields, enhancing the quality

and skills of those involved. We see investing in education and training is fundamental to broadening the future of the One Health scope, increasing the diversity of scientific research.

The OHEJP scope has focused on addressing the domains of foodborne zoonoses, antimicrobial resistance, and emerging threats, as identified in the initial <u>Strategic Research Agenda published in 2018</u>. However, we also recognise environmental health, social sciences, and humanities have a big part to play in the One Health principle and should be included in future collaborations to embrace and build upon a true One Health vision. To this end, an updated <u>Strategic Research and Innovation Agenda</u> (SRIA) was published in 2022.

One of the OHEJP legacies is how we have demonstrated that collaborations between the medical, veterinary, and environmental professions can work. This is needed to tackle emerging cross-sector issues, ultimately improving food security and human, animal and environmental health.

We <u>guide others</u> towards continued initiatives using a One Health approach and encourage further uptake of the instruments and opportunities arising from our <u>outcomes</u>; the MVNA has taken up a key role in sustaining many of the activities and outcomes, including the <u>One Health EJP website</u>.

All those involved in the One Health EJP during its five years should feel extremely proud of the important scientific results achieved, the generated global reach of the One Health message, the knowledge that has been imbibed to future One Health researchers, and the foundations created for future cross-sector collaborations.



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joint Integrative Projects



The One Health EJP Strategic Research Agenda (SRA) proposed six components of the prevention, detection, and response chain needed to deal with foodborne zoonoses, AMR, and emerging threats. Along this so-called integrative strategy matrix six Joint Integrative Projects (JIP) were conducted (Table 1).

established in response to the COVID-19 pandemic to address this new global viral disease threat. The integrative strategy matrix encompasses surveillance programmes; detection/typing methods and protocols; strain collections, reference materials and biobanks; digital infrastructures, including interpretation of surveillance data and surveillance data communication; and finally, prevention and response activities. The activities undertaken in these integrative projects strengthened both the scientific capacity within the partner institutes and the collaborations occurring at the European level now and for the future. The One Health EJP SimEx project was an additional integrative activity that aimed to test the capability, capacity, and interoperability of actors in public health, animal health and food safety in countries to work together to deal with a fictitious foodborne outbreak.

In addition to the five original integrative projects, the COVRIN project was

Table 1 shows the integrative projects together with their associated outputs and outcomes. These scientific achievements and practical methodologies are intended to be used by our stakeholders (ECDC, EFSA, EEA, WOAH, FAO, WHO, EMA, JAMRAI, jpiamr, COMPARE, and EFFORT) and others interested to work following the One Health approach now and in the future.

What has the One Health EJP achieved through its integrative projects?

The JIPs research has involved extensive multi-national and multi-sectoral collaborations, sharing of resources and knowledge in an effort to increase capabilities and a common understanding on interdisciplinary collaborations (i.e., implementing a One Health approach). These JIPs and their associated outcomes will support the continued collaboration amongst actors with increased co-operation on the design and implementation of surveillance activities (i.e., MATRIX), laboratory methods (i.e., OH-HARMONY CAP), reference material and data (i.e., CARE), interpretation of surveillance data (i.e., COVRIN), cross-sector communication (i.e., ORION) and actions (i.e., COHESIVE).

The MATRIX JIP created solutions for European countries to support and advance the implementation of One Health Surveillance (OHS). These solutions, known as the MATRIX Solutions for OHS, are: i) the OH-EpiCap Tool that evaluate the capacities and capabilities for the OHS of a hazard of choice;

INTEGRATIVE STRATEGIC ACTIVITIES	JOINT INTEGRATIVE PROJECT SCIE OUTPUT(S) AND OUTCOME(S)
Design and implementation of surveillance activities	MATRIX: Solutions to support and a One Health surveillance: the OH-EpiCa a roadmap to develop national OHS, manual for OHS Dashboards, guide checklists such as an interactive gui facilitate the development of multi-se OHS frameworks, best-practices to oper cross-sectoral collaborations a guid design, implement, and evaluate off controls within the food safety sector.
	<u>COHESIVE</u> : Pathway analysis of outbody detection.
Laboratory methods	OH-HARMONY-CAP: Diagnostics, lak capabilities, capacities, and interope collection tool.
Reference material and data	CARE: Database of strains and geno quality control analysis in food safety
Interpretation of surveillance data	<u>ORION</u> : Framework for understand information exchange – <u>One Health Secodex</u> .
	COVRIN: Models for the risk assesses SARS-CoV-2.
	<u>COHESIVE</u> : Information system that genomic data and metadata of path from different countries (<u>demo</u>).
Cross sector communication of data	COHESIVE: Risk Analysis System for a FoodChain-Lab web application to t spurious food items; quantitative sh application assessment toolbox; ris assessment Decision Support Tool.
	ORION: Solutions for interoperabilit improve data FAIRness – OHEJP Glo One Health Linked Data Toolbox, He Surveillance Ontology, Food Safety Knowledge Exchange Format.
Action (prevention and response)	<u>COHESIVE</u> : Review on the economic analysis of foodborne zoonoses.

Table 1. Research outputs and outcomes from OHEJP integrative projects in relation to the prevent-detect-response chain, the integrative strategic matrix.



TIFIC	SIMEX PROJECT SCIENTIFIC OUTPUT(S) AND OUTCOME(S)
vance protool, practical nes and e to toral tionalise to cial	SimEx: Foodborne disease outbreak simulation exercise on a national level <i>Salmonella</i> Typhimurium outbreak that involved the food chain and pet feed chain. Practical exercise used the <u>COHESIVE</u> <u>FoodChain-Lab</u> web application.
eak	
oratories ability	<u>SimEx</u> : Foodborne disease outbreak simulation exercise to highlight the importance of harmonisation of data collection and data sharing.
nes for	
g and veillance	SimEx: Foodborne disease outbreak simulation exercise on a Salmonella Typhimurium outbreak. Practical exercise used the <u>COHESIVE Food-Chain-Lab</u> web application and interpreted the findings.
ent of	
tores ogens	
oonoses; ace <u>ny Risk</u>	SimEx: Foodborne disease outbreak simulation exercise facilitated cross-sector discussions on lessons learned from the outbreak investigation and identified the gaps to be addressed to improve coordination in the future (detailed in this <u>publication</u>).
to <u>sary</u> , <u>alth</u>	
	SimEx: Foodborne disease outbreak simulation exercise provided evidence to support the improvement of future foodborne outbreak management strategies (detailed in this <u>publication</u>).

Joint Integrative Projects

ii) roadmap to develop national OHS that countries can use to develop OHS according to their needs and resources; *iii)* a practical manual for OHS Dashboards developed to facilitate the design and implementation of OHS dashboards using open-source tools; *iv)* guidelines and checklists to facilitate the development of multi-sectoral frameworks, operationalise cross-sectoral collaborations and establish official controls for One Health surveillance.



The OH-HARMONY-CAP JIP aimed to develop and produce tools and recommendations on how to harmonise sampling and testing, characterisation of isolates, and data management and harmonised reporting at both the national reference laboratory and the primary diagnostic level across Europe. OH-HARMONY-CAP created three core outputs; these were a OHLab-<u>Cap tool</u>, a survey of food business operators HACCP-based self-control programmes, and criteria for ranking and evaluating laboratory protocols to benefit foodborne sectors (Table 1). These resources, if implemented, may contribute to an improvement in the standardisation and harmonisation of protocols for model organisms.

The <u>CARE</u> JIP was formed out of the need to develop new One Health concepts for proficiency testing, reference materials, and to improve the quality and availability of demographic data as current methods and resources are highly fragmented between member states. CARE created a large reference of well-characterised database reference strains on foodborne pathogens, which was made public; whole genome sequencing of non-clustering clustering and Campylobacter, Listeria monocytogenes and Salmonella isolates; cross -sectorial proficiency tests/external

quality <u>assurance guidance</u>; and a <u>guide</u> for accessing relevant data and models for quantitative microbial risk assessments (*Table 1*). These CARE resources were designed to ensure the accessibility and sustainability of reference materials, facilitate proficiency testing at the European level, and raise awareness among EU authorities about relevant materials for the analysis of microbial risk.

The <u>ORION</u> JIP developed and optimised resources that support the implementation of the One Health paradigm for disease surveillance. One of the project's main output is the OHS Codex: The Knowledge Integration Platform, that integrates a broad spectrum of innovative solutions, resources, and findings in an overarching framework. Among others, the OHS Codex encompasses the One Health Report Annotation Checklist (OH-CRAC), the One Health EIP Glossary, National OHS Report Templates, a OHS Inspiration catalogue, the OH Surveillance Pathway Visualisation, the OH Knowledge Base, the Sequencing for Surveillance (SfS) Handbook and the Health Surveillance Ontology. The Food Safety Knowledge Exchange (FSKX) Format, a format that supports the One Health community in sharing and re-using mathematical models and data analysis procedures, was also developed during the ORION project before being promoted and expanded by the MATRIX project. Several national One Health pilots, such as Campylobacter surveillance systems in Sweden and Denmark, IRIDA in Norway, Sweden and national surveillance system for antimicrobial resistance and Antimicrobial Use (AMU) in Denmark, used ORION solutions, that created direct impact on cross-sector communication, surveillance data exchange, and interpretation. On an international level, the ORION project performed several activities to share knowledge with international stakeholders such as EFSA and ECDC, for example, in dedicated pilot projects. In addition, a number of ORION solutions were integrated into the Surveillance and Information Sharing Operational Tool (SISOT) of WHO/FAO/WOAH.





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Joint Integrative Projects

The <u>COHESIVE</u> JIP aimed to develop sustainable cross-sector approaches with respect to surveillance, assessment, and control of zoonoses at the national and regional level within EU countries and across borders, thus implementing the One Health approach. COHESIVE designed several tools, such as a new version of the <u>FoodChain-Lab</u> web application and risk assessment <u>Decision Support Tool</u> (*Table 1*), to be used in integrated risk analysis systems for emerging zoonoses and foodborne diseases that are applicable across health sectors. The wide variety of COHESIVE resources can be used to facilitate international coordination, improveing the efficiency of joint One Health risk analysis and surveillance for zoonotic pathogens, and benefit pandemic disease preparedness.

The <u>COVRIN</u> JIP was formed during the COVID-19 pandemic to integrate research activities among OHEJP partners. The overall objective of the JIP was to identify the <u>drivers for the emergence</u> and <u>spread</u> of SARS-CoV-2, generate data and build models for the risk assessment of SARS-CoV-2. COVRIN developed a range of tools that <u>reinforce collaboration and integrative activities</u> within the OHEJP (*Table 1*). Overall, COVRIN deliverables can be used in the preparedness of future coronaviruses, the molecular and biological characterisation of SARS-CoV-2, and the <u>surveillance and risk assessment</u> at the animal-human interface for infection, in accordance with the prevent, detect, and respond strategy.



