D1.1 Summary Progress Report Year 1

WP1 Coordination

Responsible Partner: ANSES
Contributing partners: all partners

GENERAL INFORMATION

European Joint Programme full title	Promoting One Health in Europe through joint actions on foodborne zoonoses, antimicrobial resistance and emerging microbiological hazards
European Joint Programme acronym	One Health EJP
Funding	This project has received funding from the European Union's Horizon 2020 research and innovation programme under Grant Agreement No 773830.
Grant Agreement	Grant agreement n° 773830
Starting Date	01/01/2018
Duration	60 Months

DOCUMENT MANAGEMENT

Deliverable	D1.1 Summary Progress report
WP and Task	WP1; Task 1.2
Leader	ANSES
Other contributors	All partners
Due month of the deliverable	M9
Actual submission month	M10
Type *R: Document, report* *DEC: Websites, patent fillings, videos, etc.* *OTHER*	R
Dissemination level *PU: Public* *CO: confidential, only for members of the consortium (including the Commission Services)*	PU

1 Table of Content

2 Publishable summary

2.1 Summary of the context and overall objectives of the project

2.1.1 What is the problem/issue being addressed?

The One Health EJP is a policy driven research network addressing issues related to needs identified in the food safety area.

- Need to strengthen the links between human health, animal health and environmental aspects: One Health approach
- Need to further integrate surveillance and response capacities, preventive approaches, detection systems as well as preparedness and response to disease outbreaks
- Need of collaboration in Joint Research and Joint Integrative Projects, as well as Training and Education activities throughout a consortium of national public mission organisations
- Need to foster interaction between European, national authorities and stakeholders
- Need to update policy makers on these achievements and, built on this knowledge, to take appropriate action

2.1.2 Why is it important for society?

The integrated health approach, known as 'One Health', is based on strengthening collaboration between human health, animal health and environmental management. It focuses on developing surveillance and response capacities, strengthening early-warning and detection systems; reinforcing the capacities of public health and veterinary authorities as regards prevention, preparedness and response to disease outbreaks; evaluating the social and economic impact of diseases; promoting inter-sector collaboration for the health of the livestock, wildlife and ecosystems concerned; research on the conditions under which diseases emerge and spread. Thus coordination between the different health systems, which are generally run separately, must enable economies of scale by encouraging synergies, and guarantee improved health security. Particular attention is paid to the communication of risks at all levels of action.

2.1.3 What are the overall objectives?

The overall objective of the One Health EJP is to develop a European network of research institutes, mainly with reference laboratory functions, integrating medical, veterinary and food scientists in the field of food and feed safety in order to improve research on the prevention and control of mainly foodborne zoonoses, while taking into account the public health concerns of consumers and other stakeholders throughout the food chain.

2.2 Work performed from the beginning of the project to the end of the period covered by the report and main results achieved so far

2.2.1 WP1

The coordinator set in place all procedures for the One Health EJP, especially the management structure such as the PMC (Programme Managers Committee), the POC (Programme Owners Committee), the SSB (Scientific Steering Board), the ESAB (External Scientific Advisory Board), the Stakeholders Committee, and organized a kick-off meeting. A website was built for collaboration and exchange of information internally.

2.2.2 WP2

After expert consultation a new version of the strategic research agenda has been drafted. The interfaces with the EU funded projects has been defined and the priority topics of EFSA and ECDC taken into consideration. A set of priority topics has been established, in preparation of the Call2.

2.2.3 WP3

A set of 11 Joint Research Projects has been launched, previously selected. The first year has been dedicated to start the JRP. A second call is in preparation.

2.2.4 WP4

A set of 2 Joint Integrative Projects has been launched. The first year has been dedicated to the start of these integrative initiatives. These integrative projects are the basis for a scale up by introduction of new partners.

2.2.5 WP5

The purpose of this WP was to establish a dialogue with EFSA and ECDC as major stakeholders of the One Health EJP and also with other relevant policy makers (FAO, WHO). The need identified by the risk-assessors has been taken into account in the strategic priorities defined in WP2. WP5 will also function as a channel for the One Health EJP to disseminate new scientific data to these stakeholders.

2.2.6 WP6

The main activities was related to the PhD grants allocation and selection of the PhD students. The modalities of selection of the students have been defined and the interaction with the Joint Research Projects defined. The aim of WP6 was starting to create a community of interest in particular by setting up new generation of scientists in the One Health area.

