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Scientific Activities

Issue Two
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The One Health EJP (OHEJP) is a unique international collaboration between partners across different fields. With strong links to both national and international stakeholders and efficient science-to-policy translation, the scientific activities of the One Health EJP will have both immediate and long-term impact.

Launched in January 2018 and working to a 5-year programme, the One Health European Joint Programme is a landmark partnership between 43 public health, animal health and food partners and the Med-Vet-Net Association, a European Network of Excellence for Zoonoses research, located across Europe.

The main focus of the OHEJP is to reinforce collaboration between public partners by enhancing collaboration and integration of activities by means of dedicated Joint Integrative Projects (JIPs), Joint Research Projects (JRPCs), and through education and training in the fields of Foodborne Zoonoses, Antimicrobial Resistance and Emerging Threats.

Through the OHEJP there are opportunities for harmonisation of approaches, methodologies, databases and procedures for the assessment and management of foodborne hazards, emerging threats and antimicrobial resistance across Europe, which will improve the quality and compatibility of shared information for decision making.
The overarching objective of the OHEJP is to develop, consolidate and reinforce a collaborative European network of public research institutes with reference laboratory functions.

A key aim of the OHEJP is to integrate medical, veterinary and food scientists to address three key research topics: foodborne pathogens, antimicrobial resistance and emerging infectious disease threats.

Research needs of stakeholders are at the forefront of the consortium's focus.

**Key objectives:**

- To bring together the major representatives from medical, veterinary and environmental scientific communities and international stakeholders with expertise in foodborne zoonoses, antimicrobial resistance and emerging threats.
- To implement the “Prevent-Detect-Respond” concept to reinforce cross-disciplinary scientific integration and collaboration for rapid response and prevention of foodborne pathogens, antimicrobial resistance and emerging threats.
- To stimulate scientific excellence by co-funding Joint Research and Joint Integrative Projects that have the potential to enhance scientific knowledge and provide tools for disease surveillance at national, European and global level.
- To foster the harmonisation and standardisation of laboratory methods by bringing together international scientific and technical expertise.
- To exchange, communicate and inform policy change by collaborating with our European and international stakeholders, including European Centre for Disease Control and Prevention (ECDC), European Food Safety Authority (EFSA).
- To promote and develop One Health research through training, education and communication nationally and internationally at all levels and career stages.
- To work to achieve a sustainable platform that can be continued to be built upon and grow, beyond the lifetime of the OHEJP and beyond Europe.
CONSORTIUM STRUCTURE

A governing and management system was established at the beginning of the OHEJP.

The governing boards specific to the OHEJP include: The Project Management Team (PMT), Scientific Steering Board (SSB) and Programme Managers Committee (PMC).

There are also important contributions from members outside of the OHEJP and these include: The Programme Owners Committee (POC), the External Scientific Advisory Board (ESAB), the Stakeholders Committee (SC), the Ethics Advisors and National Mirror Groups.

The OHEJP Coordination Team are based at the French Agency for Food, Environmental and Occupational Health & Safety (ANSES), France.

The OHEJP Scientific Coordinator resides at Sciensano, the Belgian Institute for Health.

The Project Management Team consists of all the Work Package (WP) Leaders and Deputy Leaders.
JOINT INTEGRATIVE PROJECTS AND JOINT RESEARCH PROJECTS

The ambition of the OHEJP is to align European countries through a joint priority setting in the domains of foodborne zoonoses, antimicrobial resistance and emerging threats, and joint programming of research agendas.

The OHEJP approach is to set up a common strategic research agenda among the partners, taking into account the initiatives taken by our stakeholders.

Through the existing links with the Programme Owners (national or regional authorities and policy makers) national interests are also taken account of in the OHEJP strategy.

There is considerable opportunity for harmonisation of approaches, methodologies, databases and procedures for the assessment and management of foodborne hazards, emerging threats and AMR across Europe, which will improve the quality and compatibility of information for decision making.
**ORION** focuses on the semantic and technical interoperability between the sectors, with focus on surveillance information.

The ORION project aims at establishing and strengthening inter-institutional collaboration and transdisciplinary knowledge transfer in the area of surveillance data integration and interpretation, along the One Health objective of improving health and well-being. This will be achieved through an interdisciplinary collaboration of 13 veterinary and/or public health institutes from 7 European countries. These agencies are committed to adopt best practice One Health Surveillance solutions (guidelines, methods, tools and knowledge). Specifically this project will create:

- an “One Health Surveillance Codex” (WP1) – a high level framework for harmonised, cross-sectional description and categorisation of surveillance data covering all surveillance phases and all knowledge types
- an “OHS Knowledge Hub” (WP2) – a cross-domain inventory of currently available data sources, methods / algorithms / tools, that support One Health Surveillance data generation, data analysis, modelling and decision support
- “One Health Surveillance Infrastructural Resources” (WP3) – that are practical, infrastructural resources forming the basis for successful harmonisation and integration of surveillance data and methods. Developed solutions will be exemplified and validated during several One Health pilot studies in which other OHEJP research projects may join in. These pilot studies will support the operationalisation and implementation of One Health surveillance solutions on a national level and provide crucial feedback for future development and dissemination actions. An open web-based One Health Surveillance Knowledge Hub will facilitate this knowledge exchange. Trainings and workshops will be offered to support and integrate with other OHEJP projects in their data harmonisation efforts.

**JOINT INTEGRATIVE PROJECTS**

**ORION**

**Start:** 1 January 2018  
**Status:** Ongoing  
**Contact:** Matthias Filter (BfR)

Norwegian Institute of Public Health (NiPH), Norway  
National Veterinary Institute (SVA), Sweden  
The Public Health Agency of Sweden (FoHM), Sweden  
DTU National Food Institute (DTU), Denmark  
Statens Serum Institut (SSI), Denmark  
Friedrich-Loeffler-Institut (FLI), Germany  
The German Federal Institute for Risk Assessment (BfR), Germany  
Sciensano, Belgium  
Wageningen Bioveterinary Research (WBVR), The Netherlands  
National Institute for Public Health and the Environment (RIVM), The Netherlands  
Public Health England (PHE), United Kingdom  
Animal & Plant Health Agency (APHA), United Kingdom
COHESIVE focuses on the ability to pick up, share and communicate signals as well as the ability to conduct joint risk assessments.

Working towards a world with less zoonotic disease burden requires collaboration at all levels and between the veterinary and human domain. In some European countries, risk analytical structures to deal with (emerging) zoonoses in an integrated human-veterinary setting have already been implemented. However, these structures mostly were implemented after experiencing one or more large outbreaks such as BSE in the UK or Q-fever in The Netherlands. Now, these countries experience the advantages of integrated One Health approaches to deal with (re-)emerging zoonoses, including AMR and foodborne zoonoses. Due to very different organisation of food production systems, the veterinary and human health domains, both in and between countries, it must be realised that there is no general blueprint for a One Health risk-analysis structure. In this context, the COHESIVE project aims at strengthening/improving (structured) collaboration between the human and veterinary domain in the area of risk-analysis of (emerging) zoonoses in European Member States by:

- **Stimulating One Health approaches at the national level within EU countries (OHEJP partner member states) and focusing on strengthening human-veterinary collaboration** by designing common procedures and tools while taking into account similarities and differences between countries. Importantly, the project will facilitate in the first step of creating support for a One Health structure by organising local workshops with national stakeholders.

- **Roadmap towards an EU zoonoses risk-assessment of risk-analysis structure** by bringing together existing risk analysis and epidemiological tools, skills and facilities for a One Health surveillance over member states borders, including exploration of the use and possible implementation of early warning systems across Europe.

- **Design and test a common open source platform for the collection and analysis of surveillance and outbreak data on (foodborne) zoonoses**. The aim is to provide IT tools and data that are quickly available, usable and helpful in outbreak situations and for risk assessments. Especially tools for tracing, WGS and standardised risk assessments are established, harmonised and improved. Interoperability with the main data exchange systems at EU level will be ensured such the TESSy platform and the EFSA zoonoses data collection system.

- **Capacity building within and between EU countries at several levels (executive level, communication, policy makers) within the area of zoonotic diseases**. Several pilots, within and between countries, will test the developed tools (guidelines for setting-up a One Health Structure, risk-assessment tool, early warning tool, data platform) within country through specific Vet-Med partnerships. Multiple member states Vet-Med partnerships will also assess the developed tools collectively on combined country surveillance.
The CARE project will focus on developing new One Health concepts for proficiency testing (PT) of laboratories, reference materials and quality/availability of demographic data.

PT testing, or external quality assurance (EQA) schemes, is an integrated part of quality assurance management for laboratories within the field of human, food, and animal microbiology. The aim of CARE is to develop new proficiency testing schemes that can be used cross-sectorally and thereby used to evaluate the capacity to manage foodborne problems from a One Health perspective.

Reference materials (RM) for microbiological analyses on zoonotic pathogens are available in the context of reference laboratories (e.g. EURL’s). There is no EU level combining the reference collections linked to specific reference functions and sectors. Characterisation of epidemic strains, antibiotic resistances, and virulence markers have progressed from culture-based methods to molecular fingerprints. Phenotypic and genomic data must be coupled for checking authenticity of RM and promoting their use as control strains. We aim to provide insight to available and desirable RM, identifying sources of both strains and genomic data, including the field of antimicrobial resistance, provided by reference laboratories and other relevant sources such as online repositories and national collections.

Europe, due to its long tradition of preserving the microbial diversity, has an important reservoir of strains maintained in culture collections and in microbial Biological Resources Centers (mBRCs). The supply of these resources and associated data is highly fragmented among the Member States. This constitutes a large barrier for users who must (i) consult different information systems with heterogeneous data and (ii) contact several collections or mBRCs to access the wide range of resources. The provision of reference strains is an essential component for the research, the advancement of life sciences, the support of the biotechnology sector and the further development of the bio-economy. In particular, regarding the zoonotic and foodborne pathogens, there is a need to make easily visible and accessible the offer of Reference strains for validation methods and PT. We will focus on the visibility of the reference material and data associated for the scientific community, emphasising the availability and sustainability of this reference collection in order to contribute to the long-term needs of the European research. The information will be disseminated about the accessibility of the reference collection but also of CARE partner microbial collections.

At EU or national level, risk assessment and management are highly dependent on the availability and quality of data on animal populations, food and feed consumption. The quality and availability of the demographic data including those for food consumption for risk assessment differs between countries. We will further assess the quality and availability of the demographic data and focus on how to improve and make the data better by raising awareness of EU authorities collecting and organising demographic data.

Swedish National Veterinary Institute (SVA), Sweden
The Public Health Agency of Sweden (FoHM), Sweden
DTU National Food Institute (DTU), Denmark
Statens Serum Institut (SSI), Denmark
National Veterinary Research Institute (PIWet), Poland
Istituto Zooprofilattico Sperimentale dell’Abruzzo e del Molise Giuseppe Caporale (IZ AM), Italy
Istituto Superiore di Sanità (ISS), Italy
Istituto Zooprofilattico Sperimentale della Lombardia e Dell’Emilia Romagna (IZ LER), Italy
Complutense University of Madrid (VISAVET-UCM), Spain
French Agency for Food, Environmental and Occupational Health & Safety (ANSES), France
Institut Pasteur (IP), France
French National Institute for Agricultural Research (INRA), France
National Institute for Public Health and Environment (RIVM), The Netherlands
 Wageningen University & Research (WUR), The Netherlands
Animal & Plant Health Agency (APHA), United Kingdom

CARE
Start: 1 January 2020
Status: Ongoing
Contact: Rene Hendriksen (DTU)
OH-Harmony-CAP aims to collect information on current capabilities, capacities and interoperability at both the National Reference Laboratory (NRL) and the primary diagnostic level.