The <u>OHEJP SimEx project</u> was conceptualised under the One Health approach to address a foodborne zoonotic disease outbreak. The overarching objective of the project was to assess the communication and collaboration between public health, animal health and food safety authorities and laboratories within each participating country by providing a table-top exercise that covered a realistic foodborne outbreak at a national level. Between May and September 2022, the two-day exercise was successfully delivered to 255 participants across 11 European countries, which focused on a Salmonella (enterica serotype) Typhimurium outbreak affecting both human and pet food supplies. Overall, this exercise facilitated intersectoral cooperation to find solutions to common issues between sectors and indicated the areas that require further development, improving each country's national preparedness for future outbreaks of diseases.



gaps in knowledge based in One Health surveillance, harmonised procedures, databases, and protocols for the detection and characterisation of common foodborne zoonotic microorganisms (e.g., *Escherichia coli*). The OHEJP also delivered a simulation exercise to propose ways to improve countries' national preparedness for future outbreaks of disease in Europe. These achievements were accomplished through extensive, multi-national and multi-sectoral collaborations amongst OHEJP partners and non-affiliated partners and key stakeholders (i.e., ECDC, EFSA, EEA). Overall, the JIPs outcomes have the potential to benefit sectors within Europe and more globally in the detection, preparedness, and surveillance of foodborne zoonoses, antimicrobial resistance and emerging threats. This programme has demonstrated impact in the One Health arenas of science and policy, with future potential benefits for society and economy.





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Foodborne Zoonoses

Image: Construction of the construc

The Joint Research Projects and PhD projects collaborating across borders and sectors

The JRPs and PhDs have undertaken research in three domains: foodborne zoonoses, antimicrobial resistance, and emerging threats. These JRPs, and, to a lesser extent the PhD projects, have collaborated with multi-national partners and multiple sectors to share knowledge and resources in an effort to break down barriers and increase capabilities in prevention, preparedness, detection, and response of new and old threats across Europe and globally.

The JRPs and PhDs and their associated outcomes will support the continued collaboration among actors with increased cooperation on the design and implementation of surveillance activities (i.e., AIR-SAMPLING), laboratory methods (i.e., FARMED), reference material and data (i.e., PEMbo), interpretation of surveillance data (i.e., ECO-HEN), cross-sector communication (i.e., FED-AMR) and actions (i.e., BIOPIGEE).

Domain: Foodborne Zoonoses

The first domain of scientific research based on the One Health EJP <u>Strategic</u> <u>Research Agenda</u> is foodborne zoonoses.

The domain was made up of 11 JRPs and five PhD projects outlined in *Table 2*. The scientific themes incorporated analytical methods, host-microbe interactions, epidemiology, risk assessment, and interventions to address the ongoing food safety concerns in Europe, including national and international challenges, particularly as a result of the COVID-19 pandemic which disrupted scientific activities of these JRPs. Within the domain of foodborne zoonoses, this led to an increased importance on the development and harmonisation of analytical methods and tools (i.e., next-generation sequencing based methods, *in vitro* and *in vivo* models, risk assessment tools, etc.) for the detection of bacteria, viruses and parasites within the food supply (e.g., protocols, databases, models, etc.). The main scientific outputs and outcomes from each JRP and PhD project are described according to the integrative research matrix (*Table 2*), which addresses the needs of the principal stakeholders' (e.g., ECDC, EFSA, EEA) to dynamically approach the challenges and threats posed by foodborne zoonoses from gaining European impact.

What are Foodborne Zoonoses and why are they included in the One Health EJP?

Foodborne zoonoses are diseases caused by the consumption of food or water contaminated with <u>zoonotic</u> microorganisms (i.e., bacteria, viruses, fungi, parasites, and their toxins), which can lead to illness and in severe cases death. The consumption of animal products (i.e., meat, milk, eggs, etc.) grows with the increasing global population and is subject to consumer

INTEGRATIVE STRATEGIC ACTIVITIES	JOINT RESEARCH PROJECTS SCIENTIF OUTPUT(S) AND OUTCOME(S)
Design and implementation	AIR-SAMPLE: Air filters to detect
of surveillance activities	Campylobacter in broiler houses.
	NOVA: Code to model disease spread a
	explore disease surveillance options.
Laboratory methods	METASTAVA: Guidelines for sequence- metagenomics disease surveillance.
	MedVetKlebs: The ZKIR assay, a Real-Ti PCR method for the detection of <i>Klebsi</i> pneumoniae in environmental samples
	TOXOSOURCES: Harmonised Methods detecting <i>Toxoplasma gondii</i> contamina in fresh produce.
Reference material and data	LISTADAPT: Algorithm for selecting stra explore the diversity of strains circulati Europe.
Interpretation of	ADONIS: Decision making tools and gu
surveillance data	to determine causes and <u>best interven</u> for stagnant human <i>S</i> . Enteritidis infect
	BeONE: Integrative solutions for foodb pathogens surveillance, a <u>One Health</u> Sequencing for Surveillance Handbook creating genomic repositories and <u>Rep</u> Tool.
	DISCOVER: Models and methods for attributing human foodborne infection animal, food, and environment sources
	TOXOSOURCES: Methods to evaluate to relative contribution of different source Toxoplasma gondii infections.
	MedVetKlebs: Multicentric study of Kleip pneumoniae in European food product
Cross sector communication of data	BIOPIGEE: BIOPIGEE Glossary and BIOPIGEE: Information Material for Farming Scholeducation and training resources in pobiosecurity.
	NOVA: Mathematical models for data combination and analysis for One Heal syndromic surveillance systems.
Action (prevention and response)	MoMIR-PPC: Prevention & Control Mea against <u>Salmonella</u> and <u>Campylobacter</u> a poultry production level.
	BIOPIGEE: Biosecurity measures for the cost-effective control and of Salmonella Hepatitis E Virus (HEV) in primary pig production and abattoir.

Table 2. Research outputs and outcomes from the OHEJP projects in relation to the integrative strategic activities

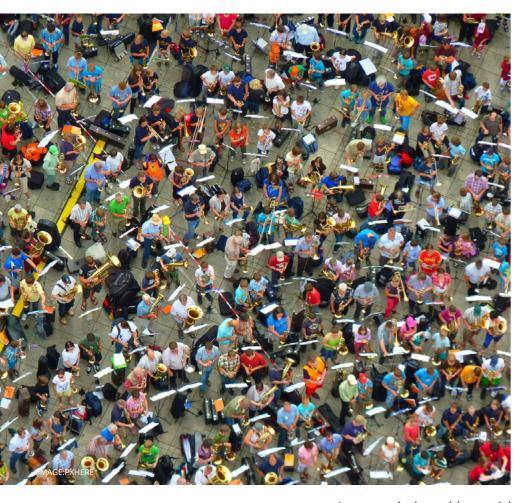




	PHD PROJECT SCIENTIFIC OUTPUT(S) AND OUTCOME(S)
nd	
ased	AptaTrich: A whole-larva systemic evolution of ligands by exponential enrichment (SELEX) method for <i>Trichinella spiralis</i> .
ne la	TRACE: A novel <u>HEV-probe enrichment</u> <u>method</u> for the sequencing of phylogenetically different HEV strains.
or ion	
ns to g in	
lance ons ons.	EnvDis: An environmental and disease model for determining the influence of weather on the incidence of salmonellosis.
rne and r <u>Tree</u>	ToxSauQMRA: Quantitative Microbiological Risk Assessment for the detection of <i>Toxoplasma gondii</i> in pork carcases, sausages, and dry ham.
to	MACE: Model to allow for key players to evaluate interventions to control <u>cystic echinococcosis</u> in resource constrained countries.
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ı	
ures the	MACE: Mathematical model for the surveillance of <u>cystic echinococcosis</u> life cycle.
and	

HEALTHEJP Foodborne Zoonoses





demand, urbanisation, and globalisation. This situation places a higher demand on the food chain and results in intensive farming practises (i.e., mass production and global movement of products), which can lead to an increased risk of farm-to-fork contamination¹ if defective processes are not amended. Contamination of food products can occur at various stages of the food chain (i.e., during production, processing, distribution, preparation, and final consumption) based largely on the health status of the food handlers, and their knowledge of best practises of personal and food hygiene. Despite rigorous strategies to prevent foodborneoutbreaks in Europe, 4,005 foodborne outbreaks were recorded in 2021, which is a 29.8% increase compared to 2020. Because foodborne zoonoses spread through a complex network of countries, food markets, human and veterinary

sectors, it can only be addressed by using a One Health approach. The foodborne zoonoses domain of the OHEJP research aimed to protect human and animal health by reinforcing early detection methodologies, increasing educational resources, and creating an array of models to carry out surveillance on common pathogens (i.e., Campylobacter, Salmonella, Trichinella, Toxoplasma, etc.). EFSA, a key stakeholder within the OHEJP, highlights that controlling the presence of zoonotic microorganisms is one of the most effective ways of reducing the burden of human illness, through a cross-sectoral One Health approach, which through the OHEJP has led to effective surveillance models (i.e., epidemiology), detection, and control and prevention of recurrence strategies (Table 2).

What has the One Health EJP scientific research achieved in the field of Foodborne Zoonoses?

The research undertaken in the domain of foodborne zoonoses has involved surveillance activities, laboratory methods to improve the detection of common zoonotic pathogens, interpretation of surveillance data (i.e., determine the outbreak source), cross-sector communication of surveillance data (i.e., educating key players on biosecruity) and intervention and control, such as biosecurity measures for common zoonotic pathogens. These JRPs and PhD projects and their associated outcomes will help to create trust among public institutions when a cross-border outbreak are managed, and will ensure consistency in the application of techniques across European laboratories and stakeholders.

The approach taken within this OHEIP domain was focused on the developmentof new tools for the surveillance of zoonotic pathogens (i.e., Toxoplasma gondii, Salmonella), the detection of pathogens (i.e., Klebsiella pneumoniae, Trichinella), and the creation of new risk assessments and mathematical models for supporting disease prevention and response, at the national, European, and international levels. The aims of these OHEJP devised methods and tools are to address foodborne zoonoses risks globally, with methods and tools made publicly available for widespread use across public health, animal health, and food safety sectors. A One Health approach was used to ensure standardisation of procedures for the detection, identification, and characterisation of new and ongoing foodborne zoonotic infections in Europe. These strategic activities were supported through transdisciplinary collaboration and alignment between OHEJP partners in the medical, veterinary, and food sectors.

Two JRPs focused on the design and implementation of surveillance activities. The AIR-SAMPLE JRP developed and harmonised sampling and detection methods for Campylobacter in chicken (broiler) houses, by producing protocols for collecting air samples, DNA extraction from filters, and Real-Time Quantitative PCR (qPCR) specifically for Campylobacter. The final guidelines and tool are capable of implementing air-sampling and qPCR to improve detection, allowing the veterinary and food production sectors to confirm the cleanliness of broiler houses before inserting new chicks. In a similar effort, the NOVA JRP created several novel methods to enhance the surveillance and response, adding efficiency and cost-effectiveness across the food chain. More specifically, syndromic surveillance was used to develop and implement tools to advance methods for the real-time and near-real-time dection of early outbreak signals using exisiting survillance sources. In addition, NOVA refined the BfR-developed FoodChain-Lab, by developing a model for a fast recognition of products protentially involved in foodborne outbreaks and intergrated this into the FoodChain-Lab eco-system. The further development of this resource offers public health institutes a route to determine the source of contamination, allowing appropriate prevention strategies to be utilised and to prevent redistribution for human consumption in Europe.