2.2.7 WP7

The first year has been dedicated to explore the putative options for the long term (Sustainability) in collaboration with the Programme Owners.

2.3 Progress beyond the state of the art, expected results until the end of the project and potential impacts

Consistent with the “Prevent-Detect-Respond” concept, integrative activities will feed the approach of evidence based risk assessment and therefore risk management by the competent authorities.
Intensive collaboration between the most relevant partners in Europe in the field of foodborne zoonoses and antimicrobial resistance contribute to help to reduce unnecessarily duplication of work on these topics.
It is of importance to efficiently organize knowledge dissemination to the appropriate stakeholders (ECDC, EFSA, DG AGRI, DG Santé, the national authorities and beyond); these tasks were and will be taken forward by WP2 (Strategic Research Agenda), WP5 (Science to Policy) and WP6 (Education & Training)
The EJP aims at enhancing harmonization, alignment and integration of activities in these domains, but this process may not be finalised at the end of the 5-year programme. To make sure that the integrative

activities will last beyond the lifespan of the One Health EJP, a specific WP (WP7) is dedicated to create a significant long term capacity building and alignment among all EJP partners.

3 WP1 - Coordination and Management

3.1 Work carried out to date

3.1.1 Task 1.1: Management of EC contractual obligations

Regarding contractual procedures, the One Health EJP Coordination Team (CT) has prepared the Grant Agreement which has been signed by all the partners as well as the Consortium Agreement. The One Health EJP Support Team (ST) has ensured a strict monitoring of the deliverables and milestones which has allowed the timely submission of the deliverables due in the period as well as the notification of the milestones achieved. The WP1 deliverables (Summary Progress Report and Annual Work Plan) have been prepared by the Coordination Team in order to report to the REA. The ST has also prepared the first amendment to the Grant Agreement including budget adjustments, clarification of articles 11, 12 and 15 of the Grant Agreement used by some Beneficiaries, withdrawal and fusion of partners and update of the work programme.

3.1.2 Task 1.2: Project management

The CT, consisting of the Coordinator, Deputy Coordinator and Support Team, has provided effective management support to ensure the quality of the work both in terms of results and timing and to manage the relationships between partners and to ensure an effective internal communication. The CT has organised weekly teleconferences to monitor the project's progress and to ensure the timely implementation of the AWP year 1. When any important issue has arisen, the Coordination team has liaised with the Research Executive Agency (REA) to inform the Project Officers (PO) in the first place and request a delay in the submission of deliverables or a change of content of Annex 1 of the Grant Agreement whenever needed and relevant.
The CT and the Project Management Team (PMT) have had monthly teleconference to monitor the progress of the activities per work package (WP). The PMT reviewed, commented and provided relevant guidance and input on important WP documents. They also validated the deliverables which have been prepared and submitted during this period. This has been facilitated with some face-to-face meetings, shared monitoring tools, regular phone meetings and mail exchanges.
Also, a manual of procedures, which will continuously be updated, has been developped and made available to all partners. It includes templates for meetings (attendance list, agenda, minutes) and for reporting.

3.1.3 Task 1.3: Organisation of EJP management and governance meetings

All consortium gouvernance bodies (Coordination Team, Programme Management Team, Scientific Steering Board, Programme Manager Committee) have been established and have been operating since the project start. The CT has provided logistic and organisational support to meetings organisation to ensure that they run smoothly.
The Scientific Steering Board (SSB) members have been regularly informed of the One Health EJP progress and their input has been requested on several occasions such as when ranking the selected PhD programmes. The first face-to-face meeting of SSB is scheduled on 2 October 2018 in Brussels at Sciensano's premises.
The Programme Manager Committee (PMC) is the Governing Board of the OHEJP will have their first face-to-face meeting on 11th October 2018 at Anses' premises.

Externally to the consortium:
The Programme Owner Committee (POC) composed of the Beneficiaries' line Ministries Representatives has had their first teleconference in June 2018 with the following agenda items: debriefing of the Kick Off Meeting, presentation of the updated Strategic Research Agenda (SRA), update on the PhD grant programme and on the JRPs and JIPs progress. They will meet face-to-face in November 2018 at ANSES headquarters.
The External Scientific Advisory Board (ESAB) was formed and a teleconference was held in June to introduce the aims of the OHEJP, discuss the mandates of the ESAB members and plan future meetings.