The quantitative description of current and best practices and the development of harmonised protocols will identify and possibly close the gaps and suggest future studies of how best to detect and characterise foodborne pathogens across the One Health sectors. A global strategic overview of laboratory capacity in the animal-food field, as provided by EULabCap, will be provided, updated and expanded.

The project will develop and test an OHLabCap survey at the NRL level in all EU/EEA countries followed by an adjusted OHLabCap survey of the primary diagnostic laboratories in countries that have been identified during the first survey. It will focus on six high priority bacteria, ten high priority parasites and AMR for *Salmonella* and *Campylobacter*. The project will also quantify current practices, and describe procedures and methods in the detection of foodborne pathogens and AMR for *Salmonella* and *Campylobacter*. Upon review, we will produce recommendations and guidelines on how to improve the quantitative data on foodborne pathogens. Focus will also be on selected bacteria and parasites. We will collect, analyse and rank current protocols according their ability to detect the model organisms Shiga toxin producing *E. coli* (STEC)/enterotoxin producing *E. coli* (ETEC) and Cryptosporidium.

Specific protocols of the highest quality will be designed to be tested, and will test the developed protocols in practical training seminars, and through E-learning, and include training in how to organise national networks and exercises in communication on both national and EU/EEA levels.
**MATRIX** aims to advance the implementation of One Health Surveillance in practice, by building on existing resources, adding value to them and creating synergies among the sectors. In particular, identifying and describing existing cross-sectorial One Health Surveillance programmes or potential programmes, extending the efforts of existing integrative OHEJP projects which focus on separate or only two sectors.

The previous integrative projects were funded to strengthen collaboration and communication at the end of the surveillance continuum in each sector. **MATRIX** takes advantage of this linkage by strengthening the practice of surveillance along the whole process of surveillance, from implementation to output, reviewing existing structures, and proposing guidelines for either adaptation of new or improvement of already existing One Health Surveillance collaborations.

The plan is based on two fundamental premises: 1) the need for a problem-based approach using real-life cases; and 2) the understanding that different countries have different realities, and proposed solutions must therefore consider how implementation can be addressed under different resource settings.

The project will collate and review all available descriptions of national and multi-national frameworks which already function or can function in a One Health approach. This will provide a foundation for the development of best-practice One Health Surveillance guidelines. Where possible, surveillance on output-based measures will be recommended to strengthen the general guidelines. To make **MATRIX** context aware, we will take explicit account of a country's resources and capacity to carry out surveillance and provide an assessment tool for surveillance capacity. Once strengths and weaknesses are identified, a country can situate themselves in the roadmap for One Health Surveillance development. A key aim is to share surveillance inputs and outputs across sectors, providing digital integration centres for decision making.

The problem oriented vision of the project is reflected in the creation of hazard specific tracks that will apply and evaluate methods with particular reference to the identified hazards, in order for the methods to be useful for as many zoonotic hazards as possible.
Coronavirus disease (COVID-19), which is caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), was first identified in December 2019 in Wuhan, China, and has since spread rapidly, evolving into a full-blown pandemic. This COVID-19 pandemic has an unprecedented societal and economic impact.

A main focus of the COVRIN project will be to reinforce collaboration and integration of research activities on SARS-CoV2. This project aims to integrate coronavirus research activities of all project partners. The project will have two main operational objectives:

1. To identify the drivers for the emergence and spread of SARS-CoV2.
2. To generate data and build models for risk assessment of SARS-CoV2.

Activities to connect with stakeholders and avoid overlaps with other projects will be a key focus and the project will split into four key research activities:

1. Research on detection of SARS-CoV2 in animal species and the environment
2. Research on SARS-CoV2 molecular and biological characterisation
3. SARS-CoV2 surveillance and risk assessment, focussed on the animal human interface
4. Coronavirus preparedness.

Within the overall One Health EJP strategic goals, the overall aim of the COVRIN project will be to generate and share data of integrative research activities on virus-host interactions, virus evolution and drivers for emergence, risk assessment and risk modelling, in order to increase the preparedness for future Coronavirus outbreaks.
The NOVA project strives to develop new surveillance tools and methods and to harmonise and optimise the use of existing surveillance system data.

19 Med and Vet institutions from 10 European countries are collaborating for this project. The project consists of five topics. Three of the five (1, 2 and 3) concern the development of targeted surveillance tools, whereas the remaining two (4 and 5) concern integrative measures:

1. **Syndromic Surveillance**: to develop and implement tools to advance methods for real-time and near real-time detection of early outbreak signals using existing surveillance data sources.

2. **Spatial risk mapping**: to advance the use of geographical mapping and analysis for understanding zoonotic disease risks to farm animals and humans.

3. **Food purchase data**: Create methods to acquire and analyse (large) datasets from food purchases from consumers and institutions, in order to develop the novel field of understanding of risks for sporadic disease and outbreaks via patterns in the food that we buy. The two integrative or overarching research umbrellas concern:

4. **Mathematics and Economy**: To develop advanced mathematical modelling tools for better analysis of existing surveillance data, with a particular aim of conducting cost effect analyses.

5. **Terminology, data sources and barriers**: within a One Health perspective, to define common surveillance concepts, locate and make use of available data sources and understand impediments in the use of surveillance data and tools that may exist in some countries or sectors.

NOVA, is expected, through its collaborative structure, to help advance the use of modern surveillance principles across Europe. Moreover, the outcomes developed will have practical and cost saving impacts on how surveillance of existing and emerging zoonotic agents is being conducted within the EU.
The **LISTADAPT** project aims to decipher the molecular mechanisms of the adaptation of *Lm* to its various ecological niches by comparing both genotypic and phenotypic data from a large and balanced set of strains from environment, animals, foods and clinical cases in several European countries.

The foodborne bacteria, *Listeria monocytogenes* (*Lm*), which is causing listeriosis, is together with *Salmonella* and STEC, the main causative agent for foodborne infections in EU, in terms of severity of the illness and fatality rate (EFSA-ECDC, 2015). It is a life-threatening disease with high mortality (20-30 %) and hospitalisation (98.9 %) rates. A significant increase in the occurrence of listeriosis has been recorded since 2008 in Europe. In 2014, 2,161 confirmed human cases of listeriosis have been reported in Europe (ECDC atlas, EFSA-ECDC, 2015). The ecology of *Lm* is still poorly understood and the capacity of some strains to adapt to the environmental conditions found in the food industry makes production of high quality, safe food a major challenge.

To elucidate which genes and molecular mechanisms underlie the adaptation of *Lm* to its different ecological niches, LISTADAPT will use standard operating procedures (SOPs) for the production and analysis of Whole Genome Sequencing (WGS) data and bioinformatics tools previously developed for EU Horizon 2020-COMPARE project. The LISTADAPT consortium includes the European Union Reference laboratory (*EURL*) for *Lm*, 7 National Reference Laboratories (NRL) for *Lm* of which two also are National Public Health Laboratories and the EURL for antimicrobial resistance. The NRLs expert in WGS will train the others to COMPARE Standard Operating Procedures and bioinformatics toolbox and will stimulate them to use WGS for the surveillance of *Lm* in their country. This multidisciplinary project will benefit from the (i) expertise of partners in food safety as well as animal and public health, (ii) high-level infrastructures and (iii) 9000 strains already available within the consortium of which 2000 are whole sequenced.

The project will improve scientific knowledge on the ecology of the bacteria by gaining insight into the adaptation, evolution and genetic make-up of strains that are successful in some environmental niches and not in others. The project will train Reference Laboratories to use WGS using COMPARE Standard Operating Procedures and will stimulate them to use WGS for the surveillance of *Lm* in their country. Finally, the new diagnostic tests aimed at identifying strains in food and animal reservoirs may arise from this project. These new tests should become key tools to improve the surveillance system, to assist the food industry in improving food safety and may have a significant economic impact and important benefit for society.
METASTAVA aims to evaluate the potential use of metagenomic analysis to the public health reference laboratory by targeted collection of reference data and reference materials, by generating focused validation data, and by proposing criteria and tools for a robust quality assurance of metagenomic workflows from sample selection to interpretation of results.

Metagenomic analysis is increasingly used to identify possible causes of unexplained disease outbreaks, to complement routine diagnostic evaluation, and to study the role of the microbiome and virome in health and disease. Currently, standardisation of metagenomics data generation and analysis tools is being sufficiently covered by other ongoing initiatives (including COMPARE). However, translating these promising technological developments into diagnostic tools for veterinary and public health laboratories requires careful validation, which is the focus of this project.

In order to use Metagenomic analysis for robust diagnostics, METASTAVA identified several important gaps in our knowledge of NGS and metagenomics that must be filled:

1. Development of a set of reference data for the model pathogens, representing most common sample types
2. Development of harmonised workflows for the generation and analysis of metagenomic data fitting to a defined diagnostic scope for the model pathogens
3. Development of a validation protocol for metagenomic diagnostics (including quality assurance and robustness testing).

The METASTAVA project is addressing the identified gaps and using hepatitis E virus (HEV), norovirus (NoV), zoonotic pox viruses, antibiotic resistant bacteria and Shigatoxigenic Escherichia coli (STEC), as model pathogens in developing the methods and reference datasets.

In short, where ongoing initiatives invest in the standardisation of metagenomics tool sets, METASTAVA wants to bring metagenomics to the diagnostic laboratory.
AIR-SAMPLE aims to develop and validate air sampling as a low cost and multi purpose alternative to fecal droppings or boot swab for surveillance, monitoring and eradication of Campylobacter in confined and biosecured broiler production.

Campylobacter is a bacterium that can cause campylobacteriosis in humans. This is the most frequently reported food-borne illness in the European Union, with over 190,000 human cases annually (EFSA). Therefore, monitoring of Campylobacter in poultry is mandatory according to Directive 2003/99/EC. However, the current sampling techniques are mostly a century old and need modernization in order to adapt to automated and molecular detection techniques, reduce the cost of handling and transport, and provide faster laboratory results close to, or in real-time for multi-pathogen testing (Hoorfar, 2011). At present, on-farm sampling of poultry is done by taking fecal droppings or boot swabs. Lately, a novel method that consists of sampling air on gelatin filters has been developed to demonstrated the presence of Campylobacter in ambient air from broiler flocks in production houses (Olsen et al., 2009; Søndergaard et al., 2014). As part of the EU project CamCon, the air sampling approach was further showed to be highly sensitive, cost effective as well as user friendly under various poultry farming conditions (Søndergaard et al., 2014). Moreover, no technical skills are required to perform air sampling in poultry flocks, and the sample is microbiological stable and thus can be shipped for analysis by ordinary mail, rendering the approach suitable for self-regulation.