Three foodborne zoonoses JRPs produced laboratory methods to address the role of specific bacteria and parasites, through the detection and characterisation of fresh produce and environmental samples. Specifically, the METASTAVA JRP created guidelines for sequence-based metagenomic



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Foodborne Zoonoses



disease surveillance, proposing criteria and tools for the robust quality assurance of metgenomic work from sample selection for interpretation of results using model pathogens including, hepatitis E virus (HEV), <u>norovirus</u> (NoV), zoonotic pox viruses, antibiotic resistant bacteria and Shigatoxigenic *Escherichia coli* (STEC). METASTAVA also produced a range of resources for SARS-CoV-2, specifically a <u>rapid SARS-CoV-2</u> whole genome sequencing <u>method</u>, which was used during the pandemic to inform decision-making in real-time at the Netherlands National Public Health Department.

With a similar aim, <u>MedVetKlebs</u> JRP created a novel tool, <u>ZKIR qPCR</u> ('*Klebsiella* MALDI-TypeR') which is capable of detecting *Klebsiella* pneumoniae in food products (i.e., chicken, vegetables, etc.). The innovative tool has made it possible to detect all members of the *Klebsiella* pneumoniae complex quickly. MedVetKlebs also created a model capable of defining the most appropriate genetic threshold based on individual outbreak properties. The model has made it possible to broadly determine foodborne or environmental source case clusters or outbreaks. MedVetKlebs research outputs have the potential to be implemented in human and veterinary health services.

The TOXOSOURCES JRP has harmonised methods for detecting *Toxoplasma gondii* contamination in fresh produce, <u>meat products, and environmental</u> <u>pathways</u>. The JRP created a <u>Quantitative Microbiological Risk Assessment</u> (QMRA) model, which allows for the quantitative estimates of the contribution of the main sources and transmission routes of *T. gondii* infections based on <u>improved source attribution models</u> (e.g., partitioning of human illness into sources, such as animal reservoirs or food vehicles). The potential for this model to be implemented at the national, European, and global level were planned, allowing for the development of informed interventions.

One JRP, <u>ListAdapt</u>, focused on deciphering the molecular mechanism of the adaption of the microbial zoonotic *Listeria monocytogenes*, by creating an algorithm for selecting strains to explore the diversity of strains circulating



in the environment. This was achieved by creating a <u>dataset</u> of high-quality genome sequences originating from strains collected in <u>20 European countries</u>, to improve our understanding of *Listeria monocytogenes* ecology and diversity, with the potential to aid in surveillance at the national, European, and global levels.

Five JRPs were involved in the interpretation of surveillance data of foodborne zoonoses. The <u>ADONIS</u> JRP created a <u>multi-criteria decision analysis</u> model to assist with decision making by ranking potential determinants and options for the intervention for the stagnating *S*. Enteritidis trend in Europe according to relative importance. <u>EFSA</u> documented an outbreak of *S*. Enteritidis in Europe in 2021, which resulted in 272 cases, 25 confirmed hospitalisations, and two deaths, highlighting the extremely relevant objectives of the ADONIS project to understand why the *S*. enteritidis prevalence in humans is no longer decreasing in Europe.

The **BeONE** IRP focused on integrative solutions for foodborne pathogen surveillance, combining epidemiological and genomic data (the ReporTree tool), with a specific focus on Listeria monocytogenes, Salmonella enterica, Escherichia coli, and Campylobacter jejuni. BeONE data sets were created for these zoonotic pathogens, to potentiate the use of genetic diversity data necessary for outbreak detection, representing a useful asset in future surveillance- and research-oriented studies. The DiSCoVer JRP followed a similar approach and focused on source attribution, first by creating comprehensive and standardised data sets for foodborne pathogens (i.e., Salmonella, Campylobacter, STEC, and ESBL). These unique multi-country datasets are freely available and provide researchers with novel insights into the epidemiology of foodborne hazards, which may further inform on strategies to deal with future outbreaks in Europe. Within DiSCoVer, recommendations were made based on source attribution models to inform actions on where targeted future control and intervention could be implemented to significantly reduce the burden of human infectious.

TOXOSOURCES produced new data sets on the contribution of the main sources and transmission routes of *Toxoplasma gondii* infections based on source attribution models. Furthermore, a novel typing method was created to improve preparedness to detect the introduction of atypical *T. gondii* strains by import and to trace the infection sources in outbreaks. These resources have the potential to impact on the veterinary and food production sectors now and in the future. Lastly, an additional output of MedVetKlebs was a <u>multicentric study</u> that produced a novel isolation strategy for *Klebsiella pneumoniae*. The study identified that the presence of *K. pneumoniae* in salad and chicken meat was high across the food sector. These findings need to be further explored to define possible control strategies, to understand the degree at which food contamination by *K. pneumoniae* contributes to human infection.



Foodborne Zoonoses





Two JRPs focused on improving cross-sector data communication in the domain of foodborne zoonoses. The <u>BIOPIGEE</u> JRP focused on a range of outputs to benefit a stakeholder, specifically farming students. A <u>BIOPIGEE</u> Information Materials for Farming Schools was developed to evidence good biosecurity practices on pig farms in Europe, accompanied with pictures and research findings to support the effectiveness of these strategies. While, <u>NOVA</u> produced a <u>mathematical model</u> capable of simulating sampling schedules and standard laboratory procedures to inform on the time required to detect emerging infections. Furthermore, the model took in a range of factors, including the location of contamination and consumer food purchase data, which allowed the model to determine which country (i.e., Denmark, Netherlands, UK) had the highest preference for risk based sampling (i.e., sausage/<u>pork chops</u>). The model has practical and cost-saving impacts on how the surveillance of existing and emerging foodborne zoonotic agents is carried out within Europe.

Lastly, two JRPs focused on prevention and response. The MoMIR-PPC JRP achieved four core outcomes, which have the potential to impact on the prevention and control of Salmonella. The identification of the role of animal-animal recontamination was evidenced to be driven in some part by host factors and the gut microbiota. A mathematical model of indirect transmission of bacteria between broilers was developed, assessing the biosecurity-based intervention strategies against Campylobacter and Salmonella. MoMIR-PPC further identified several predictive biomarkers to predict the levels of Salmonella shedding in pigs and chickens in infected animals. Additionally, this project created several preventive measures based on the use of pre- and pro-biotics to prevent salmonellosis, as an alternative to the inappropriate use of antibiotics. The outcomes of the MoMIR-PPC may sustainably improve safe animal food production and trade by providing information and tools leading to on-farm control of bacteria (i.e., Salmonella). Resources developed by the **BIOPIGEE** JRP further aimed to improve the biosecurity on pig farms against Salmonella and Hepatitis E Virus (HEV), through a **BIOPIGEE Glossary**, BIOPIGEE Biosecurity Protocol, BIOPIGEE Checklists, BIOPIGEE Slaughterhouse Guidance Manual, and the BIOPIGEE Cost-effectiveness Support Tool. These resources were created with users in mind, ensuring that these tools could be used by farming students, individual farmers, veterinarians, researchers, policymakers, and industry stakeholders, improving the general knowledge of biosecurity by breaking down knowledge barriers.

Further foodborne Zoonoses research was carried out by five co-funded PhD projects. The <u>AptaTrich</u> PhD produced a whole-larva SELEX method (i.e., a technique by which random libraries of DNA can be screened for selection using targets and can then be amplified by PCR), which can be used to isolate specific <u>aptamers</u> specific for the muscle larvae of *T. spiralis*. This method has the potential to enable specific and early detection in both humans and

pigs from the diagnostic testing and monitoring of *Trichinella*. The <u>TRACE</u> PhD developed a novel Hepatitis E (HEV)-probe enrichment set that uses a <u>probe</u> <u>capture enrichment</u> processes and <u>shotgun metagenomic sequencing</u>. HEV is a globally reaching virus, which is estimated to cause ~ 20 million infections worldwide, with 44,000 deaths reported globally in 2015 by <u>WHO</u>. Therefore, the method may prove to be useful throughout Europe and globally to determine the HEV transmission in Europe and prevent the consumption of raw or undercooked pork products contaminated with HEV at the source of infection.

A further two PhD projects focused on interpretation of surveillance data. The <u>EnvDis</u> PhD created an environmental and disease model to investigate the influence of weather on the incidence of <u>salmonellosis</u>. The <u>model</u> focused on potential influences on bacterial growth at the final stage of the food chain, relevant for human consumption in the UK and the Netherlands. The development of an evidence-based surveillance model has provided information on how changes in environmental factors influence foodborne zoonoses. Similarly, the <u>ToxSauQMRA</u> PhD created a quantitative microbiological risk assessment model on the persistence of *Toxoplasma gondii* in pork carcases, sausages, and dry ham. The novel <u>QMRA model</u> will provide an effective tool in the development of preventive strategies against *T. gondii* in the European food chain.

Finally, one PhD had a multi-pronged approach, for the interpretation of surveillance data and action (prevention and response). The MACE PhD produced a mathematical model for the economic evaluation of cystic echinococcosis (CE) control and elimination. The model captures aspects of CE life cycle and host interactions, allowing for the evaluation of intervention strategies in resource-constrained settings. The development of this novel model contributes to providing insights on the effectiveness of strategies in reducing disease prevalence and assisting evidence-based decision making for CE management.

In summary, the research undertaken in the domain of foodborne zoonoses has successfully addressed the strategic goals of the OHEJP, by addressing foodborne zoonotic pathogens using the One Health approach. This has been achieved through extensive, multi-disciplinary collaborations among public health, animal health and food safety sectors (i.e., expertise, data and resource sharing) amongst EJP partners, non-affiliated partners, and key stakeholders (i.e., EFSA, EEA). The methods, tools, and resources created under this domain have the potential to be utilised during surveillance activities, in laboratory settings, and for preventative actions against foodborne disease outbreaks. Collectively, the outputs and outcomes from these JRPs and PhD projects have strengthened the scientific capacity within the project partners. While ensuring a strong emphasis on contributing to the prevention, preparedness, detection, and response of new and old foodborne zoonotic threats across Europe and globally.



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Domain: Antimicrobial Resistance

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The second domain of scientific research based on the One Health EJP <u>Strategic Research Agenda</u> is Antimicrobial Resistance (AMR). The domain includes seven JRPs and nine PhD projects, as listed in *Table 3*, with a focus on sustainability and the needs of the main One Health EJP stakeholders - including, but not restricted to ECDC, EFSA, DG HEALTH and DG AGRI.