3.1.4 Task 1.4: Communication tools

In order to ensure better internal and external communication, a Communication Contact Person by institute has been appointed to create the Communications committee. The first communication activities were developing the One Health EJP visual identity and all the corresponding communication tools, both offline and online. It involved disseminating relevant information about the project's progress and results through various communication supports such as social media. The One Health EJP social media accounts have been set up (LinkedIn, Twitter) and they are regularly updated according to the corresponding developed guidelines. As all EJP social media posts will have hashtags #OneHealthEJP or #OHEJP, it will be a useful tool to monitor and track the posts over the course of the project.
The One Health EJP website has been launched; there is a public area detailing the project, which is aimed at providing general information to the public. In addition, there is a private area (EJP consortium members only) to be used as a project management tool, where users can track their deliverables and milestones, store and share updated versions of key documents with other relevant EJP partners. It also provides a communication platform between the EJP consortium through the use of discussion forums and a private messaging functionality.
A bi-monthly newsletter will be produced by the communications committee for the EJP partners. The Communications committee was setup at the start of M5, and so the first bimonthly newsletter will be published in M7. There was also very limited content in the first 5 months of the EJP project for a newsletter. However, the next newsletters can now include updates on the EJP Doctoral Programme, Website and Social Media accounts, JRPs and JIPs, together with project related information including information on project meetings and deliverables.

3.1.5 Task 1.5 Ethics

The principles of ethics and research integrity are dealt with in the Grant Agreement in general terms (Article 34). In the Ethics Summary Report of the One Health EJP (11 May 2017), the evaluators required "at least two independent external Ethics Advisors … to assess all proposals recommended for funding for ethical issues. The independent external Ethics Advisors must also produce a report describing any ethical issues raised by this project and the sub-projects to be funded and confirming that these have been adequately addressed. These reports should be presented to the European Commission at the time of the periodic reports."
The Coordination Team asked PMT members per mail (20 July 2017) to come up with names of Ethics Advisors candidates. A list of 8 candidates was drawn from which two experts were selected, i.e. Kate Millar (University of Nottingham, UK) and François Hirsch (INSERM, FR). Both were appointed as independent external ethics advisors (Deliverable 8.1).
Based on the available information in the Grant Agreement, personal contacts with the selected experts and mail discussion with the REA Project Officers (e.g. mail 31 October 2017), an ethics work plan including a putative time schedule and a procedure with specific actions were drafted.

In parallel, based on the Horizon 2020 guidance document on the ethics self-assessment, a questionnaire (Excel document) was elaborated and sent to the leaders of the Joint Research and Joint Integrative projects (mails 19 October 2017). This ethics self-assessment identified all ethics issues in the 13 projects that start from January 2018, and also included a reminder for project leaders to comply with the legal ethics requirements.
Finally, all full project proposals and the self-assessments were sent to the ethics advisors for evaluation (mail 24 November 2017). At the end of January 2018 (31 January), the ethics advisors listed the recommendations for each of the 13 projects. All project leaders were informed per mail (5 February 2018) about these recommendations related to their JRP or JIP. In order to remind project leaders on their task to comply with these recommendations, the ethics issue was clearly described in the guidelines for Project Leaders to report (Deliverable 3.1). Also during the videoconference that explained these guidelines (25 April 2018), the ethics issue was mentioned.

3.1.6 Task 1.6 Declaration of Cofund

The Support Team has gathered from all consortium members, except two partners, the completed template of the Participant Declaration. All declarations have been compiled in deliverable D1.28 "Correctly signed, dated and stamped participant declarations filled by each participant [Programme Owner and/or Programme Manager] delivered to the REA" which has been submitted on 31 January 2018.
The Support Team has gathered from all consortium members, except two partners, the completed template of the Mandate. All mandates have been compiled in one deliverable D1.29 "Correctly signed, dated and stamped Mandate to Programme manager for the European Joint Programme Cofund action 773830 One Health EJP filled by each Programme Owner to the REA" which has been submitted on 31 January 2018.