The AIR-SAMPLE project will provide the European community (authorities and industry) with a low cost and harmonised tool for interventions as well as codes of best practices. The main outcome will be a harmonised and standardised, filter based sampling protocol that can replace the current cumbersome and time consuming microbiological methods. Air sampling should be feasible for surveillance, monitoring and eradication of Campylobacter in confined and biosecured broiler production.
MoMIR-PPC aims to develop new approaches to predict, identify and prevent the appearance of animal and human Super-shedders based on immune response and gut microbiota composition.

Early studies on infectious disease epidemiology assumed that susceptible hosts within a population had equal chances of becoming infected. Consequently, the majority of control measures and intervention strategies are based on this paradigm as well as the mathematical models of pathogen transmission. Recent studies have uncovered the importance of host heterogeneity in infection and it has been shown that a minority of the infected individuals are responsible for the majority of the infections. In the case of pathogens transmitted via the faecal oral route, these individuals are those that shed the highest numbers of bacteria and are known as Super-shedders. The most important zoonoses (salmonellosis, colibacillosis and campylobacteriosis) are no exception (Marshall & French 2011 MAF; Bearson et al. Infect Genet Evol, 2013).

MoMIR-PPC’s main objective is to improve EU industry sustainability and safe trade by providing information and tools leading to on-farm control of the bacteria. To maximise the feasibility of the project, the focus is put on *Salmonella* infection, which is a priority for Europe (The EFSA Journal, 2013 11(4)). Salmonellosis will serve as a model for other zoonotic bacteria as *Campylobacter* and *E. coli*. The biomarkers, diagnostic tools and the control measures obtained in this project should be easily translated to these bacteria in a future project.

The main achievements will be the development of:

1. Predictive markers based on that will sign the risk to become a Super-shedder of *Salmonella*
2. Immune and microbiota biomarkers of excretion that will be useful to detect animal Super-shedders and/or human prolonged carriers
3. Preventive measures and/or control measures of this zoonotic problem by the characterisation of prebiotics, probiotics and nutraceutical products, which could be use in animals but also in human
4. A pool of biosecurity measures at the farm levels, with a cost effectiveness, thanks to the mathematical models at between and within host scale. These mathematical models will provide new tools to risk managers for prevention and control of *Salmonella* infections but which should be easily adapted to other zoonotic pathogens.
MedVetKlebs is a multidisciplinary international project that aims to define the ecology of *Klebsiella pneumoniae* (*Kp*) and the sources of infections of humans and animals in order to investigate transmission routes and to find an optimal way to control them.

*Klebsiella pneumoniae* (*Kp*) is a major cause of hospital-acquired infections such as pneumonia, bloodstream infections, infections in newborns and intensive-care unit patients. In 2014, *WHO’s global report on AMR* revealed that the resistance to the treatment of last resort (carbapenem antibiotics) for life threatening infections caused by a common intestinal bacteria, *Kp*, has spread to all regions of the world. In the western world, *Kp* represents nearly 10% of nosocomial infections and is one of the most problematic multidrug resistant (MDR) organisms, with increasing resistance to carbapenem and other ‘last resort’ antimicrobial agents (colistin, tigecycline). The European Parliament report on Antimicrobial Resistance (*IP/A/STOA/SC/2005-173*) stated: “The increasing development of such pan resistant organisms has the potential to become a worldwide catastrophe.”

In this context, MedVetKlebs aims to improve of public and animal health through a better control of *Kp* infections by:

1. Developing and harmonising detection and isolation methods;
2. Ensuring a broad sampling of ecological niches and deep sampling of potential sources;
3. Performing genomics analysis and transmission modeling, including development of new methods for source attribution and risk assessment.

To achieve the above objectives, MedVetKlebs brings together partners from different sectors (fundamental microbiology, medical, veterinary, food, environmental sectors, and bioinformatics) located in different European countries in order to ensure sufficient geographical coverage of sampling.

Furthermore, MedVetKlebs will develop an efficient scheme of dissemination and implementation of obtained results to all concerned parties and to general public.
The DiSCoVeR project brings together experts from different disciplines (microbiology, bioinformatics and epidemiology) and sectors (veterinary science, food safety, public health and environmental health) from 19 institutions in 13 European countries into a unique consortium to address the challenges of source attribution in an interdisciplinary manner. As there is no gold standard for source attribution, we will take a comprehensive approach applying several different methodologies and models in a comparative fashion.

The project will map the existing knowledge gaps and recommend new studies and/or methods that are needed to fill them. The work will start by mapping existing data and establishing a joint data sharing platform for the project partners. We will include data from a broad range of reservoirs and sources, including those that are not traditionally part of existing monitoring and surveillance activities, e.g. pets (incl. reptiles), wildlife, and environmental sources.

The work will also focus on cataloguing, evaluating and advancing existing methods for source attribution and develop methods for the critical assessment of source attribution models. Novel approaches for source attribution will also be explored, developed and assessed. Existing approaches that will be investigated include the microbial subtyping, meta analysis of case control studies and outbreak data, and risk assessment based methods. The source attribution estimates will focus on three pathogens (Salmonella, Campylobacter, and STEC) and AMR.

We expect by the end of the project to have identified and filled important knowledge, methodological and data gaps for source attribution of zoonotic pathogens and AMR determinants through systematic collection and analysis of existing and new data and by applying existing, modified and novel approaches. We will make recommendations on how source attribution estimates can be translated to policy action to support the surveillance, control and prevention of foodborne infections in EU. These recommendations will be presented for and discussed with stakeholders such as ECDC and EFSA, and farmer and consumer organisations.
Salmonella and Hepatitis E virus (HEV) are zoonotic pathogens which are in general subclinical in pigs. Salmonellosis can cause gastrointestinal diseases in humans with over 90 thousand confirmed cases and 156 deaths in the EU in 2017. HEV infections in humans can be fatal; it is considered an emerging problem in the EU. Biosecurity protocols are highly important tools to reduce the load of such pathogens along the food chain, leading to safe and healthy animal derived food.

We built a dense network of European research organisations including public health from all European regions, joining expertise in veterinary epidemiology, microbiology, veterinary and human medicine, agronomy, econometrics, bacteriology. This BIOPIGEE project concentrates on the pathogens Salmonella and HEV.

A biosecurity protocol for the primary production will be developed. Applying this protocol, herds in the project partners’ countries identified as being at high or low pathogen risk will be assessed for their biosecurity to find best practice at different production stages. Additionally, field and intervention studies will be completed in areas where current evidence is weak, e.g. effectiveness of management controls on HEV prevalence. Furthermore, a protocol for slaughterhouse biosecurity will be developed and applied in partner countries. The persistence of Salmonella, HEV and other pathogens in reservoirs (biofilms) will be evaluated in depth together with studies of disinfection effectiveness.

The consortium partners’ disease transmission models (stochastic, network trade, quantitative microbial risk assessment) will be improved by newly gained empirical data. Scenarios on country specific biosecurity measures and on the measures’ impact on human infection rate will be run. Results will be used to assess the economic profitability of the implementation of standard and specific intervention measures along the pig supply chain and to assess projected future pork product derived human salmonellosis cases.

A catalogue of biosecurity measures will be continuously filled with the findings on the measures’ effectiveness and costs for Salmonella and HEV. A benchmarking of biosecurity practice (measures, categories and overall) will be developed which considers different production stages as well as European regions. Finally, dissemination activities include comprehensive education material for e.g. farming schools and online use, a support tool to calculate cost effective measures and a workshop series that will connect researchers and stakeholders and help to exchange knowledge and experience all along the chain “from farm to fork”, with special focus on primary production.
TOXOSOURCES is a unique international collaboration with optimal complementary expertise on the zoonotic parasite *Toxoplasma gondii* at the interface of humans, animals, food, and environment.

The TOXOSOURCES project will address the research question – What are the relative contributions of the different sources of *T. gondii* infection? – using several multidisciplinary approaches and novel and improved methods to yield the most robust estimates possible that can inform risk management and policy makers.

The main outcomes of TOXOSOURCES are quantitative estimates of the contribution of the main sources and transmission routes of *T. gondii* infection based on improved source attribution models, new data filling the key knowledge gap about the role of increasingly popular but unstudied ready to eat fresh produce, a novel serological method that aims to specifically detect infections caused by oocysts, and a novel typing method to improve preparedness to detect introduction of atypical *T. gondii* strains by import and to trace the infection sources in outbreaks.

All the results are integrated to contribute to developing efficient interventions at national, regional, European and global levels. TOXOSOURCES will have immediate and long-term societal impact, and has potential, ability and ambition to advance science.

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Swedish National Veterinary Institute (SVA), Sweden
Institute of Food Safety, Animal Health and Environment (BIOR), Latvia
DTU National Food Institute (DTU), Denmark
Statens Serum Institut (SSI), Denmark
Friedrich-Loeffler-Institut (FLI), Germany
The German Federal Institute for Risk Assessment (BfR), Germany
Robert Koch Institute (RKI), Germany
National Veterinary Research Institute (PIWet), Poland
National Institute of Public Health (NIPH), Czech Republic
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Istituto Superiore di Sanità (ISS), Italy
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French Agency for Food, Environmental and Occupational Health & Safety (ANSES), France
National Institute for Public Health and Environment (RIVM), The Netherlands
Wageningen University and Research (WUR), The Netherlands
University of Surrey (UoS), United Kingdom

This project also includes external partner(s).
Salmonellosis remains the second most common zoonosis in humans in the EU despite a significantly long term decreasing trend in human cases since 2008. In recent years this decreasing trend has levelled off. In laying hens, the prevalence of positive flocks for the target serovars, and especially for S. Enteritidis, has also increased after a long period of documented reduction.

Several hypotheses have been made, including more complete reporting and improvements in the surveillance of human salmonellosis, premature relaxation of Salmonella control measures at primary production, possible deficiencies in the enforcement of existing control measures and sensitivity of statutory sampling programmes, and changed/increased exposure patterns.

The ADONIS project will identify determinants underlying the stagnation/reversal of the decreasing trend in Salmonella Enteritidis incidence in humans and poultry in the EU. We will apply a cross sectorial approach where we will investigate possible explanatory factors at the levels of primary production, epidemiology/exposure, and the pathogen itself.

At the primary production level, the project will evaluate possible changes in flock management and possible insufficiencies in control measures implemented to date in poultry farms related to the implementation of vaccination programmes as well as the application of strict farm hygiene controls and sensitivity of the statutory sampling implemented in commercial flocks.

At the public health level, this project will evaluate national surveillance systems for S. Enteritidis in humans, assess changes over time regarding epidemiological characteristics, and calculate the total reservoir output exposure loads.

At the pathogen level, we will assess whether the recent plateau in salmonellosis incidence in Europe could be related to the genetic variation of the Salmonella bacterium, primarily S. Enteritidis, such as the emergence or clonal expansion of specific bacterial strains with increased fitness in the form of e.g. increased bacterial division, increased virulence or antibiotic resistance. Finally, the data and information gathered will be ranked and prioritised by a Multi Criteria Decision Analysis modelling.
BeONE will develop an integrated surveillance dashboard in which molecular and epidemiological data for foodborne pathogens can be interactively analysed, visualised and interpreted by the relevant experts across disciplines and sectors.