A list of the main scientific outputs and outcomes have been established for AMR projects, comprising harmonised protocols, databases, tools, and recommendations, which are arranged according to their <u>integrative strategic</u> <u>activity</u>. These activities address analytical methods (laboratory methods and reference material and data), epidemiology (interpretation of surveillance data), risk assessment (interpretation of surveillance data) and intervention (cross-sector communication of data).

What is antimicrobial resistance?

AMR occurs when microorganisms (i.e., bacteria, viruses, fungi, and parasites) evolve to resist a substance that would normally stop their growth or kill them. As a result, this resistance means it is becoming more difficult to find efficient treatment for a growing number of infections. AMR increases the risk of disease spread and serious illness, such as sepsis and, if not addressed, would significantly increase the risks associated with key medical procedures (O'Neill, 2016; WHO – Antimicrobial resistance Key facts).

Considered a silent pandemic, AMR is a global One Health problem and has been recognised by the World Health Organisation (WHO) as 'one of the most urgent health threats of our time'. With 1.27 million deaths directly attributed to antibiotic-resistant bacterial infections in 2019¹, AMR is a worldwide problem and has significant economic impact on European health care systems, into the billions (\in) (European Commission – AMR: a major European and Global challenge, 2020). This issue is projected to rise, causing 10 million deaths annually and costing 100 trillion US Dollars by 2050² if not addressed.

Because AMR organisms can be transmitted between people and animals (and *vice versa*), through the environment or from food origin³, AMR can only be tackled using a One Health approach.

Murray *et al*, 2022
<u>O'Neill, 2016</u>
<u>Woolhouse and Ward, 2013</u>
<u>McEwen & Collignon, 2018</u>;
<u>Holmes *et al*, 2016</u>

AMR is a natural evolutionary trait of all microorganisms which is accelerated by several factors such as the misuse and overuse of antimicrobials in human and veterinary medicine, poor infectious diseases prevention and control measures in healthcare facilities and farms, <u>a lack of access to</u> <u>sanitation</u>, hygiene, and medicines, and the use of heavy metals and biocides in agriculture⁴. The OHEJP scientific strategy included research on this growing threat by looking at the factors affecting transmission

INTEGRATIVE STRATEGIC ACTIVITIES	JOINT RESEARCH PROJECT SCIENTIFIC OUTPUT(S) AND OUTCOME(S)
Laboratory methods	IMPART: Updated and improved detection
, i i i i i i i i i i i i i i i i i i i	protocols for AMR Enterobacterales. New ECOF
	for veterinary antibiotics. New rapid diagnostic
	AMR in Clostridium difficile.
	FARMED: Detection and Characterisation of AM
	pathogens and genetically modified microorganis
	using long-read <u>metagenomics</u> .
	WORLDCOM: Portable nucleic acid diagnostics workstation and assays for the detection of AM
	biomarkers for on-site AMR detection.
	FULL-FORCE: lab protocols for the creation of lo
	read sequencing dataset. Open source
	bioinformatics pipeline for automated analyses
	sequencing data and plasmid assembly: the Fu
	Force Plasmid Assembler
	FED-AMR: Harmonised protocols for C. difficile
	collection and isolation in animal, food and
	environmental samples.
Reference material	ARDIG: Collection of large number of genomes that
and data	be used as reference material for AMR confirmation
	WORLDCOM: reference database of sequences
	from currently circulating AMR pathogenic stra
Interpretation of	ARDIG: Comparison between antimicrobial
surveillance data	usage and AMR data to improve AMR surveillance
	EULL-FORCE: Data on plasmid structure and
	variability of drug resistant organisms.
	RaDAR: COMPASS a large curated database of A
	plasmids from a range of different bacterial
	species and sources.

Table 3. Research outputs and outcomes from the Antimicrobial Resistance OHEJP projects in relation to the integrative strategic activity





	PHD PROJECT SCIENTIFIC OUTPUT(S) AND OUTCOME(S)
<u>Fs</u> s for	LIN-RES: Molecular tool for the detection of AMR genes. Pipelines for the automatic analysis of Next-generation DNA sequencing data for Enterococci and Staphylococci.
R, ims,	VIMOGUT: Semi-automated <i>in vitro</i> chicken gut model.
<u>R</u>	<u>Codes4strains</u> : Innovative genomic nomenclature and typing approach, called <u>cgLIN codes</u> , for <i>Klebsiella pneumoniae</i> .
ong- s of L	<u>UDoFRiC</u> : Model systems to study interactions between fluoroquinolone resistant <i>Campylobacter</i> and chicken.
	KENTUCKY: Construction of <u>reporter</u> plasmids and fluorescent recipient strain for the study of AMR transfer dynamics in <i>S</i> . Kentucky.
	METAPRO: Method of detection of the <i>npmA</i> gene (AMR) reservoirs.
can 1.	LIN-RES: Collection of linezolid resistant bacteria, with their genomes and AMR profiles.
ns.	<u>VIMOGUT</u> : Data on the <u>microbiota composition</u> and diversity of broiler chicken colonised by AMR <u>Escherichia coli.</u>
	<u>Codes4strains</u> : Identification and characterisation of a new species of <i>Corynebacterium</i> : <u><i>C. rouxii</i></u> .
	<u>HME-AMR</u> : Collection of AMR Enterobacterales isolated from soil, spinach, and bovine milk filters samples collected from areas with high and low zinc concentrations.
	WILBR: Collection of pig and gull faeces from a low antimicrobial usage pig farm. Collection of <i>E. coli</i> isolated from these samples, with their AMR profiles.
	ECO-HEN: Collection of <i>E. coli</i> isolated from a commercial layer (egg production) farm with low antimicrobial usage and their phenotypic and genotypic AMR characterisation.
<u>.</u>	LIN-RES: Identification of a large reservoir of Ente- rococci carrying linezolid resistance genes in food producing animals. Data on <u>colistin-resistant <i>E. coli</i></u> .
	<u>UDoFRiC</u> : Trend of fluoroquinolone resistance in <i>Campylobacter</i> derived from UK broiler chickens over 25-years.
MR	<u>HME-AMR</u> : Scoping <u>literature review</u> on the impact of heavy metals on AMR in the primary food production environment.
	METAPRO: Metagenomics study on Spanish samples from human, animal and environment.
	WILBR: Comparison of AMR and multi-drug resistant (MDR) <i>E. coli</i> strains isolated from different host species.
	ECO-HEN: Identification and characterisation of the AMR determinants and plasmids carried by the isolated <i>E</i> coli

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of AMR and how to curb them. The OHEJP research on AMR contributed to protect all pillars of health and harmonise approaches for more sustainable ways to keep antimicrobials working and improve antimicrobial stewardship. It has successfully delivered project outputs and outcomes to improve the detection, prevention, and control.

What has the One Health EJP AMR scientific research achieved?

Much of the OHEJP funded research on AMR has involved improving upon, or developing new laboratory methods for the detection, identification, and characterisation of AMR determinants. This work also included the harmonisation and standardisation of reference methods, material, and data as well as diagnostic tests, and bioinformatics tools. Some of the research projects also investigated the transmission mechanisms of AMR, its epidemiology and its association with antimicrobial usage or heavy metals use in agriculture. These projects' outcomes contribute to ensure consistency in the detection, prediction, and surveillance of AMR across laboratories in Europe. The OHEJP-devised solutions can be widely applied across public health, animal health and food safety sectors, creating a standardised and harmonised approach and supporting transdisciplinary collaboration.

Five of the OHEIP IRPs worked to advance detection methods and reference databases, to improve AMR surveillance and help monitoring the emergence of new types of AMR. More specifically, the IMPART JRP worked in close cooperation with the European Committee on Antimicrobial Susceptibility Testing (EUCAST), to establish new epidemiological cut-off values (ECOFFS) for animal pathogens, that are available on the EUCAST website. IMPART also built and tested harmonised protocols for the isolation of acquired colistin-resistant Enterobacterales and for the monitoring of carbapenem-resistant Enterobacterales from food producing animals and food products; and developed a robust and simple method to test the antimicrobial susceptibility of *Clostridium difficile* strains. These protocols could be of interest for EFSA and the EU Reference Laboratory for AMR (EURL-AR). With the similar aim to improve AMR surveillance in Europe, the WORLDCOM JRP developed a portable nucleic acid diagnostics workstation and assays for the detection of AMR biomarkers from environmental water and pig faecal samples, for use in a laboratory setting and for on-site diagnostics. A reference database of sequences from currently circulating AMR pathogenic strains was also generated during the WORLDCOM project and could be used for further comparative genomics and data analyses.

2021 6 Kirstahler *et al.*, 2021; Teudt *et al.*, 2022 7 Nunez *et al.*, 2022; Storey *et al.*, 2022; Savin *et al.*, 2021; Massot et al., 2020; Patino-Navarrete *et al.*, 2020; Gay *et al.*, 2019 8 Getino *et al.*, 2022; Thomson *et al.*, 2022; Juraschek *et al.*, 2021; Brouwer *et al.*, 2020; Duggett *et al.*, 2020; Rodriguez-Rubio *et al.*,

2020; Brouwer et al., 2019

<u>D'aes et al., 2022; Buytaers et al.,</u>

As part of the <u>FARMED</u> JRP, European institutes validated and implemented protocols for long-read <u>metagenomics</u> and <u>resistome</u> sequencing. This technology allowed the detection and characterisation of genetically modified microorganisms in microbial fermentation products and has the potential to rapidly monitor AMR and pathogens in many different environments⁵.

The <u>FULL-FORCE</u> JRP also worked towards improving AMR surveillance by working on methodologies and tools for <u>Mobile Genetic Elements</u> (such as plasmids carrying AMR determinants) typing. FULL-FORCE constructed and benchmarked an open source <u>bioinformatics</u> pipeline, the <u>Full Force Plasmid</u> Assembler, that can be readily implemented in public health and veterinary labs. FULL-FORCE produced lab protocols for the creation of <u>long-read</u> sequencing datasets that were applied to a variety of study cases; such as the study of AMR in sewage water⁶, the surveillance of <u>multi-drug resistance in</u> *Salmonella enterica* serovar Infantis and the clinical relevance of <u>*E. coli* isolates</u> from poultry and pig slaughterhouses in Germany.

The ARDIG JRP studied the dynamics of AMR between humans, animals, food, and the environment, by performing extensive comparative genomics studies on AMR bacteria from different sources⁷ and providing an important overview into the types of AMR plasmids commonly circulating at the interface between human, animal and environmental health⁸. ARDIG also compared antimicrobial usage and AMR data in the human and livestock sectors, to assess the effectiveness of AMR stewardship measures. ARDIG's recommendations to improve AMR surveillance strategies were disseminated to experts in the field, from EFSA, EMA and ECDC and other European projects.