3.2 Deliverables and Milestones

3.2.1 Deliverables

Del Rel No	Del no	Deliverable tittle	Submission
D1.28	D1	Correctly signed, dated and stamped participant declarations filled by each participant [Programme Owner and/or Programme Manager] delivered to the REA.	M1
D1.29	D2	Correctly signed, dated and stamped participant declarations filled by each participant [Programme Owner and/or Programme Manager] delivered to the REA.	M1
D1.1	D3	Website and social media accounts and power-point template	M8

3.2.2 Milestones

Mil Rel No	Milestone tittle	Notification
MS1	One Health EJP Kick-off meeting	The Kick Off meeting has been held at ANSES headquarters on 30&31 January 2018.

	Agenda, participant folder and presentations are available upon request.

4 WP2 – Integrative strategic research agenda

4.1 Work carried out to date

4.1.1 Task 2.1: Development of the SRA

In the first months of the OHEJP a provisional Strategic Research Agenda was delivered and a procedure for updating of priority research and integrative topics was developed. A gap analysis was performed by the OHEJP domain and theme secretaries to assess the extent to which the first round priority research and integrative topics are covered by the first round of granted projects. Topics that are insufficiently covered have been (re)included in the prioritization process for the second call. In June, an experts meeting was organized in Bilthoven, the Netherlands (at RIVM), including one representative from each partner organization, to narrow down the first round research topics and to prioritize both research and integrative topics by using a multi-criteria decision analysis (MCDA) procedure. Also, EU stakeholders' needs were taken into account in the procedure and after discussion of the resulting lists of priority topics with the Stakeholders Committee, topic descriptions were developed in collaboration with the domain and theme secretaries. During this reporting period (M1-M9) four deliverables (D2.1, D2.2, D2.5 and D2.6) and three milestones (M2.1, M2.2, M2.3) have been submitted.

4.1.2 Task 2.2: Strategic interactions with EU projects and initiatives

In order to fulfil the objective of fostering strategic interactions with related EU projects and initiatives an analysis of the relevant EU-projects/initiatives and potential strategic interactions was done during the first months of the OHEJP. The CORDIS (Community Research and Development Information Service) database was used as the main tool to identify projects relevant to the OHEJP. Moreover, information was obtained from the EJP partners. All the compiled information was centralized in a repository of EU projects/initiatives that will be available to all partners through the OHEJP website. This repository includes a descriptive sheet of each project/initiative (name of the project, acronym, objectives, coordinator, period and financing entity), a gantt chart, the OHEJP partners and the relevant projects/initiatives included in the OHEJP strategy matrix. This repository will be updated three times a year. This information will have an impact in several OHEJP activities as for example the SRA (WP2), the JRP/JIP (WP3), the organization of cogwheel workshops (WP4) and the International Stakeholders (WP5). During this reporting period (M1-M9) two deliverables (D2.3 and D2.4) and one milestone (MS22) have been submitted.

4.2 Deliverables and Milestones

4.2.1 Deliverables

Del No Rel	Del no	Deliverable tittle	Submission
D2.1	D30	Provisional strategic research agenda	M1
D2.2	D31	Report on the procedure for updating of priority topics	M2

D2.3	D32	Report on the identification of relevant EU-projects and initiatives and the procedure to identify potential strategic interactions	M2
D2.4	D33	Report on potential strategic interactions with EU projects and initiatives	M4
D2.5	D34	Report on the experts meeting	M6
D2.6	D35	Updated list and descriptions of priority research and integrative topics	M9

4.2.2 Milestones

Mil No	Rel	Milestone tittle	Notification
M2.1		Meeting with WP leaders to establish procedure for SRA update	During this meeting, which took place on May 11 in Amsterdam, the gap analysis was validated and the procedures for the experts meeting were established.
M2.2		Meeting with domain/theme secretaries	During this meeting, which took place on April 20 in Amsterdam, a gap analysis of the first round projects was performed and the procedures for the experts meeting were developed.
M2.3		Experts meeting	During this meeting, which took place on June 4-5 in Bilthoven, NL, priority research and integrative topics for the second round were identified and prioritized by using a multi-criteria decision analysis (MCDA) procedure.
M2.5		Inventory of relevant EU research projects and related initiatives	The document "Inventory of relevant EU research projects and related initiatives" has been shared with relevant beneficiaries and will be used as a tool for WP2 expert meeting to be held in June 2018. The document is available upon request.

5 WP3 - Joint research projects

5.1 Work carried out to date

5.1.1 Task 3.1: Drawing up of guidelines for submission, selection and evaluation of JRP proposals as well as request of extension of accepted JRPs.