Surveillance of foodborne infections and outbreak detection/investigation is primarily handled at the national or regional level with several institutions/parties spanning different sectors and disciplines. The continuous increase in the complexity of data to be analysed and integrated, e.g. epidemiological and genomic data, as well as the need for international cooperation in solving multiple country outbreaks enhances the needs for informatics tools that can allow integration of the various types of data and facilitate their visualisation and interpretation.

Building on previous experiences and existing components, a tool tailored specifically to institutions in the public health/animal health/food safety sectors will be created. The use of dynamic similarity thresholds for different epidemiological situations and investigate cluster congruence between different genome sequence-based typing approaches will be introduced. The developed dashboard will aim at meeting the needs of the national institutions for communication with the EU wide systems, e.g. TESSy and the future ECDC/EFSA joint database of genomic data.

The project will bring us beyond the state of the art by developing a tailored surveillance system, facilitating consistent definition of outbreaks across domains and countries by the use of new algorithms based on integrated genomic and epidemiological data, as well as facilitating communication and flexible data sharing.

With input from a broad range of partners and experts, the development in the project will mainly be performed by partners with experience in using molecular epidemiology, WGS and bioinformatics in the surveillance. The project aims to fulfil the needs of partners at all levels of experience and it is the goal that the project can assist a smooth and efficient transition to a WGS based and integrated surveillance across Europe.
**IMPART** consists of four topics related to the development and harmonisation of phenotypic methods for detection of antimicrobial resistance, in line with the Commission’s Action Plan Against the rising threats from Antimicrobial Resistance: Road Map (updated on November 2016):

1. selective isolation and detection of colistin resistant Enterobacteriaceae
2. selective isolation and detection of carbapenemase-producing Enterobacteriaceae
3. development of a standardised disk diffusion method for susceptibility testing of *Clostridium difficile*
4. setting ECOFFs for specific pathogen/antibiotic combinations.

This project will result in a validated and sensitive method to detect colistin resistant (carrying *mcr*) and carbapenemase-producing Enterobacteriaceae (CPE) in caecal samples from animals and in food. This is essential for the monitoring of the current prevalence and spread of bacteria carrying these emerging resistance genes in animals and the risk of transmission of these genes via food.

Additionally, in order to provide a suitable and cost effective method for antimicrobial resistance surveillance of the zoonotic pathogen *C. difficile*, a disk diffusion method will be developed and standardized for a broad range of antimicrobials. The generated distributions of inhibition zone diameter will support future work on setting epidemiological cut-off values (ECOFFs). Furthermore, the setting of ECOFFs for veterinary pathogens will highly improve harmonisation of monitoring of resistance in animal pathogens and support the process for defining animal species specific clinical breakpoints for veterinary antimicrobials which will ultimately lead to more effective and prudent use of antimicrobials in animals.
The ARDIG project examines the dynamics of AMR in the human, animal, food and environment epidemiological unit from 6 European countries (UK, Norway, France, Netherlands, Germany, Spain), which represent significant difference in their usage of antimicrobial agents and AMR prevalence, as well as different climate and management systems, and the potential for transmission of resistance.

The project explores the ecological impact of administration of antibiotics to humans and animals, and their environment, across six countries using a One Health approach. This will provide a better understanding of the types of resistances, their prevalence and variation in different populations over time, so the occurrence of multi-drug resistant (MDR) superbugs can be controlled. Moreover, the work will help overcome the immense limitations in comparability between data from the different sectors and countries, as highlighted in the JIACRA report.

It is expected that the results will help identify factors influencing the transmission of AMR between animals, humans, food and the environment which can be applied not only to provide a basis to improve existing national surveillances, but also to aid in the design of new or improved global AMR surveillances strategies, as well as risk and transmission models for assessing future control measures and mitigation of risk posed by AMR. The knowledge gathered can also serve, in the future, for development of novel targeted diagnostic applications for rapid surveillance and control.
The RaDAR project aims to generate consensus estimates for sources attribution, risks of exposure and disease burden of AMR by integrating available data from various sources.

Resistance mechanisms emerge and spread globally. Circulation of antibiotic resistant bacteria in food and the environment and the resulting exposure of human beings to these bacteria may be significant. In general, information on the overall exposure to AMR from food and the environment is scarce. Therefore efforts are needed to fill data gaps and systematically integrate data into consensus estimates for sources attribution, risks of exposure and disease burden.

The RaDAR project aims at filling these gaps with a multidisciplinary and cross member state approach by:

1. Addressing the relative and absolute contribution of animal and environmental sources to the public health burden of AMR
2. Linking data on antimicrobial consumption and the effects of different kinds of antimicrobial use on AMR in animal husbandry
3. Modeling the spread of resistance determinants in microbial communities, the environment and along the food chain
4. Quantifying human exposure and disease burden.

The project will develop generic risk and transmission models that may be adapted to various bacterial species and resistance determinants. It will generate consensus estimates for sources attribution, risks of exposure and disease burden of AMR by integrating available data from various sources and will lead to a consolidation of the international cooperation with respect to the assessment of risks related to the complex AMR problem.
Antimicrobial resistance (AMR) threatens some of the greatest medical advances in modern times. Current AMR and pathogen detection is primarily reliant on classical culturing techniques, which may be slow. The development of new tools for real-time detection of resistant pathogens is a priority topic of the One Health EJP. On-site and real-time analysis requires independence from culturing techniques to facilitate rapid interventions, especially during outbreaks. Furthermore, it requires robust protocols using minimal technical equipment that can be used outside of the normal laboratory environment. Metagenomic sequencing using short-read data can detect the composition of microbial communities for the assessment of potential pathogens and AMR or virulence genes, which could become an invaluable diagnostic tool. However, short-read technologies cannot reliably associate individual genes in a community to specific organisms and is a potential limitation for detecting AMR in pathogens.

The FARMED project aims to address these issues by using the ONT MinION, comparing this technology to other metagenomic sequencing technologies, and assessing its ability for diagnostic use on a range of sample matrices within both the laboratory and the field. Using long-read metagenomic sequencing, the local genetic context of AMR genes can be derived, and as such, the presence of the AMR genes can be attributed to specific species and plasmids, within the bacterial community. This technology will enable the identification of a plethora of bacterial species and linkage of particular species to a range of AMR genes. We will create harmonised protocols for on-site metagenomic DNA extraction and sequencing library preparation on the MinION, and simultaneously adapt existing methods for DNA extraction with the ONT VolTRAX system. We will develop efficient real-time mapping strategies that identify the origin of the genetic context of AMR genes, identify the host bacterial species to enable specific pathogen detection.

In addition to on-site metagenome analysis, we will investigate and establish best practice for ‘off-site’ analysis of plasmids sequences by comparing with purified isolates. We will compare the use of long-read and short-read data, as well as a combination of the technologies such as Hi-C, to assemble complete plasmids from metagenomics data. Hi-C sequencing is a novel method that uses proximity ligation of DNA molecules to determine the genetic context of AMR genes in relation to linkage to the bacterial host chromosome. Defined communities, containing isolates harbouring known plasmids, will be used to determine whether plasmid sequences can be derived from these metagenomic data.

We will provide an interactive workshop to transfer our extensive wet- and dry-lab experiences, including molecular and bioinformatic expertise, gained from this project. We predict that the methodologies and tools emerging from FARMED will be highly attractive and imminently applicable to a wide range of users beyond the consortium, to rapidly monitor AMR present in pathogens in many different environments. We envisage this technique, will be especially useful in low or middle income countries where the burden of pathogen occurrence and AMR may be high but there is limited access to specialist or even ‘standard’ laboratory equipment for diagnosis.
Current European monitoring systems for antimicrobial resistance (AMR) fall short in dissecting clonal from horizontal transmission of AMR genes. Although an increasing emphasis is put on genomic based surveillance, mobile genetic elements (MGEs) remain challenging to reconstitute due to their chimeric, modular and repetitive nature. These MGEs often encode resistance to critical antibiotics and can spread within or across species and genera, making them a central part of any AMR transmission study.

The **FULL-FORCE** consortium will broadly introduce single molecule real-time (SMRT) sequencing in EU veterinary and public health institutes. This technology allows real-time sequencing with long sequence reads, providing additional information of where a read should be placed in the genome. Building on JPIAMR’s SOLIDNESS results, we will harmonise, build and test each institute’s SMRT sequencing capacity.

We will apply this knowledge on six study cases which will greatly profit from MGE sequencing, including samples isolated in the context of national surveillance programmes, EFFORT and ARDIG projects. This will be followed up by detailed investigation of prominent MGEs, and by applying this knowledge to modelling efforts of AMR dynamics in closed production systems. At the same time, high quality MGEs sequencing will provide an excellent dataset to test the performance of public and in house developed tools for MGE typing, and to study associations between AMR genes and MGEs in metagenomic datasets from the EFFORT project.

In conclusion, **FULL-FORCE** will supply 17 EU partners with a technological toolbox and hands on training in SMRT sequencing. This will allow a paramount step for the effective integration of MGE typing in One Health AMR surveillance, whilst delivering an unprecedented insight in dominant MGEs which are driving resistance among commensal and pathogenic Enterobacteriaceae in Europe. Full Force ahead.
The work to be undertaken in this WORLDCOM project will involve the development of real-time diagnostic on-site tools for the detection of zoonotic pathogens focusing on *E. coli*, *Salmonella* and *Campylobacter* together with resistance markers for identification of AMR including CTX-M-15, NDM-5, KPC-2, OXA-48 and MCR-1. Multiplex assays for both pathogen and resistance genes using novel isothermal technology Loop Mediated Endonuclease Cleavage-Loop Mediated Isothermal Amplification (LEC-LAMP) will be developed and evaluated in the first instance for use in a laboratory setting on standard laboratory platforms.

The use of isothermal amplification technologies including LAMP and LEC-LAMP (developed at NUI Galway), with the capacity to detect and differentiate single nucleotide polymorphisms (SNPs), will enable the development of AMR detection assays which will be suitable for use both in a laboratory setting and on site, since complex instrumentation will not be required for amplification or for product detection. It is planned to incorporate the assays into a nucleic acid lateral flow (NALF) device, which will be evaluated for on site application, with particular focus in the first instance on pen side use in a farm setting. Additionally, the tests developed will be evaluated for use in environmental (irrigation, recreational and drinking water) and clinical settings (human samples).

The output of the on site NALF assays will be communicated via a custom designed smartphone application, which will link to relevant reference laboratories. This platform will facilitate early warning of potential zoonotic threats and enable follow up epidemiological investigations to be conducted using the full complement of lab developed tools if warranted, including phenotypic and genotypic characterisation following isolation of the pathogen of interest from the corresponding sample.

A genomics approach will be used to develop a reference database of sequences from currently circulating AMR pathogenic strains, which will complement the IT and diagnostic assay tools in the WorldCom project. This task will involve curating relevant available sequences and targeted *de novo* sequencing of currently circulating and phenotypically characterised pathogens from the farm, environmental and clinical settings.