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Douarre et al., 2020

Two further JRPs focused on the attribution of AMR sources and the study of AMR transmission between the pillars of One Health. The RaDAR JRP investigated the contribution of animal and environmental sources to the public health burden of AMR. A large database of AMR plasmids from a range of different bacterial species and sources, COMPASS, has been created and curated by RaDAR⁹ and can be used for the study of plasmids' transmission routes. RaDAR also produced AMR risk assessment models for different food chains, such as the likelihood of AMR *E. coli* in slaughter-aged pigs, and built an infrastructure for exchanging and annotating such models. Finally, RaDAR designed and validated a mathematical model that has been applied to AMR *E. coli*, for source attribution and for modelling their persistence during food preparation.

Meanwhile, the <u>FED-AMR</u> JRP studied the dissemination of AMR in the environment and food/feed chain. Harmonised protocols for *Clostridioides difficile* isolation allowed to study *C. difficile* transmission between human and companion animals, investigate its airborne dissemination, and assess its transmission dynamics in a farm environment. FED-AMR also conducted a study of <u>bacteria at the human/animal/environment interface</u>, that suggested an AMR transmission chain between pig production and farm related environments through free extracellular DNA. Finally, FED-AMR created protocols for the systematic review of <u>factors influencing the</u> prevalence of AMR in the environment. The results of this project could help improve the surveillance of AMR in farm related environments and agricultural soils, as well as impact on strategies to upgrade wastewater treatment plants.

Two of the 17 OHEIP PhD projects worked on AMR detection methods. The LIN-RES PhD developed a molecular test (AMR-ARRAY), that can detect many resistance genes at the same time and showed very good performance. In parallel, a study carried out on colistin-resistant E. coli from food-producing animals identified the AMR genes associated with colistin resistance. Finally, linezolid resistance surveillance, carried out in Belgium in 2019, revealed a large reservoir of Enterococci carrying linezolid resistance genes in food producing animals. These key results were shared with Belgian institutions (FASFC, FAMHP, AMCRA) and European institutions (EURL-AR, EFSA and ECDC); with the EURL-AR planning to make a survey to assess the interest and feasibility of conducting linezolid selective monitoring in the other EU member states. With a similar aim of improving AMR surveillance, the METAPRO PhD focused on the application of a metagenomics approach for the study of resistance to next generation aminoglycosides. The results showed that the enzyme npmA, conferring resistance to all known aminoglycosides, is found in both humans and animals in high prevalence and is spread worldwide. A detection method (single cell genomics) for npmA was developed to be used in environmental samples. Aminoglycosides being currently a critical component of the antibacterial arsenal due to their broad

spectrum of activity and rapid action, it is important to identify and survey resistance to this class of antibiotics.

Five of the PhD projects focused on the study of AMR transmission, trends and dynamics in different environments and using different model organisms. The <u>VIMOGUT</u> PhD studied the role of the chicken gut microbiota in the spread of AMR genes in the environment. The project uncovered that the <u>colonisation of the chicken gut microbiota by AMR *E. coli* is associated</u>

with modifications in microbiota's composition. An *invitro* chicken caecal model has also been developed and optimised, to be used as a research tool to explore microbiota -based strategies to reduce the spread of AMR genes. These results have been shared with the Dutch Ministry of Agriculture, Nature and Food Quality.

With a similar aim, the KENTUCKY PhD investigated the use of various genetic engineering techniques to visualise AMR transfer dynamics. Salmonella enterica serovar Kentucky (S. Kentucky), a common causative agent of gastroenteritis in humans strongly associated with AMR has been chosen as a model organism. A <u>reporter</u> plasmid and a fluorescent recipient strain have been successfully constructed, to visualise in real time the transfer of the AMR carrying plasmid. Understanding better the molecular mechanisms behind the AMR genes' transfer has the potential to improve AMR surveillance.



The <u>WILBR</u> PhD explored the likelihood of wild birds as a vector of AMR to farms. <u>Whole genome sequencing</u> was performed on large collection of pig and gull faecal samples collected on a low antimicrobial usage pig farm. The results highlighted the presence of multi-drug resistant (MDR) bacteria in both pig and gull isolates across multiple timepoints, suggesting that wild birds are contributing to the persistence of MDR bacteria in the pig populations, even in the absence of the selective pressure of antimicrobials in the

Antimicrobial Resistance





farm. This work has been shared with the <u>Veterinary Medicines</u> <u>Directorate</u>, an executive agency of the Department of Environment, Food and Rural Affairs (<u>Defra</u>) within the UK Government.

Meanwhile, the UDoFRiC PhD investigated fluoroquinolone resistance in UK broiler chicken (meat production) flocks. The project collated UK national surveillance data from the Animal and Plant Health Agency (APHA) archives (1995 - 2020) and identified significant trends in fluoroquinolone resistance in Campylobacter strains isolated from broiler chicken. An in vitro study provided insight into the ability of fluoroquinolone-resistant Campylobacter mutants to pass not only within a broiler flock but to humans through contaminated food produce. The ECO-HEN PhD focused on the dynamics of AMR in E. coli from a commercial layer farm (egg production) where antibiotics were sparsely used. Whole genome sequencing was performed on a large collection of E. coli isolates,

identifying around 30 AMR determinants and multi-resistance regions. The study of the <u>flow of AMR determinants in the full laying hen production cycle</u> identified the predominant AMR genes and highlighted the importance of including <u>commensal</u> bacteria in AMR surveillance.

The <u>Codes4strains</u> PhD focused on the detection, identification, and <u>epidemiology</u> of *Klebsiella pneumoniae*, one of the most concerning multi -resistant bacteria, and *Corynebacterium diphtheriae*, which causes diphtheria. The PhD project identified and successfully identified and characterised a new species, *C. rouxii*; and contributed to epidemiology studies of diphtheria in different regions of the world, from animal and human clinical sources⁶. <u>DIPHTOSCAN</u>, a <u>genotyping</u> bioinformatics tool designed by Codes4strains, will advance the genomic epidemiology of *C. diphtheriae*, the clinical management of patients and knowledge on the links between animal and human diphtheria cases. Codes4strains also developed a new genome-based

approach for classification and nomenclature of bacterial strains, called cgLIN codes, that will endow surveillance networks with the capacity to efficiently monitor and control the emergence of bacterial sub lineages of high public health relevance.

Finally, the <u>HME-AMR</u> PhD project studied the role of heavy metals as a selective pressure for AMR in the primary food production environment. <u>A literature review</u> showed a clear link between heavy metals and AMR in the primary food production environment, with heavy metals facilitating the dissemination of AMR genes. Field-based studies conducted on soil, spinach samples, and bovine milk filters collected from areas with high and low zinc concentrations demonstrated that primary food production environments can harbour clinically relevant AMR Enterobacterales. Findings of this work will contribute to meeting the objectives of <u>Ireland's Second National Action Plan on Antimicrobial Resistance</u>, and to the <u>European Antimicrobial Resistance</u> <u>Surveillance Network (EARS-Net)</u>.

In summary, the JRPs and PhD projects under the AMR domain have successfully created harmonised detection methods, references databases and bioinformatics tools as well as gathered new evidence on AMR transmissionand dynamics. These outcomes can be used to advance AMR surveillance and control measures. This has been achieved using a One Health approach, thanks to interdisciplinary collaborations among partner institutions from the public health, veterinary and food sectors across Europe. A wide range of stakeholders have already taken interest to apply OHEJP devised tools to their AMR surveillance activities. Overall, the project outcomes have the potential to improve the detection, prediction, and surveillance of AMR across Europe in the future.



6 Hennart et al., 2020; Badell et al., 2021; Guglielmini et al., 2021; Hennart et al., 2023; Museux et al., 2023; Tessier et al., 2023

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Emerging Threats



Domain: Emerging Threats

The third domain of scientific research based on the One Health EJP <u>Strategic Research Agenda</u> is emerging threats. This domain includes six JRPs and two PhD Projects, as listed in *Table 4*.

The scientific themes (e.g., analytical methods, host-microbe interaction, epidemiology, risk assessment, and intervention) integrated into these projects evolved over time in response to the changing trends in One Health research and national priorities of the OHEJP partners, particularly in response to the COVID-19 pandemic. Within the emerging threats domain, this led to the increased importance for the development of analytical methods and tools for the early detection and identification of pathogens. The main scientific outputs and outcomes (i.e., protocols, databases, models, and other tools) from each project are described according to their integrative research activity (*Table 4*), which address the principal stakeholders' needs to the challenges posed by emerging threats for gaining optimal European impact.

What are Emerging Threats and why are they included in the One Health EJP?

Infections that are transmitted directly or indirectly between animals and humans (zoonoses) lead to diseases, which pose major risks to public health. Additionally, reverse zoonoses are infections that are transmissible from humans to animals, potentially threatening the health of animal populations. Zoonoses can be caused by a variety of infectious agents, including viruses, bacteria, parasites, fungi, and prions. Around 60% of known human infectious diseases and 75% of emerging infectious diseases are zoonotic¹; thus, zoonotic infectious diseases pose an important One Health issue. The emerging threats domain of the OHEJP research aimed to tackle the global health challenge of emerging and re-emerging zoonoses, defined as newly appearing in a population or have existed previously but are rapidly increasing in incidence or geographical range (WHO). These emerging threats can be caused by known zoonotic pathogens (e.g., Mycobacterium bovis, Brucella canis) or by unknown or previously undetected zoonotic pathogens (e.g., Marburg virus, Severe Acute Respiratory Syndrome Coronavirus 2: SARS-CoV-2). An abundance of societal and environmental factors influence the emergence/re-emergence of zoonoses, such as land use changes (e.g., agriculture, urbanisation), population changes, microbial and industrial pollution, climate change (e.g., increased mean temperature), wildlife trade (e.g., introduction of non-native species), and biodiversity loss².

Understanding how these factors affect the transmission of zoonotic pathogens between humans and animals and identifying ways to reduce the infection risks are essential. Hence, the OHEJP scientific strategy included research on emerging threats, focussing primarily on threats emerging since 2017 with a suspected zoonotic potential. The scope of this research

INTEGRATIVE STRATEGIC ACTIVITIES	JOINT RESEARCH PROJECT SCIENTIFIC OUTPUT(S) AND OUTCOME(S)	PHD PROJECT SCIENTIFIC OUTPUT(S) AND OUTCOME(S)
Design and implementation of surveillance activities		DESIRE: Development of an evidence-based surveillance for emerging rat-borne zoonoses in changing environments, using specific metagenomic tools in microbiome- profiling techniques. Evidence of <u>urban</u> greening influence on rat-borne zoonotic disease hazard.
Laboratory methods	<u>TOX-Detect</u> : <u>Database</u> of protein profiles of foodborne toxigenic bacteria.	<u>PEMbo</u> : Genomic analyses on a panel of <i>Mycobacterium bovis</i> strains in France, with key <u>publication</u> .
	MAD-Vir: Tool to detect known viruses and discover new viruses.	
	TELE-Vir: Portable Point Of Incidence (POI) toolbox, consisting of the INSaFLU-TELEVIR platform and the POI protocol for identification and characterisation of emerging virus threats.	
	IDEMBRU: Toolkits for the rapid detection/ identification of emerging <i>Brucella</i> threats.	
	MEmE: Detection tools standardisation and data collection on <i>Echinococcus multilocularis/ granulosus</i> in the food chain. Key <u>publication</u> on cystic echinococcosis.	
	PARADISE: Novel genotyping schemes and detection strategies for <i>Cryptosporidium parvum</i> and <i>Giardia duodenalis</i> . <u>Standard Operating Procedures</u> developed.	
Reference material and data	and outcomes from One Health FID projects in	PEMbo: Collection and characterisation of complete reference genomes of <i>Mycobacterium bovis</i> strains in France, with key <u>publication</u> .