For the preparation of the first internal call, procedures for submission and selection of project proposals were developed in 2016. For the second call that will be launched in autumn 2018, not only the timeline and the paragraphs dealing with the topic descriptions and the budget to be allocated to these topics need modification, also practical issues that were identified during the first round have to

be adapted. An online questionnaire was sent out on 26 April 2018 to PMT and SSB members to ask for their feedback on the existing procedures and for new suggestions. The outcome of this survey (document and PPT) was discussed with PMT members during a videoconference (13 June 2018) and served as input for the adapted guidelines (Deliverable 3.3, delivered in M7: July 27th, 2018).
The possibility to extend JRP or JIP with a limited number of months, without additional budget, was discussed. As for enlarging existing JIP consortia (not allowed for JRP), specific integrative support functions are foreseen under WP4. In addition, enlarging consortia with organisations outside the OneHealth EJP, would be possible under strict conditions. Draft guidelines are available and were sent on June 26th 2018 to the REA officers for feedback.

5.1.2 Task 3.2: Supervision of the JRP in the first round of projects.

To support the project leaders of JRP and JIP in reporting on their activities to the WP3 team, guidelines were developed (Deliverable 3.1). The expectations on reporting were preliminary discussed during the pre-kick off meeting held in Brussels in 15 December 2017 (Milestone M25) with all project representatives. The guidelines specify a first feedback on the newly started projects (online questionnaire), the input project leaders have to give to the Summary Project Report (their 9 month report to WP3), the annual (at 12 months) report and the final report at the end of the JRP or JIP. The templates for these reports are also defined in the guidelines. As a supportive measure, a videoconference with project leaders was organised on 25 April 2018 to explain the various expectations. These guidelines for project leaders include to a large extend the way the research projects are monitored by WP3 (which is deliverable 3.5, due for M10).
Project leaders gave a quick feedback on their freshly started projects by means of an online questionnaire (Milestone M26; sent out by Ann Lindberg, WP4 on 28 February 2018). The results of this survey were described in a document and summarised in a presentation that was communicated through videoconference with the project leaders on 1 June 2018. Comments from the project leaders and from PMT members were included in the final report on the recently started projects of the first call (Deliverable 3.4, delivered in M8: 27 August 2018).
Through their 9 month report, all project leaders confirmed that their research projects have started and have held their kick-off meeting. Recruitments are done or on-going. Most of the milestones and deliverables are on time. More detail on the Joint Research Projects progress can be found below (see 5.1.2.1 to 5.1.2.11).

5.1.2.1 IMPART

5.1.2.1.1 Summary

On 20 January 2018 the IMPART consortium started with sending out an invitation for a kick-off meeting. The meeting was held on 20 February 2018 at Schiphol Airport in Amsterdam (NL) attended by fifteen persons representing all thirteen partner institutes. After a general introduction by the IMPART project leader information about the different work packages was provide by the work package leaders. Former to the kick-off meeting a questionnaire was sent around to all partners in order to gather relevant information about the subject involved before the kick-off meeting. The received information was used as input for the actual kick-off meeting to speed-up the process. IMPART WP leaders communicate via Skype at least every two weeks (and Skype meetings have been planned every two weeks for the rest of the year). Notes are taken by the WP2 leader. No other teleconference meetings have been planned so far for the individual work packages.

The setup of WP1 (Selective isolation, detection and characterization of colistin-resistant Enterobacteriaceae) and WP2 (Selective isolation, detection and characterization of carbapenemase-producing Enterobacteriaceae) was discussed during the kick-off input at which feedback was given. All the samples for the pre-ring trials and the final ring trials will be prepared at Anses Fougères and sent around in parallel for both WP1 and WP2. Recently, a new person has been hired to organize and assist with the sample preparation. Currently, the protocols for the pre-ring trials are in preparation and will be sent to all partners for comments during the upcoming two months.

For WP3 (Establishing epidemiological cut-off values (ECOFFs)) the setup was discussed during the kick-off meeting and based on the information collected via the questionnaire, a principal consensus was reached on potential bacterial strains and antimicrobials to be tested. Three different antimicrobial panels will be sufficient to test most bug/drug combinations. The design of the plates was delayed. Recently, the proposed lay-out of the three panels has been sent around for comments to all partners involved. In addition, partners have been asked to give an estimation of the number of plates they would like to use for this project. The plates have been ordered in the end of July (2000 plates per panel) and probably delivered and distributed in October.