The sequence information in the reference database will be used to design the diagnostic assays and to develop and train novel Machine Learning algorithms for the detection and prediction of antimicrobial resistance from sequence data.

The novel combination of modified isothermal amplification technology, NALF devices capable of being used on site and mobile technology will be the basis of an innovative, early warning toolkit for prediction of antimicrobial resistance in various environments.
Over the course of the FED-AMR project, the relevance of horizontal antimicrobial resistance gene (ARG) transfer on free extracellular DNA (exDNA) over ecosystem boundaries relative to bacterial conjugation will be evaluated.

ExDNA is widely present in natural environments and sufficiently stable to constitute an important reservoir for ARGs. The dissemination of AMR on exDNA over ecosystem boundaries will be monitored under controlled but naturally occurring environmental conditions in an open-air agricultural research area: The Hydrology Open Air Laboratory (HOAL) in Petzenkirchen, Austria. ARG concentrations, diversity, dynamic variability, mobility and bacterial biodiversity will be determined in an annual longitudinal study covering a crop growing period, different fertilisation and land management techniques and various different – but interlinked – environmental compartments along the route: pig farm -> manure -> soil -> crop/food/feed -> ground/surface water -> pig farm (and other associated human compartments). The results obtained from HOAL will be compared with data retrieved from equivalent compartments in Northern, Eastern and Southern Europe. Movement of ARGs over ecosystem barriers will be inferred by sequence comparisons and construction of phylogenetic trees of ARGs and ARBs. The linkage between human and non-human reservoirs of AMR will be investigated exemplarily with *C. difficile* as ARG transfer platform over ecosystem boundaries and conjugation as means for HGT.

The prevailing selection pressure in each tested habitat during the longitudinal study will be determined by quantifying antimicrobials, herbicides and trace elements in the tested compartments. Environmental conditions which may induce or inhibit the expression of competence genes that are necessary to enable the uptake of free extracellular DNA by bacteria will be identified in soil microcosms and in a pig gut model. The impact of transformation relative to conjugation will be evaluated using *Acinetobacter* sp. (transformation) and *C. difficile* (conjugation) as model organisms in these experiments.

Experimental data obtained during the project will be used to feed and tune probabilistic modelling of the emergence of AMR in target bacteria and to delineate the relative contribution of transformation and conjugation to ARG acquisition in soil environments. Mechanistic models will address key questions regarding the spatio-temporal changes observed in microbial communities and shall support the identification of critical control points for intervention to reduce the spread of AMR from environmental sources.
The MAD-Vir Project aims to further develop a metagenomics microarray technology with adequate sensitivity for clinical application to improve fast detection of viral FBZ agents and emerging threats.

Epidemics and outbreaks of emerging viral diseases are a growing global threat. The recent Ebola, MERS-CoV and Zika virus outbreaks illustrate this. It is vital for the control of spread of any infectious disease to identify the pathogen and source of disease rapidly and accurately. Early, rapid and bio safe diagnosis of unusual and imported cases offers the best preparedness. However, many infections show similar symptoms (syndromes) or initially non-specific symptoms, making them clinically difficult to recognise. It can also be difficult to distinguish disease syndromes caused by an emerging or new virus from those of other common diseases.

In order to improve fast detection of viral FBZ agents and emerging threats, a metagenomics microarray technology (Pan-Virus-Array) with adequate sensitivity for clinical application was developed. It provides rapid simultaneous identification of all known virus but also all virus families. This approach is very fast, easy and cheap (compared to NGS) and can eliminate the need for a specific clinical hypothesis.

The MAD-Vir project aims at further developing this microarray chip to allow easy update with new virus probes and to implement the Microarray chip method in 4 EU reference laboratories. This metagenomic microarray will also be compared to other diagnostic methods that have already been developed (e.g. pathogen specific PCRs, Microfluidic PCRs, Nanostring) and used in the testing of suspicious and imported disease cases as well as surveys.

The development and harmonization of this non NGS based metagenomics method for detection of viral FBZ agents and emerging threats might aid in an early identification of zoonotic pathogens and may aid in outbreak preparedness.
The TOX-detect project aims to contribute to an increased consumer health protection by filling the critical gaps of lacking methodologies to detect bacterial toxins and characterizing foodborne toxigenic bacteria.

Every year, around 5,000 foodborne outbreaks (FBOs) are reported in the EU (EFSA), with bacterial toxins produced by *Staphylococcus* spp., *Bacillus* spp. and *Clostridium* spp. Overall, nearly 10,000 human cases caused by bacterial toxins are annually reported in the EU (EFSA). However, the true incidence of FBOs caused by toxigenic bacteria is underestimated for many reasons (misdiagnosis, under reporting, improper sample collection and laboratory examination). Moreover, FBOs caused by toxigenic bacteria share a common symptomatology, leading to difficulties in outbreak investigation to clearly identify the responsible causative agent. All this may also explain why the proportion of “weak evidence” FBOs is particularly high in case of bacterial toxins being the causative agent.

To contribute to the detection of bacterial toxins and characterising foodborne, the main objectives of TOX-detect are:

1. The establishment of an EU wide network focusing on the detection and identification of the toxigenic bacteria * aureus, B. cereus* and *C. perfringens* and all agents being at the interface of human and animal health, as well as food safety.
2. Screening for information within Europe, resulting in the evaluation of existing and developed methods for screening/confirmation and identification of toxigenic bacteria.
4. Implementation and development of:
   a) New (“non-NGS”) approaches for a better detection and quantification of bacterial toxins or factors involved in the virulence of toxigenic bacteria, including those that remain currently undetectable (emerging threats)
   b) Rapid (pen side) methods allowing to discriminate between pathogenic and non pathogenic bacteria and further to analyse their toxin gene expression will be developed and harmonised as complementary tools.
5. Exchange of information and know how between network partners, including information on protocols, reagents etc., to establish a European network of national reference, verification and diagnostic laboratories working on toxigenic bacteria.
The TELE-Vir project key aim is to develop a very fast point-of-incidence toolbox for identification and characterisation of emerging virus threats for humans and/or domestic and wildlife animals. Third-generation sequencing using the MinION device (Oxford Nanopore Technologies) has shown to be a promising fast diagnostic sequencing tool. We believe that when combined with a suitable field deployable point-of-care approach, and a direct upload of genomic, phenotypic and epidemiological data into a user-friendly bioinformatics toolkit, a very fast identification and characterisation can be performed.

The poi toolbox will be built on already developed point-of-care virus inactivation and nucleic acid extraction methods and expanded to a standardised protocol for the MinION sequencing of both DNA and RNA virus in clinical specimens. The bioinformatics part will be built on an already existing bioinformatics platform like the INSaFLU and will enroll user friendly graphical interfaces from the very beginning of the workflow (assessment of quality of sequencing reads) until the final outputs (e.g., phylogeography charts enriched with associated sample metadata and relevant viral genotypic and phenotypic features such as the available data on virulence, host and, if applicable, vector) ranges, transmissibility, persistence in the host and in the environment, drug resistance, antigenicity, etc.).

In addition, a graphical output of results will be accessible to a non expert audience. This point-of-incidence toolbox allows for an easy, rapid and user friendly in situ identification with immediate characterisation and hence a very fast response and improved decision making during an outbreak or a potential outbreak of an emerging or re emerging virus threat, which will aid in the overall outbreak preparedness in Europe.
**MEmE** is a multicentre collaborative international project aiming to fill the research gaps highlighted by international agencies (EFSA, ECDC, WHO) for the detection and control of cystic and alveolar *Echinococcosis* (CE and AE, respectively).

MEmE, expanding the results of previous European projects, will focus on both the standardisation, harmonisation and validation of existing parasitological and molecular methods, and the development and comparative assessment of innovative molecular tools and biomarkers to detect *Echinococcus multilocularis* (Em) and *Echinococcus granulosus* sensu lato (Eg) in the food chain. These tasks will be conducted in line with OIE principles and methods of validation of diagnostic assays for infectious diseases. A biomarker discovery task will also focus on the proteomic analysis of exosomes in sheep plasma, to develop innovative tools for the detection of CE the natural intermediate host.

Production of epidemiological data on the presence of Em/Eg eggs in the food chain will focus on vegetables for human consumption as well as dogs’ faeces in selected endemic countries. Moreover, food source targeted questionnaires will be developed and administered to a sample of patients with CE, in selected hospitals, including those registered in the European Register of CE (ERCE), and AE and matched controls, to advance our knowledge on food related risk factors for human infection.

Long term capacity building and alignment of European research strategies at national and EU level is expected through the MEmE network, which includes inter alia the European Reference Laboratory for Parasites, WHO Collaborating Centres, OIE Collaborating Centres, National reference laboratories for parasites/*Echinococcus* and the HERACLES Extended Network. Organisation and delivery of parasitological and molecular Proficiency Testing Schemes on the validated techniques will be organised by the MEmE network, after organisation of specific training through short exchange visits for key personnel between network laboratories. Some of the techniques validated for detection of Em/Eg may also be translated to epidemiology and diagnosis of human infections, within a One Health approach.

Altogether, MEmE will provide a comprehensive set of relevant integrative activities (including development and validation of protocols, collection of biological material, capacity building, and epidemiological investigations). These will allow partner organisations to harmonise procedures, improve detection of Eg and Em, and define control strategies based on the occurrence of these pathogens in the food chain and the relative importance of their foodborne transmission.

Norwegian Veterinary Institute (NVI), Norway
Swedish National Veterinary Institute (SVA), Sweden
Veterinary and Food Laboratory (VFL), Estonia
Statens Serum Institut (SSI), Denmark
Friedrich-Loeffler-Institut (FLI), Germany
National Veterinary Research Institute (PIWet), Poland
Istituto Superiore di Sanità (ISS), Italy
National Health Institute Dr. Ricardo Jorge (INSA), Portugal
The National Institute for Agrarian and Veterinarian Research I. P. (INIAV), Portugal
French Agency for Food, Environmental and Occupational Health & Safety (ANSES), France
National Institute for Public Health and Environment (RIVM), The Netherlands

This project also includes external partner(s).
**Foodborne parasites (FBPs) are major contributors to the global burden of gastrointestinal disease. In Europe, according to recent estimates, protozoa of the genera Cryptosporidium and Giardia are of particular relevance. These parasites are transmitted through direct and indirect routes, and cause large outbreaks linked to contaminated water and food. Outbreak investigation and source attribution remain difficult, also due to the existence of genetically highly variable species and genotypes of zoonotic origin.**

**PARADISE** aims to deliver informative typing schemes and innovative detection strategies applicable to food matrices for both parasites. Using NGS technologies (genomics and metagenomics), the project will generate much needed data that will enrich our understanding of the epidemiology and genomics of these organisms, and provide the basis on which improved strain typing schemes will be developed and rigorously tested. In parallel, strategies (nanobodies, aptamers, use of hybridisation probes) to enrich for the target pathogens in different matrices will also be developed and tested.