Table 4. Research outputs and outcomes from One Health EJP projects in relation to the integrative strategic activity

was expanded in response to the COVID-19 pandemic in 2020, which led to the establishment of the COVRIN Joint Integrative Project to specifically address SARS-CoV-2, as explained under the Joint Integrative Projects -Addressing Challenges through a One Health Scope section. The OHEJP has successfully delivered project outputs and outcomes to improve preparedness to emerging threats in line with the 'Prevent-Detect-Respond' concept.

What has the One Health EJP scientific research achieved in the field of Emerging Threats?

Much of the research on emerging threats has involved improving upon or developing new laboratory methods for the detection, identification, and characterisation of zoonotic pathogens. This work also included the harmonisation and standardisation of the reference methods, diagnostic tests, and protocols. These project outcomes help to ensure consistency in the application of techniques across laboratories in Europe and obtain comparable epidemiological data. Another key aspect of the OHEJP research

1 <u>Salyer *et al.*, 2017</u> 2 <u>Amri *et al.*, 2020</u>



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Æmerging Threats

has focused on providing novel tools for disease surveillance of emerging threats at the national, European, and international levels. The aim being that OHEJP-devised tools can be widely applied across public health, animal health and food safety sectors, creating a standardised approach to the detection, identification, and characterisation of emerging threats. These strategic activities were supported through transdisciplinary collaboration and alignment between the medical, veterinary, and food institute partners.

Two JRPs worked to advance laboratory techniques that would address the emergence of viral threats and better control future viral outbreaks. More specifically, the MAD-Vir JRP developed a novel tool using metagenomics microarray technology to improve fast detection of viral pathogens causing foodborne zoonoses and emerging threats. This tool can be applied in clinical settings to facilitate early identification of zoonotic pathogens and assist in outbreak preparedness. With the similar aim to improve outbreak preparedness in Europe, the TELE-Vir JRP produced a portable Point Of Incidence (POI) toolbox for the identification and characterisation of emerging viral threats. This innovative toolbox consists of a free bioinformatics web-based platform and POI protocol for viral detection using metagenomics techniques. TELE-Vir's toolbox has the potential to be applied in the field for rapid detection of any virus in diseased humans and animals.

Other JRPs focused on the emerging threats posed by bacterial and parasitic pathogens. Two JRPs addressed bacterial pathogens and bacterial toxins, since some bacteria can produce toxins that are hazardous to health. The TOX-Detect JRP developed and harmonised detection methods for foodborne toxigenic bacteria (toxins produced by bacteria that are transmitted via contaminated food and causing disease), including species of Staphylococci, Bacillus and Clostridia. TOX-Detect produced a reference database of protein profiles for specific toxin-producing bacterial strains. This research will help to timely identify these pathogens and prevent foodborne disease outbreaks caused by these toxigenic bacteria. Meanwhile, the IDEMBRU JRP aimed to address the emerging bacterial threat of Brucella species that cause the highly contagious zoonotic disease of Brucellosis. The IDEMBRU project created a variety of different innovative toolkits that have integrated the data from emerging Brucella species and the reservoirs of infection, which act as a resource to guide the characterisation of emerging Brucella species. Overall, IDEMBRU research will inform Brucella surveillance activities, which are essential to protect humans and animals against this zoonotic threat.

Two further JRPs targeted research on parasitic threats found in Europe and more globally. The <u>MEmE</u> JRP aimed to tackle the parasitic threats posed by *Echinococcus granulosus* and *Echinococcus multilocularis* in the food chain responsible for <u>echinococcosis diseases</u>. This was achieved through the development and standardisation of diagnostic tests and epidemiological data collection tools for improved detection and control of <u>cystic echinococcus</u> species.

Applications of MEmE research impacted on public health, animal health, and food safety sectors. Since the foodborne zoonotic parasites, *Cryptosporidium parvum* and *Giardia duodenalis*, are responsible for causing major outbreaks of gastrointestinal diseases in Europe, the <u>PARADISE</u> JRP focused on these two pathogens. PARADISE successfully delivered novel genotyping schemes and innovative diagnostic strategies for detection of these *Cryptosporidium* and *Giardia* species, with the development of <u>Standard</u> <u>Operating Procedures</u>. PARADISE project outputs can be applied to food matrices, so that this research will benefit foodborne disease outbreak investigations.

The <u>PEMbo</u> PhD, aimed to improve understanding of the genetic evolution of *Mycobacterium bovis* causing <u>bovine tuberculosis</u> in France. This disease is recognised as a re-emerging zoonotic threat in regions of France, associated with transmission of infection between domestic animals and wildlife. The PEMbo project successfully collected and analysed <u>new reference</u> <u>genomes of *M. bovis* strains</u> from across France for epidemiological studies on transmission dynamics, useful for bovine tuberculosis surveillance activities.

Furthermore, since rats carry a multitude of pathogens with public and veterinary health importance, the DESIRE PhD aimed to design and test an effective surveillance system for rat-borne zoonotic diseases in urban environments within the Netherlands. Specific metagenomic sequencing tools were tested to screen for zoonotic pathogens in rats based on microbiome-profiling techniques. The development of an evidence-based surveillance system has provided insights into the epidemiology of emerging rat-borne zoonotic disease hazard detected in greener urban areas. This surveillance system also contributes to planning risk assessments and intervention strategies to mitigate against health threat at the human-wildlife-environment interface.

In summary, the research projects under this domain have successfully addressed emerging and re-emerging threats posed by a wide range of viral, bacterial, and parasitic pathogens using the One Health approach. This has been achieved through the interdisciplinary collaborations among partner institutions that enabled scientific expertise, equipment, and facilities to be shared across European countries to advance diagnostic techniques and tools. Project objectives for this domain evolved over time to effectively respond to stakeholders' needs and address the changes in European and international policies focused on disease outbreak preparedness, thus increasing our research impact. A wide range of stakeholders have already started to apply OHEJP devised emerging threats tools to their activities (e.g., EFSA, ECDC, EU reference laboratories), which will continue into future initiatives. Overall, the project outcomes have both strengthened the scientific capacity within the OHEJP and will benefit the prevention, preparedness, detection, and response to emerging threats across Europe in the future.







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Education and Training



Education and training of a next generation of One Health scientists was an integral part of the One Health EJP in the form of the Work Package on Education and Training.

The team aimed to develop and deliver innovative training platforms and materials with a specific focus on the OHEJP domains (foodborne zoonoses, antimicrobial resistance, and emerging threats) and to provide a sustainable framework throughout the OHEJP partner network. This was achieved through 16 co-funded PhD projects, with an additional PhD project focusing specifically <u>Sustainability of the One Health approach</u>. Activities brought together students, early career researchers, and key experts with diverse expertise in the human, animal, and environmental fields with Summer Schools, continuing professional development modules, short-term missions, webinars are workshops, many of which were fully funded.

These opportunities enabled the PhD students to explore and share skills, expertise, and knowledge internally and externally of the OHEJP consortium and with key stakeholders (ECDC, EFSA and EEA). Collectively, the PhD projects have produced more than 34 peer-reviewed publications and have disseminated project outcomes at more than 104 national and international conferences.

The annual Summer Schools and one Final School - 2019, 2020, 2021, 2022 – brought together delegates from a range of educational levels and interdisciplinary backgrounds, creating a diverse pool of experience and knowledge to promote interesting interactions and collaborative discussions. Specifically, the Final School attracted 246 delegates from around the globe, all of whom benefitted from the OHEJPs knowledge and extensive network.

The OHEJP CPD modules brought together trainers and trainees with experience in different domains and encouraged them to seek new synergies and collaborations. Three CPD modules were organised by OHEJP consortium members between 2020 and 2022 and were fully funded by the OHEJP. These grants allowed over 100 PhD students, Early Career Researchers, and OHEJP consortium members to be trained through a well-balanced mixture of teaching styles using classical joint plenary presentation sessions, moderated interactive workshops, and practical exercises in the areas of <u>Outbreak Preparedness</u>, <u>Digital Innovation for One Health Predications</u>, and <u>Rapid Diagnosis and Harmonisation of Diagnostic Tests</u>. Through the One Health framework, people were brought together from health disciplines, making these CPD modules cross-disciplinary, which is highly advantages for the One Health approach.

The OHEJP also co-funded 19 STMs, which involved 22 Early Career Researchers and 27 institutes within the OHEJP consortium, from 13 countries.

These travel grants facilitated the exchange and harmonisation of scientific expertise, methodologies, equipment, and facilities between members of our Consortium. They drove research forward in a collaborative and non -duplicative fashion to strengthen the scientific capacity within the OHEJP. The STMs researchers shared and implemented their newly acquired skills and knowledge within their host institutes. Four research publications, a conference, and a poster were produced using the developed frameworks and results (for more information, read the <u>report on outputs of STMs</u>).

All PhDs participated in the yearly OHEJP Annual Scientific Meetings (ASM) via individual the 3-minute competition, round table discussions and poster or physical presentations, all of which help in the development of soft skills. Following on from the proceedings were the ASM Satellite Workshops with training and discussion in the areas of <u>digital innovation and data</u> management, <u>digital solutions to disease surveillance and outbreak</u> investigation, and <u>diagnostics</u>. These workshops were interactive events to facilitate learning and interactions amongst over 250 students at various academic levels, Early Career Researchers, and members of the OHEJP consortium. The workshops were in part a great success of the OHEJP and an exemplary demonstration of how the use of training opportunities is an effective way to facilitate a One Health compliant exchange of information between sectors.

A further workshop, Integrated approaches to zoonoses: a systems thinking primer, used systems thinking to enhance collaboration between sectors using case studies ensuring a real world response. Moreover, a dissemination webinar series 'New Tools for Detection and Surveillance', which covered New Tools for Surveillance and Risk Assessment and New Tools for Detection and Surveillance together tools created from within the OHEJP consortium and demonstrated the utility of these tools in a One Health setting. The webinar series was attended by more than 160 delegates and 34 countries. The webinar series ensured the dissemination of tools and their practical uses created during the OHEJP, which were presented in a free, accessible, and global manner.

In summary, the education and training activities of the OHEJP have contributed to the development of a sustainable education and training framework, which has strengthened the scientific capacity within the OHEJP and more widely. These activities further highlight the ability of OHEJP to bring together and train experts from across our European network and share knowledge and cooperate to promote a sustainable One Health approach into the future. Developing capability, building capacity and reinforcing preparedness needs to be done in 'peace time', to create trust among institutions across sectors and borders, which will be crucial in responding to future outbreaks and recovering from them.