For WP4 (Developing and optimizing a disk diffusion method for antimicrobial susceptibility testing of Clostridium difficile) the set-up of the work package was also discussed during the kick-off meeting. Eight different antimicrobials were chosen to be analysed during the project. Due to a delay in finding a technician, the laboratory work was delayed and will approximately be started in July 2018. A strain collection plan including app. 520 isolates of human, animal, environmental and food origin was established. The isolates were sent to the BfR in May / June 2018 and subsequently characterized. MIC-determination for all isolates has been carried out using agar dilution as described by CLSI. In uncertain cases, the results have been confirmed using E-Test.

WP5 (Coordination of the four work packages and knowledge dissemination both internally within and externally beyond the IMPART consortium) is about knowledge dissemination. Since July, 6th, 2018, the One health EJP intranet platform is in place. We will use the private space on the platform to share our documents within IMPART.

5.1.2.1.2 Project-specific milestones and deliverables

5.1.2.1.2.1 Deliverables

JRP name	Project deliverable number	Deliverable name	Delivery date from AWP	Actual delivery date	If deliverable not submitted on time: Forecast delivery date	Comments
IMPART	D-JRP1-5.1	Invitation to the Kick-Off meeting sent to participants	1	22-01-2018		Kick-off meeting was organized on Tuesday 20 February at Schiphol airport in Amsterdam
IMPART	D-JRP1-3.1	Priority list	3	20-02-2018		Agreed on during kick-off meting
IMPART	D-JRP1-5.2	Kick-off meeting notes sent to participants	3	22-02-2018		
IMPART	D-JRP1-1.1	Protocol of methods ready to be used in the pre ring trial	6		10	A Junior scientist was hired begin of July. Progress are already being made, but details but need to be set
IMPART	D-JRP1-2.1	Protocol of methods ready to be used in the pre-ring trial	6		9	Only a draft of the WP2 protocol ready for the pre-ring trial. Have to narrow down the choices of methods.

5.1.2.1.2.2 Milestones

JRP name	Milestone number	Milestone name	Delivery date from AWP	Achieved (Yes/No)	If not achieved: Forecast achievement date	Comments
IMPART	M-JRP1-1	Kick-off meeting (notes of meeting)	2	Yes		
IMPART	M-JRP1-2	Ordering of microtiter plates with antimicrobials (WP3)	4	No	6	Creating the layout of the microtiter plates was more complicated than expected.
IMPART	M-JRP1-3	IMPART EXTRANET in place	6	Yes/no	9	Temporary virtual workplace will be set through Anses website and switched to OH-EJP website as soon as it is operating
IMPART	M-JRP1-4	Established disk diffusion method (WP4)	8	No	11	Advertised technician position could not be staffed on time.
IMPART	M-JRP1-5	Completed strain collection (WP4)	9	Yes	9	

5.1.2.1.3 Description of the project activities per task

5.1.2.1.3.1 WP1: Selective isolation, detection and characterization of colistin-resistant Enterobacteriaceae

JRP1-WP1-T1: Describe existing methods to be evaluated in a ring trial (M1-M6)
All existing methods used at the partners' laboratories are listed. A list of available selective agar plates has been made and an evaluation of pre-enrichment conditions (medium, selection) is expected. Person to be hired : Tifaine Hechard joined the team on a 6 months (9-JUL-2018 to 8-JAN2019)
JRP1-WP1-T2: Preparation of the samples for the pre-ring trial (WP1 and WP2; M7-M8)
Not yet ready

5.1.2.1.3.2 WP2: Selective isolation, detection and characterization of carbapenemase-producing Enterobacteriaceae

JRP1-WP2-T1: Describe existing methods to be evaluated in a ring trial (M1-M6)
All existing methods used at the partners' laboratories are evaluated. A list of available selective agar plates has been made and an evaluation of pre-enrichment conditions (medium, incubation temperature) has been discussed. A draft of the pre-ring trial protocol for WP2 is written and is ready to be sent out to the IMPART partners.

JRP1-WP2-T2: Preparation of the samples for the pre-ring trial (WP1 and WP2; M7-M8)
No samples are yet prepared for WP2.