Furthermore, PARADISE will engage in multicentre studies to validate the newly developed methods, testing their applicability across the spectrum of relevant matrices in an unprecedented effort at the EU level. These new methodologies will form the basis for integrated approaches aimed at controlling FBPs in the European food chain.
Brucellosis is a highly contagious zoonosis usually caused by ingestion of unpasteurised milk or undercooked meat from infected animals, or close contact with their secretions. Brucellosis is one of the most widespread zoonotic diseases globally, with 500,000 new human cases estimated each year. For many years six ‘classical’ Brucella species were identified but, since the late 1990’s, several new Brucella species (including B. inopinata, B. microti and B. vulpis) were isolated from humans, wild animals and/or environmental sources demonstrating a wider range of hosts and new potential zoonotic threats. Some of these species are genetically and/or phenotypically atypical in comparison to the ‘classical’ species.

In 2017, European amphibians were reported to be infected by one such recently identified species (B. microti), already reported in rodents, foxes and wild boar, thus confirming the broad host range of emerging atypical Brucella. These emerging Brucella isolates need to be further investigated to evaluate their geographical distribution and host range, to assess their zoonotic potential, and to compare their virulence and persistence markers with classical species.

Other emerging situations concern classical Brucella species, such as Brucella suis and Brucella melitensis, which circulate in wildlife reservoirs with the potential to spillover to domestic animals and humans or which are emerging in Western Europe as a result of pet movements (Brucella canis). Currently only some classical Brucella species are subject to statutory control and surveillance strategies in domestic animals in Europe. Therefore, these species are potentially underdiagnosed in wildlife. Some Brucella species are classified into biovars, and species and biovars vary in terms of pathogenicity for humans. The most studied Brucella species and biovars correspond to those presenting the known highest risk of transmission to humans while others are poorly characterised. Finally, emerging reservoirs of classical Brucella could be linked with new consumption patterns, with developing practices of organic and raw milk products, with imported animal-derived products from different origins or with emerging animal movement pathways.

An exhaustive evaluation and understanding of emerging non classical Brucella and emerging reservoirs of classical species is needed to protect people and animals from infection. This IDEMBRU project aims to develop a toolbox focusing on emerging Brucella species and reservoirs in order to ensure rapid detection, identification and characterisation. The project will include i) the detection and investigation of these pathogens from different sources under various epidemiological contexts in terms of natural landscape, livestock demographics, and wildlife populations (Mediterranean, East, North and West Europe); ii) the characterisation of the emerging Brucella species by identification of genomic and phenotypic variability via high throughput methods (NGS, molecular tests, proteomics, metabolomics); iii) the understanding of virulence and zoonotic potentials through in vivo and in vitro infection models; iv) the development of a toolkit for the integration of data from emerging Brucella and as a resource to guide characterisation of emerging Brucella.
**PhD Projects**

The One Health EJP funds 17 PhD projects. These projects aim to train the next generation of One Health scientists by facilitating a cross disciplinary approach to research.

One Health EJP PhD grants aim to help reinforce the collaboration between our partner institutes by enhancing transdisciplinary cooperation and integration of activities. As these PhDs progress, the PhD students will have the opportunity to expand their network, and to be part of a unique One Health EU community - for example, together with those who attend the other Education and Training activities such as the summer school and Short Term Missions or establishing links with JRPs and JIPs which would also form links between JRPs and JIPs. The PhD students also have the opportunity to present their progress annually at our Annual Scientific Meeting.

The OHEJP PhD projects provide excellent opportunities to:

- Provide interdisciplinary (med-vet-environment) training for the next generation of One Health researchers in Europe contributing to the sustainability of the One Health approach.

- Allow greater flexibility in the PhD projects to ensure innovative hypothesis driven research. To clarify, JRPs and JIPs align very stringently with the priority research and integrative topics defined in the Strategic Research Agenda (SRA), whereas PhD projects are relevant and within the scope of the SRA topics and align with the general objectives of the OHEJP i.e. prevent-detect-respond, in order to improve integration and societal preparedness to deal with foodborne zoonoses, antimicrobial resistance and emerging threats within the mandate of the OHEJP.

- Maximise international and interdisciplinary networking among OHEJP partners. In addition to interacting with the JRPs and JIPs, PhD students also have opportunities to interact with OHEJP stakeholders and national and international surveillance programmes to promote collaborations and ensure the sustainability of the OHEJP network.

- Explore and share skills, expertise and knowledge with the consortium, thus accelerating the rate and quality of research.

- Build a sustainable cohort with organised events throughout the OHEJP.
Trichinellosis is a zoonosis caused by the consumption of raw or undercooked meat of animals (mainly pigs, wild boars, horses) infected with the nematode *Trichinella* spp. Over the past decades, human trichinellosis incidence has decreased in the EU due to improvement of pig farming conditions and to stringent control measures implemented by controls at the slaughterhouse. The cost of trichinellosis control in pigs is estimated at 220 millions euros per year in EU. To date, *Trichinella* spp. remain in the top three of prioritised foodborne parasites in Europe (Bouwknegt et al., 2018). This parasite is still of major public health and economic importance at international level (Codex Alimentarius).

EFSA identified the type of production system as a main risk factor for *Trichinella* infections, and that the risk of *Trichinella* infection in pigs from officially recognised controlled housing conditions (ORCHC) is negligible. Therefore, EU regulation 2015/1375 introduced possible derogations from the necessity of testing each slaughter pig, if specific conditions are met. In order to verify that *Trichinella* is truly absent in such a population and to identify changes in disease prevalence at an early stage, monitoring programmes are recommended (EU 2015/1375). To date, serological methods have been identified, but are fraught with problems concerning specificity (false positives) and detection of infection at an early stage.

Due to the very low *Trichinella* prevalence in pigs from ORCHC, a test specificity bordering 100% is needed, as false positive samples would need to be retested with a second serological method (e.g. Western Blot). Such tests can only be performed by specialised laboratories, making the testing logistics more complicated and expensive.

Therefore, new diagnostic methods with higher specificity and earlier detection are needed for prevention at the slaughterhouse and to improve human disease detection, which will do in the AptaTrich project.
*Toxoplasma gondii* is an intracellular coccidian parasite and one of the most successful parasites worldwide.

Sexual reproduction resulting in shedding of oocysts occurs only in felids (definitive hosts), but virtually all warm blooded animals can carry tissue cysts and act as intermediate hosts. Humans, as intermediate hosts, become infected with *T. gondii* through ingestion of oocysts (e.g. when handling soil or cat litter, or on unwashed vegetables) or tissue cysts in raw or undercooked meat.

Meat appears to be a major source of *T. gondii* infections in Europe, as in an European multi-center case control study 30 to 63% of infections in pregnant women were attributed to meat, whereas 6 to 17% were most likely soil borne (Cook *et al.*, 2000).

Pigs, like other livestock, can harbour tissue cysts following the ingestion of oocysts or dead animals. The surveillance plan conducted by the Ministry of Agriculture of France in 2013, and carried out by ANSES in collaboration with URCA, showed that 3.0% (CI95-[0.9-5.0%]) of pigs raised in an indoor system and 6.3% (CI95-[2.6-9.9%]) of pigs raised outdoor were seropositive for *T. gondii*. This seroprevalence reached 13.5% (CI95-[13.1-13.9%]) in outdoor breeding sows. Viable parasite could be isolated in 22% (25/113) and 47% (16/34) of the indoor and outdoor pig carcasses analysed respectively.

With 40.4 kg per household in 2014, pork is the first meat consumed in France, whose ¾ is eaten in the form of sausage and salami products (FranceAgriMer, 2015). Among raw cured meats, dry sausage is the most widely consumed (about 75,000 tonnes of dry sausage per year in France). France alone produced just over 108,000 tonnes of sausages and dry sausages in 2015, representing about 9% of the total tonnage of all sausages (FICT data, 2016). The health safety of these products is therefore a major issue. The share played by the consumption of pork meat in human contaminations is not known, nor is the risk of transmission of the parasite via the consumption of cured meat products.

The TOXSauQMRA project aims at answering this lack of knowledge, providing though the bases for a robust QMRA analysis in France, an European country with a high *Toxoplasma* positive rate among humans.
Foodborne diseases remain an important cause of morbidity, mortality, and healthcare costs worldwide. For instance, in 2015 diarrhoea alone caused more than 1.3 million deaths and 71.59 million DALY globally. The problem is expected to be exacerbated by population growth and the rising of resistance to antibiotics. Furthermore, anthropogenic activities are constantly changing the environment (here and throughout we refer to weather, climate, land use and also socio economics factors as environment or environmental factors) which is a well recognised driver of diseases. The environment can affect pathogen abundance, survival, and virulence, host susceptibility to infection as well as human behaviour. It is thought that the accelerating rate of global climate and other environmental change will impact the distribution, frequency and patterns of established diseases as well as the emergence and re emergence of new and old ones. As a society, it is our duty to be prepared.

Our ultimate goal is to develop a tool to assess the public health risk of foodborne zoonosis based on information of relevant environmental factors. Accordingly, we are interested in the following overarching questions:

• Can we identify the key environmental processes triggering and propagating foodborne zoonoses?
• Can we disentangle the role of animal, human (including socio economic factors) and environmental factors in foodborne zoonoses?
• Can we identify the delay between variations in the environment (e.g. increase in the temperature or behavioural change) and the occurrence of a foodborne outbreak?
• How can we quantify their impact on Public Health?

For this EnvDis project we will focus on Salmonella, for which the mechanism of transmission is relatively well known (e.g. effects of temperature and water activity), which will help in validating our approach.
Cystic echinococcosis (CE) is a zoonotic parasitic disease of significant public health concern in many parts of the world. For example, over 5,000 new CE cases are reported in South America every year and a recent study has estimated that more than 150,000 people in Bulgaria, Romania and Turkey might be affected by CE. The burden, extending to include economic impacts, is mostly felt in subsistence livestock keepers and other marginalised rural and peri urban populations where other health competing threats persist. Under reporting of the condition is large and the evidence to inform efficient surveillance and control approaches scarce. The large range of surveillance and control measures across all hosts, and their heterogeneous application across geographies further complicates the aggregation and comparison of evidence to assess the performance of control programmes.

The MACE project will inform the most efficient portfolio of surveillance options and interventions towards CE control and elimination, accounting for the varying risks, disease control capacities, and risk preferences across geographies. The project is novel in the joint application of mathematical modelling and economic evaluation at fine spatial resolutions, and in the active elicitation of risk attitudes towards CE and related control measures to formally model their impact on the uptake of interventions and their efficacy.

We target two highly CE endemic areas in the world: south America, where CE control programmes have been operating for decades and the evidence is best to inform our models. The applicants have recently applied state-of-the-art analyses to integrate multiple surveillance sources (e.g. sampling of dogs, passive surveillance, and ultrasound screening on children) in Rio Negro (Argentina) to exhaustively map CE risk. The logical next step, as suggested here, is the integration of the existing risk maps with economic evaluations of the portfolio of interventions (e.g. sheep vaccination) adjusted for risks preferences (e.g. risk aversion, loss aversion). Our second geographical target is Albania where little evidence of CE exists. Here, one of the applicants will conduct a comprehensive survey of the country to collect ultrasound evidence of CE. The survey is planned to start in September 2019. The ultrasound data will then feed the model developed with the Argentinian data, to infer the true magnitude of CE in Albania. As the model contains the economic evaluation component, we will be able to generate multiple disease control scenarios (updated with local costs). Given that risk preferences may be context specific, we will also elicit risk preferences in Albania.