Science to Policy Translation



To maximise the impact and exploitation of the One Health EJP -developed solutions and its outcomes, a Work Package was established to specifically interact with the stakeholders, namely <u>Science to Policy Translation</u>. In particular, the aims were to disseminate in a targeted manner the outcomes, to facilitate operationalisation of such outcomes, to discuss stakeholders' evolving needs, to support the stakeholders and their policy initiatives, and to advocate for the One Health approach at the EU and international level.

SCIENCE

The two internal calls implemented by the OHEJP's aiming to launch Joint Research Projects (JRPs) and Joint Integrative Projects (JIPs) were based on the needs communicated by national stakeholders and Key EU stakeholders ECDC and EFSA, ensuring, from an early stage, the usefulness of OHEJP -developed solutions. However, this exercise was only performed at specific time points. To be able to follow - and address - the stakeholders' evolving needs, the OHEIP set up a Stakeholders Committee with the participation of appointed representatives of the European Centre for Disease Prevention and Control (ECDC), European Food Safety Authority (EFSA), European Environment Agency (EEA), European Medicines Agency (EMA), Food and Agriculture Organisation of the United Nations (FAO), World Organisation for Animal Health (WOAH), World Health Organisation Regional Office for Europe (WHO/EURO). These representatives had knowledge of the strategic directions of their respective agencies/organisations, were experts in cross-sectoral collaboration, and, in time, became increasingly familiar with the OHEJP and its potential. In addition, contacts with the EU funded projects COMPARE, EFFORT, EU-JAMRAI and JPI-AMR were kept to ensure synergies and avoid duplication of work.

Contacts with the Stakeholders Committee were regular, with meetings taking place twice per year, in addition to rich in-between communications and interactions. The Stakeholders Committee meetings were a chance to discuss the development of the Consortium and of the stakeholders' needs, to disseminate in a targeted manner the OHEJP results, but more importantly, to discuss the impact and foremost potential uptake and use of the developed results. Stakeholder representatives were briefed by means of the Targeted Reports.

The OHEJP took a number of targeted dissemination initiatives to make sure that the results timely reached the appropriate audience, in a way that was useful and interesting for that specific audience in terms of content, format, and language. Important activities were the publication of Thematic Reports, relating the needs of the stakeholders with OHEJP expertise and outcomes. Thematic reports were appreciated by the stakeholders, and were disseminated internally in the various agencies.

Such reports were:

- Link between needs of international stakeholders (FAO, OIE, WHO) and OHEIP expertise
- Link between needs of EMA and OHEJP expertise
- Link between needs of the European Environment Agency and OHEIP ٠ expertise
- Links between COVID-19 related needs of stakeholders and OHEIP • activities
- **OHEIP Thematic Report on AMR**
- OHEJP Thematic Report on environmental aspects addressed in OHEIP activities.

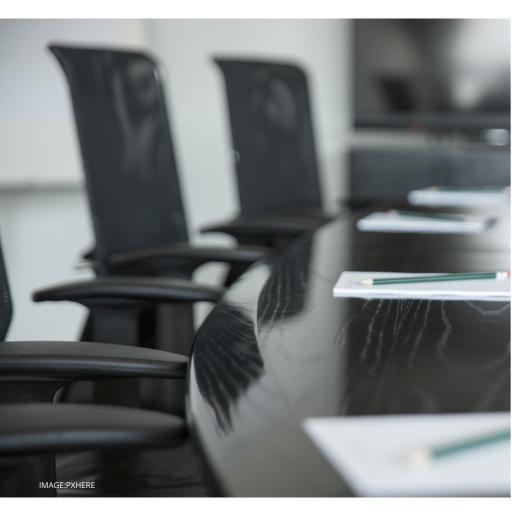
Another initiative was the set-up of Dissemination Workshops, dedicated to decision- and policymakers at the national level: representatives of ministries, national authorities and agencies. The topics of such workshops were directly suggested by the stakeholders, and most of these events were by invitation only, in order to provide a safe space for discussion between the decisionand policy- makers, and the scientists. Given the varied technical background of the target audience, these workshops focused on practical examples, showcasing how OHEIP solutions are beneficial when applied, rather than on scientific details. Although these workshops were by invitation only, the resulting reports have been made publicly available through the One Health EJP webpage to maximise fairness. The workshops were always evaluated very positively by the participants. Such workshops were:

- **Dissemination Workshop on Metagenomic**
- Dissemination Workshop on Improving One Health Preparedness to (re)emerging infectious threats
- Joint SimEx/Dissemination Workshop 'A One Health Simulation Exercise as a roadmap for future foodborne outbreak preparedness'
- Dissemination Workshop 'Communication, education and training, and science to policy translation. Lessons learnt and legacy of the OHEIP'.





Science to Policy Translation



An additional tool for dissemination. this time dedicated to any audience with a technical background, was the OHEJP Outcome Inventory (OHOI): an online, open access database of scientific and integrative outcomes. It includes descriptions of databases, strain collections, tools, and other scientific outputs (models, scripts, software, pieces of hardware, novel methods, etc.), and it facilitates the contact with projects in charge of the various solutions. To ensure sustainability, the OHOI has been taken over by the MVNA after the end of the OHEJP.

A distilled version of the OHOI, the document 'Analysis of outcomes and uptake of One Health EIP outputs by stakeholders', was also produced to target specific stakeholder organisations, namely ECDC, EFSA, EC DG-AGRICULTURE AND RURAL DEVELOPMENT, and EC DG-HEALTH AND FOOD SAFETY.

A major event organised by the One Health EIP was the Stakeholder Conference 'Collaborating to Face Future One Health Challenges in Europe'. The aim of the conference were two-fold. Firstly, it provided the opportunity to have additional impact at the scientific level (e.g., generation of new knowledge, capacity building, cross-sectoral harmonisation), the policy level (e.g., support to evidence based decision making, advocacy of One Health approach), and importantly, the long-term impact at the economy level (e.g., tools to enhance the sustainability of production that could attract the interest of the private sector), as well as at the societal level (e.g., by supporting the health of consumers, by showcasing the benefit for the society at large, and good use of EU funds). Second, it provided a forum to discuss the future of European One Health to a wide range of stakeholders. In fact, the programme brought together representatives of a large variety of interested parties, for example EC Directorate Generals, EU Agencies, the Quadripartite, representatives of the private sector and of the civil society, non-governmental organisations, etc. This was also a platform to support the sustainability of the OHEJP. The success of the event was

shown by the high interest generated (around 1000 registrations, 120 participants on site, and hundreds online), the lively discussions during, aside and after the conference, the engagement on social media, and the feedback received. Presentations delivered at the conference and other relevant material were made publicly available on Zenodo, and findable through the conference webpage.

Targeted dissemination was crucial for demonstrating, with practical examples, the closure of stakeholders' knowledge gaps, but it had another important outcome: it was also thanks to this constant exercise that the stakeholders understood and acknowledged the solidity and added value of the OHEJP, of its scientific results and of its cross-sectoral medicalveterinary-food safety network. In time, the collaborations between stakeholders and the OHEJP became more frequent, allowing the Consortium to reach additional impact at the scientific and policy level. In fact, these collaborations facilitated the operationalisation of outcomes, allowed the OHEIP-developed knowledge to inform policy, provided the possibility to advocate for the One Health approach at the EU and at global level, and supported the sustainability of the consortium and its solutions. Notable examples included:

- Targeted requests for assistance, from the Tripartite and Quadripartite, • and EU Agencies
- Requests for OHEJP outcomes to be included in stakeholders' toolboxes, e.g. Tripartite Zoonoses Guide SISOT
- Contribution to stakeholders' consultation and requests for comments on their policy documents. Of particular importance for the former are the contributions to consultations on EU policies (for example the consultation on EU4Health, that the OHEJP was also invited to present at the EC level), and for the latter, the various contributions to documents of EFSA, FAO, WHO-GOARN, and One Health High Level Expert Panel (OHHLEP)
- Contributions to stakeholders' events (e.g., ONE2022 side event, EFSA Summer Schools) and joint publications, being authored together with classic stakeholders of the OHEJP (e.g., Bronzwaer et al, 2022) or with other international parties (e.g., Streichert et al., 2022 and Hobeika et al., 2023).

The stakeholders are eager to continue the interaction with the OHEIP after the end of the EU funded project, something that is being achieved thanks to the takeover of certain OHEJP initiatives by the MVNA. Collaborations, discussions, and interactions with the stakeholders are still alive, even after the OHEJP has come to an end, either under the aegis of the MVNA, or in other frameworks, taking maximal advantage of the close relationships forged during the OHEJP.





ne HEALTHEJP Sustainability





The term 'sustainability' has a variety of meanings for different audiences and is relatable to many forms and actions aimed at the preservation of a particular resource: people, planet, purpose, profit.

In the context of One Health scientific research, sustainability aims to deliver solutions that address the interactions between the human-animalenvironment health interface, meeting present needs whilst considering the longer-term perspective with future scenarios. One prime example has been the zoonotic feature of the recent COVID-19 pandemic which heightened public awareness of how infections cross sectors (human-animal-environment) and has highlighted the relevance of the One Health approach to delivering solutions to recover from zoonoses.

For the OHEJP sustainability has been in the form of the advancement of state-of-the-art outputs in the domains of foodborne zoonoses, antimicrobial resistance and emerging threats, creating long-term approaches to address public health threats. These innovative research outputs, including databases, protocols, guidelines, models, and other novel tools, were devised to provide sustainable approaches to tackle health threats impacting both human and animal populations, some of which also consider the role of the environment.

This has been achieved through a shared roadmap, reinforcing the importance of cross-sector and transdisciplinary collaborations, enabling OHEJP researchers to combine their knowledge and resources. Adopting this approach has leveraged the strengths of each contributor and paved the way for continued innovation in the areas of research set out by the <u>Strategic</u> <u>Research Agenda and Integrative Strategy Matrix</u> that is describes. By actively bridging the gap between different health sectors the OHEJP has laid a foundation for sharing of knowledge within the scientific community and its stakeholders.

To ensure the longevity and sustainability of our valuable scientific outputs, the OHEJP has collectively generated a considerable open access <u>knowledge repository</u>, a resource that will continue to contribute to the research needed for further improvements in the public health, animal health, and food safety arenas in Europe. This knowledge repository can be used to tackle an issue or inform stakeholders and will help drive forward the One Health agenda in the EU.

By utilising from the outset the OHEJPs connections with large European agencies and global organisations that are important players in the fields of foodborne zoonoses and AMR, there was a good understanding of the needs of these national and international stakeholders, all of whom were regularly involved with discussions highlighting the impact and potential impact at the policy, societal and economic level. Additional dissemination to national decision makers was performed by targeted <u>Dissemination Workshops</u> to maximise the usefulness of OHEJP outcomes, with topics selected and based on stakeholders' input.