5.1.2.1.3.3 WP3. Establishing epidemiological cut-off values (ECOFFs)

JRP1-WP3-T1: Inventory, prioritizing and inclusion criteria (M1-M3)
The inventory of strain collections has been performed. Consensus was reached on the bacterial species and antimicrobials to be tested during the kick-off meeting based on an earlier held questionnaire by which information was gathered. . The lay-out of the panels needed fine tuning, and this was agreed upon at the end of June 2018. Subsequently, the plates (2000/batch) have been ordered in July.

JRP1-WP3-T2: Production of MIC data (M4-M18)
The production of MIC data has not started yet.

JRP1-WP3-T3: Collection and quality control of MIC data (M4-M18)
The collection of MIC data and quality control has not started yet.

5.1.2.1.3.4 WP4: Developing and optimizing a disk diffusion method for antimicrobial susceptibility testing of Clostridium difficile

JRP1-WP4-T1: Establishment of a disk diffusion method for antimicrobial susceptibility testing of C. difficile (M4-M9)
Recent literature on this topic has been reviewed regarding the state of the art and regarding differences that occur in method execution. In discussion with the project partners, eight different antimicrobials were chosen to be analysed during the project. Due to a delay in finding a technician for the project, the laboratory work regarding this task had been delayed and started in August 2018. (delay M-JRP1-4 month 8 to month 11).

JRP1-WP4-T2: Assembly and characterization of C. difficile strain collection (M4-M9)

A strain collection plan including app. 520 isolates of human, animal, environmental and food origin was established based on a questionnaire in month 1 – 2 and in consultation with the project partners 13, 31 and 38 as well as external partners from Germany and Portugal. The isolates were sent to the BfR in May / June 2018 and characterized regarding their toxin gene profile and PCR-ribotype. MIC-determination for all isolates has been carried out using agar dilution as described by CLSI. In uncertain cases, the results have been confirmed using E-Test.
JRP1-WP4-T4: Producing inhibition zone diameter distributions and proposing cut-off values for C. difficile (M7-M18)
This task has not been started yet and will follow the method description resulting from Task 4.1.

5.1.2.1.3.5 WP5 : Coordination of the four work packages and knowledge dissemination both internally within and externally beyond the IMPART consortium

JRP1-WP5-T1: Organization of IMPART (M1-M24)
All partners have participated to the kick-off meeting.

JRP1-WP5-T2: Communication within IMPART (M1-M24)
The One health EJP intranet platform is in place since the 6th of July. We will use the private space on the platform to share our documents within IMPART

JRP1-WP5-T3: Communication beyond IMPART (M1-M24)
The One health EJP website is in place: we will use the public domain of this platform to share information within EJP.

5.1.2.1.4 List of planned tele- or video conferences, face to face meetings in the next year

IMPART WP leaders communicate via Skype at least every two weeks (and Skype meetings have been planned every two weeks for the rest of the year). Notes are taken by the WP2 leader.
No teleconference meetings have been planned so far for the individual work packages.
The aim is to organize a physical meeting with all partners (or at least with the WP leaders) during the One Health EJP ASM meeting in Dublin in 2019.

5.1.2.2 ARDIG

5.1.2.2.1 Summary

Following the EJP One Health kick-off in January 2018 substantial progress has been made by all partners participating in ARDIG. Most partners that were hiring staff for contributing to ARDIG have completed their recruitment. The Institutes include APHA, BfR, NVI, RKI, UCM, UoS, and WBVR; PHE will recruit at a later stage in the project. The members of staff include PhD/MSc students, postdoctoral scientists and technical staff, who will be contributing their expertise to ARDIG in conjunction with other senior members and staff from each Institute.
ARDIG kick-off meeting was held in early March following initial planning discussions in February. At least one member from each partner Institute was present at the meeting and presented briefly on their work plan for the project. Furthermore, the PI presented an overview of the project and the work package/deputy leads for each WP. There were discussions on how to harmonise the work planned in each Institute so data sets collected can be compared across countries, as well as human and animal sectors. A follow on teleconference on 11th June attended by most partners continued with discussions on progress of work within each country and WP.
The progress made within each WP is provided in detail below within each Task. For WP1 (Comparison of antimicrobial resistance (AMR) and antibiotic sales/usage (AMU) data collected through existing surveillance, monitoring and research programs and assessment of risk factors), participating partners