Our results will inform the ongoing regional control and elimination plan coordinated by the Pan American Health Organisation. This plan set up a number of strategic outcomes that our models will be able to operationalise and optimise. We note that two of the applicants are senior members of the South America Initiative for the Control and Elimination of CE that advises countries and PAHO on technical matters. Our results will also contribute additional insight into the true magnitude of CE in south east Europe, contributing thus to WHO’s roadmap plan for CE elimination. We note that two of the applicants are members of WHO’s Informal Working Group on Echinococcosis.
Hepatitis E virus (HEV) is a zoonotic virus responsible of acute hepatitis E in human in Western countries.

HEV is widespread in a number of animal species but the major animal reservoirs of HEV are domestic and wild pigs shedding HEV into the environment. However, the main route of HEV transmission in Europe is through consumption of contaminated pork. Consumption of raw or undercooked pork products have been associated to clinical Hepatitis E.

Molecular analyses showed that HEV strains detected in pigs and humans in the same geographical region present high genetic identity, indicating that swine are the main source of infection for humans. In European countries more than 50% of the pig farms may be affected and seroprevalence within these farms can be over 80%.

To identify the contamination sources of HEV in humans, HEV sequencing, genotyping and subgenotyping is often used. Regarding HEV subgenotypes in recent years in North-West Europe, a shift is seen towards HEV subgenotype 3c. It is unknown if this is a shift towards a more virulent or a more contagious HEV variant. Since 2014, an increase in clinical cases has been observed in many EU member states including the Netherlands.

During the summer of 2017 and 2018 in the Netherlands, a temporal drop was observed in acute HEV clinical infections, after which the incidence went back up to similar numbers as had been observed before. These events have remained unexplained to this date.

To explain the predominance of certain HEV variants and to elucidate differences in virulence, TRACE will characterize HEV variants and attempt to identify virulence factors in HEV strains detected in clinical HEV patients, in the general population and in domestic swine. Given the high genetic diversity of HEV it is critical to obtain higher resolution genomic data (i.e. whole genome sequences) in order to gain more understanding on its molecular epidemiology and possible variations in patho-adaptive traits.
Linezolid belongs to the oxazolidinone family of antimicrobials and is one of the last resort drug used to fight human infections caused by multi resistant Gram positive bacteria such as Streptococci, Staphylococci and Enterococci. It is commercially available since 2000 and has not been licensed for use in animals.

In 2008, the first instance of transferable resistance to Linezolid caused by the 23SrRNA methylase Cfr (for Chloramphenicol Florfenicol Resistance) was reported in US Staphylococcal isolates recovered from human infection cases. optrA is another gene conferring resistance to Linezolid and Phenicols whose sequence was first reported in 2015. It consists in an ABC-type of membrane transporter and works as an efflux pump. After its initial finding in China, it recently emerged in animal and human Enterococci / Staphylococci on both the American and European continents.

Cfr not only confers resistance to oxazolidinones but also to pleuromutilins, streptogramins, lincosamids and phenicols. EU Staphylococcus isolates harbouring Cfr were described from 2011 onwards, mainly in intensive care units. In China, the Cfr gene was first detected in a Bacillus sp. of animal origin in 2010 and soon after in Enterococci and Staphylococci.

Cfr emerged in EU livestock first in coagulase-negative Staphylococci and very recently in Methicillin Resistant Staphylococcus aureus (LA-MRSA) strains isolated from healthy pigs.

Though currently limited in terms of frequency, emergence of cfr in European LA-MRSA is most probably attributable to a selection mechanism driven by the veterinary use of antimicrobial molecules unrelated to Linezolid but acting in a similar way on the bacterial ribosome.

This raises important questions that we want to tackle through the present PhD proposal: Are optrA – and Cfr-carrying transposons horizontally transferred from humans to animals or the other way around, from animals to humans? Are peculiar transposon variants such as Tn558: Cfr the unique source of Cfr transmission or are there other genetic carriers of concern? What is the prevalence of these genes in Gram positive indicator bacteria isolated from healthy animals in the EU? What are the risk factors favoring their dissemination?

This LIN-RES project will investigate the molecular basis, origin, transferability and risk factors associated with Linezolid resistance emergence in Gram positive bacteria of both human and animal origin.
*Escherichia coli* contribute to AMR spread by clonal strains able to survive on the food chain and by its ability for horizontal transfer of genetic platforms (like plasmids and integrons) containing AMR genes across bacteria.

The presence of AMR *E. coli* in animal intestinal microbiota is well documented, especially in those animals which are under intensive production systems like pigs and broilers. Sows are, for instance, the main source of AMR *E. coli* populations in piglets, but their fate during the lifespan of pigs depends on different factors, especially the selective pressure imposed by antimicrobial use (AMU).

On commercial table eggs production, the dynamics of AMR *E. coli* populations have been scarcely studied. It is plausible that one day chicks represent a relevant source of AMR bacteria. However, since AMU use is very limited during the egg production stage due to the zero days of withdrawal period, the main selective pressure favouring persistence of AMR populations is almost absent. Thus, if there were no additional sources of AMR *E. coli*, those deriving from one day chicks should be reduced in the intestinal microbiota of hens, and thereby faecal shedding and the consequent risk of spread to the food chain (both directly through eggs and indirectly through manure used as organic fertiliser in crops) should be limited.

The main goal of this ECO-HEN project is to fill the gap on the transmission dynamics of AMR *E. coli* in commercial laying hen production and to determine to what extent this animal production poses a public health risks via food and/or environment contamination.
Based on recent advances in 16s NGS analysis, the microbiome of humans and animals has been shown to have major health effects. As such, modification of the microbiome through changes in diet can have therapeutic effects whereas treatment with antibiotics results in a drop in bacterial abundance which is generally considered a negative effect. While a study on the development of the human infant microbiome has shown three distinct phases of microbiome progression, we have recently shown that the chicken microbiome also develops along three distinct phases, although at a much shorter timescale.

The intestinal microbiome functions as a barrier for colonisation by ingested bacteria. As such, it is likely also a barrier for bacteria resistant to antimicrobials. Antimicrobial resistance (AMR) is a major public health concern due to a predicted global rise in treatment failure, mortality and the economic burden of rising healthcare costs. Many factors contribute to this including antibiotic use and misuse, global travel, hospitalisation abroad and the use of antimicrobials for treatment or as growth promoters in livestock. Although the attribution of AMR in livestock to human health is up for debate, it is desirable to reduce prevalence of AMR in livestock, foremost to decrease the likelihood of AMR bacteria passing through the food chain, but also to retain effective therapeutic treatment of the livestock itself.

The VIMOGUT project will study the chicken microbiome development of chickens on farms to determine if the reported microbial progression is reproducible between different production rounds and farms. By screening these samples for the presence of ESBL E. coli, the significance of the reduced diversity of early colonised chickens will be determined. The in vitro chicken gut model will be set up for use at WBVR to test strategies for the reduction of ESBL E. coli and compare these with published data from in vivo studies. When the model can efficiently reproduce these in vivo studies, it can be used for further study of new ESBL E. coli colonisation prevention strategies.
The implementation of genome sequencing in public health microbiology has allowed the natural variation exhibited by pathogenic bacteria to be leveraged for infectious disease surveillance and outbreak detection. Genotype information derived from WGS allows the monitoring of pathogenic potential and the tracking of epidemic behaviour, to inform infection control, diagnostic and treatment practice.

To track strains globally, and as they spread between the environment, food, animals and humans, universal strain nomenclatures are necessary. Two main strain nomenclatures approaches are currently existing. First, core genome Multilocus Sequence Typing (cgMLST) is widely applied for bacterial pathogen surveillance. It relies on predefined gene loci, the sequence variants of which are given unique identifiers (allelic numbers). Resulting allelic profiles are given unique identifiers (cgST) or are grouped based on their similarity, generally using the single linkage clustering method.

An alternative approach known as the SNP address was developed at Public Health England. Different from MLST, it is based on single nucleotide polymorphisms (SNP) compared to a reference genome. Single linkage clustering is performed based on the resulting SNP distance between isolates. An original concept of the SNP address is to apply several thresholds upon allelic or SNP differences.

The ‘address’ is a multi positions code, where each position corresponds to the cluster membership at descending thresholds of genetic (SNP) distance among strains resulting in a multi level nomenclature which provides a good approximation of the phylogenetic relatedness among isolates. Likewise, several cgMLST thresholds can be used to provide phylogenetic information on top of classification purposes.

Providing multi level information on phylogenetic relatedness has proved helpful for epidemiological investigations and for prospective surveillance. This has facilitated outbreak detection as well as providing the framework for case/control studies at different diversity levels, depending on the length or complexity of an outbreak.

Currently, no genomic nomenclature system of bacterial pathogens exists that combines complete stability of identifiers, high standardisation and reproducibility and high resolution. This gap represents an important barrier to the field of genomic epidemiology and slows down communication and action against the transmission of pathogens across sectors, world regions and over long periods of time. We will address this critical gap in the Codes4strains project.
*Salmonella enterica* serovar Kentucky (*S. Kentucky*) is a common causative agent of gastroenteritis in humans. It is one of most notorious *Salmonella* serotypes, as it is strongly associated with antimicrobial resistance (AMR). Ciprofloxacin resistant *S. Kentucky* (CIPR *S. Kentucky*) belongs to a single sequence type (ST198), which acquired of a variant of the *Salmonella* genomic island 1 (SGI1) conferring resistance to first line antimicrobials (β-lactams, aminoglycosides, sulphonamides, tetracyclines). The MDR clone has since then also accumulated various substitution mutations in the quinolone resistance determining regions (QRDR) of DNA gyrase (gyrA) and DNA topoisomerase (parC), such that most strains carry three QRDR mutations which together confer full resistance to ciprofloxacin as well. Phylogeographic analysis indicates this clone first emerged in Egypt ca. 1989, before disseminating into Northern, Southern and Western Africa, and then further to the Middle East, Asia and Europe.

The main reservoir of *S. Kentucky* is poultry, and domestic poultry has played an important role in its global spread (most recently in South Asia and Europe). Ciprofloxacin resistance is rare in *Salmonella*, and is hypothesised to be linked to strong selective pressure exerted by fluoroquinolone use in poultry.

In the KENTUCKY project, we will investigate (i) what explains the evolutionary success of the multidrug resistant *S. Kentucky* ST198 clone, (ii) what is the mechanisms of the integration (and potential further transfer) of the ESBL gene in its chromosome, and (iii) Are there genetic determinants of different human-animal host ranges in epidemic *S. Kentucky* ST198 and ST152?
The propagation and spread of microorganisms resistant to antimicrobials is a global phenomenon that is affecting both human and animal health. To address this concern from as early as 2006 there has been a ban in Europe on use of antimicrobials as growth promoters in animal husbandry. More recently national programmes have been implemented through ECDC and EFSA for medical and veterinary institutions in Europe to annually participate in antimicrobial surveillance, so resistance trends can be monitored in some key zoonotic and commensal bacteria isolated from livestock and food products, and also associated with human infections. Antibiotic stewardship programmes have also progressed in medical and veterinary sectors in many European countries, promoting prudent use of antibiotics in the afore mentioned sectors.