Our knowledge pool has also enabled beneficial content-relevant education and training modules which have been taken up and enjoyed by over hundreds of PhDs and early career researchers from inside and outside of the Consortium, and those with a One Health interest, worldwide. The education and training component of the OHEJP has created important personal and institutional connections as part of a mutually supportive environment, allowing for insight into different fields. These professional development activities have created a solid foundation for sustainable, cross-sectoral, One Health integration to benefit the next generation, and is an essential factor in the long-term sustainability of One Health research.

The strong embedded link with the <u>MVNA</u> is an crucial factor in the long-term sustainability of the OHEJP outcomes - many of the OHEJP partners have worked together for numerous years, 18 are also part of the MVNA – and will enable continuation of OHEJP activities. Notably the MVNA will explore opportunities for education for One Health researchers such as short-term missions and workshops.

Of course, knowledge and purpose are of limited use if not shared and OHEJP dissemination activity has been an effective means to diffuse our knowledge and to keep the One Health momentum going. The targeted dissemination of results and communication of activities and practical One Health methodologies to national and international authorities and stakeholders through multiple digital and physical methods has been fundamental to sharing OHEJP outcomes to relevant audiences and has generated a global interest in the Consortium.

The <u>Strategic Research Integrative Agenda</u> is one such mechanism, highlighting OHEJP outcomes and using insights gained throughout the five-year project to provide a sustainability plan created to recommend actions to maintain its main results. An overview summarises the many present challenges and opportunities in One Health, with focus on science-to-policy translation, the role of the environment and pandemic preparedness, and an assessment of the needs of stakeholders.

In the Agenda we highlight the need for any sustainability mechanism to be effective, it will be important to place emphasis on equity and fair representation of cross-border and cross-sectoral operationalisation of One Health.

Translating the One Health concept into a collaborative operative scheme has been the goal of many scientific projects and international forums, and although many recognise the goal, the path to the goal is challenging.





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Sustainability

Targeted dissemination of OHEJP results	AUDIENCE	INFORMATION	COMMS FUNCTION	COMMS OBJECTIVE	COMMS CHANNEL
and activities	OHEJP Partners	All internal (including confidential) and external communications.	Maintain good relationships and lines of communication.	Foster integrative and collaborative work approaches. Demonstrate OHEJP impact/scientific outcomes. Demonstrate use of funds.	Website, social media, newsletters, email marketing, editorial, conferences, PR.
	Stakeholders	Internal and external (relevant) communications.	Maintain good relationships and lines of communication.	Transparency of project and progress. Demonstrate use of Grant. Demonstrate OHEJP impact/ scientific outcomes	Website, social media, newsletters, editorial, conferences, PR.
	Policy Makers	External communications.	Brand awareness. Foster relationships to grow network. Sustainability of project. To affect change.	To inform and open dialogue. Demonstrate OHEJP impact/ scientific outcomes.	Social media, website, external newsletter, editorial, PR.
	International bodies	External communications.	Brand awareness. Foster relationships to grow network. Sustainability of project. To affect change.	To inform and open dialogue. Demonstrate OHEJP impact/ scientific outcomes.	Social media, website, external newsletter, editorial, PR.
	Scientists - external	External professional communications.	Brand awareness. Foster relationships.	To inform.	Social media, editorial, website, external news, email marketing, networking, conferences, PR.
	Healthcare Professionals - external	External professional communications.	Brand awareness. Foster relationships.	To inform.	Social media, editorial, website, external news, email marketing, networking, conferences, PR.
	Students, Early Career Researchers	External communications.	Brand awareness. Create the next generation of OHEJP collaborators and One Health scientists.	To inform, educate and inspire.	Social media, website, editorial, email marketing, networking, conferences.
	General Public	Jargon-free external communications.	Image building, brand awareness.	To inform and educate.	Social media, website, newsletter, editorial, PR.

To better understand the drivers and constraints of successful One Health collaborations the OHEJP Sustainability teams co-funded PhD SUSTAIN project took advantage of the experiences and expertise of OHEJP stakeholders, and looked at how One Health practices are currently used within European institutional and political networks. The project performed

two case studies, in Sweden and Italy, to analyse the One Health approach on a national level, allowing insight into the operationalisation of One Health within government institutes, as well as their coordination and collaboration practices across institutes.

The SUSTAIN research formed part of the OHEJP Workshop on Institutionalisation, an open-discussion forum to explore the current barriers to the institutionalisation of One Health and strategies that may be employed to overcome them. The Workshop was an invitation-only event and part of the Stakeholders Conference. Discussions focussed on the barriers that are inhibiting the translation of One Health from a concept into a fully operational scheme. It was recognised that although different countries have made progressto include the One Health approach in their own procedures and methodologies, none, as yet, have been able to fully implement all the segments needed for the complete One Health approach. Considerations that need to be taken up by, and translated into actions to create a fully operative system using the One Health approach are addressed in the Document on the Institutionalisation of One Health created by the OHEJP Sustainability team.

As was clearly highlighted at the Stakeholders Conference, one strategy will be the need to collaborate with sectors not traditionally associated with One Health, like social sciences, psychology, policy, and economy. Utilising the knowledge these sectors have for community engagement will encourage the uptake of potentially impactful One Health solutions in a feasible way, thus creating continuity and sustainability for the benefit of all.

The success of the OHEJP has depended on having mechanisms in place to ensure that the project outputs and outcomes are available to the scientific community, the authorities, and policy makers to encourage their wider uptake and implementation and help inform in the decision-making process. To this end, the OHEJP Project Management Team has set up a series of bilateral meetings with its main stakeholders (EFSA, ECDC, EEA, DG HEALTH, JRC, WHO-Europe and FAO) to facilitate the uptake of the project outcomes. In these meetings the multidisciplinary cooperation of this unique European consortium was highlighted, as well as the privileged contacts with its stakeholders, which resulted in the delivery of relevant knowledge and practical methodologies that strengthen cross-sector collaborations.

Throughout the Final Report we have focussed on the sustainability of the impact and outcomes of the OHEJP and outlined a list of selected outcomes of the OHEJP for loint Intergrative Projects, and each domain: foodborne zoonoses, antimicrobial resistance, emerging threats. It is expected that the uptake and application of OHEJP tools and solutions will have important scientific and policy impact beyond the end of the Programme, and for many years to come.





HEALTHEJP CUDING CONCLUDING CONCLUDING REMARKS

The One Health EJP turned out to be an amazing adventure that started as an idea initiated by a handful of people working at ANSES and Sciensano linked to the Med-Vet-Net Association. It became a giant network of researchers, technicians, surveillance experts, risk assessors and managers across 22 European countries and 7 international organisations that were identified as key stakeholders.

The One Health EJP has successfully created an exceptional network of dedicated One Health experts that has met the demands of national and international stakeholders, and therefore constitutes a solid foundation for a future European One Health consortium." Hein Imberechts Sciensano

One Health EJP Scientific Coordinator

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This journey started well before 2015 with some ideas and handwritten notes that fitted on about half a page and ended up with voluminous reports composed of several hundreds of pages. Needless to say, that these tasks have been taken up by several collaborators that made up the superb support team at ANSES and Sciensano, plus the management team and all the researchers that collaborated intensively to this endeavour. It was a pleasure for the coordinators to be the guide to this undertaking and chair the many governance and organisational meetings for close to past six years.

One of the main reasons why the OHEJP consortium was created, was to further strengthen the cooperation between medical and veterinary (incl. food safety) public organisations in Europe. Professional networks between national reference laboratories regarding animal infectious diseases and food safety were already created by the European Commission, but the research Network of Excellence (FP6 Work Programme of the EC, 2004 to 2009) was appreciated, not only for its many scientific results and publications, but also for the tight contacts and exchanges it supported. The OHEJP partners originally set up the MVNA in 2009, but it was not until 2018 that the OHEJP brought all the relevant public entities together in the Horizon2020 project co-financed by both DG-AGRI and DG-HEALTH. Long before the term became known by the public, 'One Health' was chosen to stress the importance of cross-sector cooperation, even without the participation of a clear environment dimension at that time.

Since the COVID-19 pandemic that struck us in 2019, One Health has been on the agenda of many high-level experts discussions and conferences, both science- and policy-oriented, in the EU and beyond. It became clear that the efforts to fight infectious diseases in each of the sectors of public health, animal health and environmental health at regional, national and international levels, needed a firm coordination.

As leaders of the OHEJP, we are proud that the many results and outcomes of the 31 embedded projects that were launched in the OHEJP represent excellent examples of scientific collaboration between the medical and veterinary / food safety actors. For instance, methodologies on surveillance systems, new and improved laboratory procedures, ways to exchange surveillance and genetic data from different origins, joint risk assessment methodologies, communication of possible risks, prevention and response proposals are all very practical outcomes of this cross-sectoral work. Several hundreds of food safety experts have produced new knowledge and tools that are now accessible for everybody who is interested in food safety, infectious diseases and antimicrobial resistance. All of this was achieved despite the interuption of a global pandemic; the researchers, managers and all collaborators succeeded in advancing their work in the lab and in support of the management of this huge project. Also, many early career scientists participated in the projects, Education and Training activities and the many in person and online OHEJP events, so that the knowledge and expertise gained will not get lost. The substantial investment of the countries and the EC (\leq 45 million each) contributed to make the partners better prepared against future outbreaks, to prevent foodstuffs from being contaminated, and people and animals to get ill. The OHEJP may even have an effect on national or European policies, for instance by proposing improvement in surveillance and laboratory methodologies. The amazing work achieved in this project showed that the One Health approach is absolutely profitable to all!

Bringing experts with different expertise together and encouraging them to come up with new evidence and practical protocols is one thing, to make potential users understand what has been done and how it can help them in their daily work, is another. The OHEIP management team was very fortunate that it could rely on an exceptional team of communication experts, both for creating a strong and attractive project branding and creative, clear and engaging writing of reports, newsletters and blogs. It was obvious that both specific mailings and a broad communication through social media are essential to convey the One Health message to those audiences that can take up the outcomes of the OHEJP. Only in that way, exploitation of outcomes and gaining effect are feasible. Through the professional, attractive and recurrent communication efforts, the OHEJP management obtained the interest and support from the European agencies European Centre for Disease Prevention (ECDC), European Food Safety Authority (EFSA), European Environment Agency (EEA) and European Medicines Agency (EMA), as well as from Food and Agriculture Organisation of the United Nations (FAO), World Organisation for Animal Health (WOAH) and World Health Organisation Europe (WHO-Europe) and Directorate-General Health and Food Safety (DG-HEALTH). It is clear that the OHEJP has created a European consortium that is unique, supportive for the One Health approach and proposing practical methodologies, attractive for national and international organisations.

The OHEJP has come to an end, but the <u>Med-Vet-Net Association</u> will continue to offer a forum for all public organisations that took part in the OHEJP, even if individually they become engaged in a wide spectrum of new collaborations as well as any other relevant ones willing to join the Association in the future. Therefore, the One Health EJP Management Team wishes to thank all contributors, scientists and technical staff, as well as all their managing staff, for their contribution to this unique European One Health consortium.