Therefore, through the One Health agenda the risk posed by the medical and veterinary sectors are being assessed and addressed, but there has been limited focus both in Europe and globally on the role of the environment in propagating resistant microorganisms through inadequate treatment of contaminated/waste water, or medical, biological and food waste, which may be dispersed further through wild life such as wild birds.

Migratory birds, which represent ~40% of total birds in the world, can fly many thousands of kilometres, often overwintering in Africa and Eurasia, and returning to the northern hemisphere in spring. These birds add another level of complexity to identify and control the routes for dissemination of AMR, as they often overwinter in countries or areas where there may be paucity of information of resistance trends due to limited surveillance and diagnostic capacity, with the burden of AMR unknown.

The WILBR project will help provide an assessment of the environmental risk posed by AMR and identify management options with clear indicators of effectiveness, there is a need to understand the contribution of factors such as wild birds to dissemination of AMR in the environment in general, and on livestock farms in particular.
Plazomicin is a novel semisynthetic aminoglycoside approved in June 2018 by the FDA to be used as a last resort antibiotic in complicated urinary tract infections (UTI) caused by multidrug resistant Gram negative bacteria in humans.

Approval by the EMEA is foreseen in 2019. However, the expression of acquired 16S rRNA methyltransferases by bacteria results in complete resistance to plazomicin. Added to the high level of resistance to this novel compound, bacteria harbouring these determinants show resistance to all clinically relevant aminoglycosides.

We identified in 2005 worldwide the first bacterium from animal origin bearing one such 16S rRNA methyltransferase. Since, us and other researchers have identified 13 of such methyltransferases, and they have been found in human, animal, food and environmental sources. Recent studies show that, despite not being as prevalent as other resistance mechanisms, these methyltransferases are already globally present, jeopardising the use of this critically needed antibiotic.

METAPRO will address the presence of methyltransferases.
Since 2005, Campylobacter has been the most commonly reported gastrointestinal bacterial pathogen for people (campylobacteriosis), with an EU notification rate of 64.8 per 100,000 population in 2017. Campylobacter jejuni and C. coli accounted for 99.7% of these cases with the former linked to the majority of incidents. Across Europe, antimicrobial resistance monitoring in clinical Campylobacter isolates has reported an increasing and high levels of ciprofloxacin resistance across member states. Ciprofloxacin is an antibiotic of the fluoroquinolone (FQ) class and is regarded as critically important by the World Health Organisation and therefore this increase is a major public health concern. Campylobacter originating from poultry are considered a main source of campylobacteriosis in people. Monitoring of antimicrobial resistance of Campylobacter isolated from broiler chicken flocks and broiler products has demonstrated elevated levels of ciprofloxacin resistance which could be considered a source of the resistant isolates recovered from clinical cases.

The UDoFRIC project will aim to exploit the archives of Campylobacter and associated information (phenotypic, genomic, epidemiological metadata) from surveillance and research across the food chain to investigate temporal trends in the development and diversity of FQ resistance in UK and French broiler flocks. The study will examine the relationship between FQ use in poultry and development of resistance, assess fitness costs/benefits of acquired resistance and determine if any specific FQ resistance variants found in poultry are more or less likely to persist and cause disease in people. The project would provide data to feed into the risk assessment for ongoing use of FQ in poultry and consequent risks of FQ resistance in clinical cases.
A key element in managing antimicrobial resistance (AMR) in the One Health paradigm is to reduce the dissemination of resistance genes between microorganisms in the agri food environment. A crucial mechanism for such dissemination is horizontal gene transfer (HGT) of AMR encoding mobile genetic elements. This is particularly the case for Enterobacteriaceae where a multi drug resistant (MDR) phenotype is increasingly being observed. This mobility shapes the resistome; the collection of all genes that directly or indirectly contributes to antibiotic resistance in a particular niche. It is recognised that a reservoir of AMR genes in the environment provides the possibility for transfer of these genes to human pathogenic bacteria via zoonotic pathways.

Selective pressures drive bacterial populations to evolve and may promote the dissemination of AMR genes, in the human and animal gut, or in the environment. However, there is limited information about the impact of selective pressures in the agri-food environment on HGT between microorganisms. One of the factors which can act as a selective pressure and can influence this HGT is the presence of heavy metals.

Heavy metals occur ubiquitously in the agri food environment and sometimes in high concentrations in soil. In food animal production, heavy metals such as zinc and copper are frequently added to animal feed to promote growth and health.

It is recognised that a One Health approach is required to tackle antimicrobial resistance. This includes the role the environment, and the food production environment in particular, plays. Very limited information is available regarding the impact of selective pressures such as heavy metals which may be present in the environment on the mobilisation of antimicrobial resistance and its potential transfer into the food chain.

The HME-AMR project will address the clear need for more data on the impact of heavy metal concentrations in food production settings and their potential impact on the co selection and dissemination of AMR in the environment and the food chain, and this is therefore the driver for this project.
Bovine tuberculosis (bTB), mainly caused by *Mycobacterium bovis*, is an ancient worldwide zoonotic disease intimately and historically associated to cattle rearing. Although developing countries are most suffering from bTB, this disease remains a major problem in some industrialised countries.

When cattle breeding developed as a real industry, strong control strategies were set up first in Europe and then in other developed countries. In France, the introduction of a compulsory national wide control campaign in the sixties led to a relatively rapid decline in the number of infected herds, turning from an annual herd prevalence of about 25% to less than 0.1% in 50 years. These costly measures greatly reduced bTB incidence and offered sanitary guarantees: France obtained the officially bTB free status from the European Union in 2000. However, bTB has not been completely eradicated.

Despite considerable financial and social efforts to tackle once for all the disease, bTB seems to be slowly but continuously rising and persisting, mainly at regional levels. This indicates that either control measures are not effective or that there exist overlooked risk factors. Indeed, investigations in these endemic areas revealed that wild boar, badgers and deer were regularly found infected with *M. bovis* and thus the emergence of the disease at a domestic and wildlife interface.

It is within this framework that the thesis project of A. Hauer, took place. Her work focused on the genotyping of *M. bovis* strains available at the National Tuberculosis Reference Laboratory (ANSES) in order to obtain the data allowing to study the dynamics of this zoonotic disease and to better understand its complex nature.

Subsequent to these studies, which focused on the genotypic diversity of *M. bovis* strains, and in order to answer the hypothesis of the emergence of certain successful strains circulating in multi host systems, we propose to study the biology of these strains by genomic and biochemical-phenotypic approaches.

The aim of this PEMbo project, a collaborative study between ANSES, Animal Health Laboratory (Maisons-Alfort) and INRA, Infectiology and Public Health laboratory (Nouzilly), two French OHEJP Partners, is to better understand the complex biology of *M. bovis* through the study of the complete genomes of a large panel of isolates of interest.
Brown (Rattus norvegicus) and black rats (R. rattus) can carry a multitude of pathogens with public and veterinary health importance. Their potential to rapidly reach high population numbers creates unpredictable situations of high pathogen transmission risks.

Rat populations depend on anthropogenic factors, such as the use of rodenticides and on unintended food provisioning. They are also heavily affected by environmental changes, including urbanisation and climate change. A new phenomenon with yet unknown consequences for rat-borne diseases is the “greening” and “blueing” of cities to improve living conditions and biodiversity and to combat heat. In addition to these risks in the urban environment, there are numerous examples of the (potential) role that rats have in food contamination and the transmission of pathogens of veterinary and human health importance (e.g. avian influenza or zoonotic hepatitis E virus in rats around pig farms and antimicrobial resistance. Therefore, the wicked problem of rat borne diseases is an excellent example of a One Health topic that is highly relevant for (re) emerging threats, and is linked to the topics of antimicrobial resistance and foodborne zoonoses.

The overall aim of the DESIRE project is to design and test an effective surveillance system for rat borne diseases, using The Netherlands as a testcase. The PhD student will contribute to the surveillance of rat borne diseases by providing evidence based insights in four key elements of this surveillance system: i.e. monitoring of populations, monitoring of pathogens, risk assessment and intervention. The PhD student will build onto existing surveillance activities and extend these by collaboration with (inter)national institutes.
The PhD project lies in the field of social sciences and public health and aims to understand the political drivers and constrains for increased transboundary integration and institutionalisation of the One Health approach across EU member states.

To encompass transboundary health issues, a holistic approach, such as One Health provides a way forward. One Health joins the three interdependent sectors – animal health, human health, and environments/ecosystems – with the goal to address issues such as the spread of zoonotic diseases in its entirety. Human health does not merely result from biological or behavioural determinants. The environment also influences health through various impacts. Animal health can have direct and indirect influences on human health through zoonotic diseases, which are diseases transmitted from animals to humans.

Challenges for implementing the One Health approach are complex political and institutional structures. Complex political structures emerge through various levels on which politics can be discussed, such as local, regional, national and international levels. Additionally, problem definition as well as agenda setting opportunities, which entail policy change, are dependent on many factors and actors. Complex institutional structures are reflected by the various institutions working together on the purpose of One Health.

The first step is a literature search to inform subsequent studies. Hereafter, quantitative studies of databases and of a survey addressed to institutions working on One Health topics will follow. Lastly, a qualitative study will be conducted, which will include interviews and observations. The SUSTAIN studies will inform different aspects, such as the current state of One Health institutionalisation on EU as well as on national level, and the One Health networks’ interactions as well as relationships.
SCIENTIFIC PUBLICATIONS AND OUTCOMES

The One Health EJP is committed to sharing the results, knowledge and outcomes from all of its scientific activities. Dissemination of research is an important element of our objectives. By sharing our research findings our consortium members have the opportunity to make significant impact, both nationally and internationally, in the areas of Foodborne Zoonoses, Antimicrobial Resistance and Emerging Threats.

Utilising an established procedure, the OHEJP Communication Team work with the Communication Strategy and Plan with targeted messages to segmented audiences for enhanced knowledge translation. The process is evaluated and adapted as the OHEJP audience reach develops.

All of the OHEJP consortium members play a key role in disseminating scientific outcomes and interacting with stakeholders to inform policy change.

A variety of approaches are employed for the dissemination of research findings:

- A Data Management Plan has been developed to ensure that any data produced by the OHEJP follow the FAIR principles: findable, accessible, interoperable and reusable.
- A One Health EJP Outcome Inventory (OHOI) has been created and serves as a public database for research and integrative outcomes and updates from the OHEJP scientific activities. The Outcome Inventory facilitates communication with stakeholders and the wider scientific community by providing contact information and One Health research.
- Close relationships have been established between key Stakeholders, including ECDC and EFSA, in addition to other EU projects to ensure effective exchange of information and non-duplicative work.
- The OHEJP Annual Scientific Meeting held every spring enables further collaboration across the One Health community, and is hosted by different consortium members.
- A programme of education and training activities are available to members those outside of the OHEJP.
- All our publications are made available via the OHEJP website.
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