have started reviewing data available on antimicrobial resistance and antimicrobial usage from each country. Substantial differences have already been identified between data collected from the human and animal sectors, where preliminary analysis have been performed. Also, availability of environmental AMR data seems more limited. A data collection system is being developed to obtain an overview of the available data for the different participating countries.
For WP2 (Longitudinal studies of persistence ESBL/AmpC/carbapenem/mcr-1 and -2/PMQR producing Enterobacteriaceae on farms or hospitals) a questionnaire developed by the work package leads have helped identify the datasets that may be present in the collections of each participating Institute from retrospective studies, and the types of isolates that will be collected as part of prospective studies. A criteria for collection of human isolates from prospective longitudinal studies in hospitals has been set. For veterinary AMR monitoring by on-farm longitudinal studies, three production sectors have been identified: poultry, pig and veal calve/cattle sectors, with at least two partners involved in each sector.
In WP3 (AMR characterization, transmission of plasmids and fitness of MDR isolates) partners are progressing with molecular analysis of isolates by NGS and other methods to characterise plasmids and AMR determinants present. The focus will be on AMR determinants for the most critically important antimicrobials, following the WHO recommendations. Bacteria fitness experiments and development of the in-vitro pig and poultry gut models are also progressing. A questionnaire is being prepared as part of methods harmonization for this WP with view to a workshop being held in future to help harmonise and improve analysis of genomic data within ARDIG.

5.1.2.2.2 Progress of the project: project-specific milestones and deliverables

5.1.2.2.2.1 Deliverables

JRP name	Project deliverable number	Deliverable name	Delivery date from AWP	Actual delivery date	If deliverable not submitted on time: Forecast delivery date	Comments
ARDIG	D-JRP2-2.1	Assessment of criteria for inclusion of retrospective and prospective longitudinal studies.	2	6		A questionnaire has been completed by all partners to assess the criteria for inclusion. For both the animal and human isolates to be used from retrospective studies the criteria is still under discussion and will be finalized when data from all the strain collections become available. For the prospective studies for the human isolates the criteria is that the first 20 *E. coli* isolated from urine from each hospital at each month over a year will be included. There are no criteria for the animal isolates and we will attempt to harmonise methods as much as possible across partners.

5.1.2.2.2.2 Milestones

There are no Milestones to achieve before month 12

5.1.2.2.3 Description of the project activities per task

5.1.2.2.3.1 WP1 Comparison of antimicrobial resistance (AMR) and antibiotic sales/usage (AMU) data collected through existing surveillance, monitoring and research programs and assessment of risk factors.

JRP2-WP1-T1: Exploration and collection of data available on AMR, AMU and potential risk factors (M1-M6)
Literature and databases have been searched for data on AMR and AMU and the potential relation between the two.
To inventorise appropriate and available data sources for the analysis of AMR and AMU, a survey was sent to the ARDIG partner institutes on July 27th 2018. It consisted of a structured questionnaire using Google Sheets, and was subdivided into the following inventory-sheets: AMR in humans, AMU in humans, AMR in animals, AMU in animals, and data on AMR in food isolates. The survey collects general information on data sources, availability/accessibility, protocols, coverage, sampling, pathogens and antibiotics panels, standardization and quality. Partner institutes can provide feedback on the structure of the questionnaire until September 14th 2018. The inventory will allow to develop joint databases collating accessible data from the ARDIG partner institutes. It will guide decisions for the analysis in Task 1.2., including the identification of bacterial species / antimicrobial agent combinations. There are substantial differences between the systems and efforts will have to focus on achieving some degree of standardization and identification of overlaps with respect to bacterial species / antimicrobial agent combinations. For instance in Germany on the veterinary side bacterial isolates of zoonotic agents as well as commensal bacteria and animal pathogens are collected based on sampling plans and analysed in one laboratory against standardized panels of antimicrobials using broth micro-dilution. On the medical side, however, data on results of testing are collected from commercial and public laboratories. All laboratories are accredited and adhere to recognized standards (CLSI or EUCAST). Data collection and compilation in ARS is in addition somehow standardized through the electronic interface. These aspects need to be addressed thoroughly to avoid misinterpretation of comparative analyses. Similar discrepancies are observed for use data. In addition, at the Institute Pasteur a review of the literature on all studies dealing with molecular epidemiology of ESBL E. coli in France had been undertaken. The next step will be to collect data on ESBL *E. coli* from the Bicêtre hospital. At the APHA, published literature and reports are being reviewed to identify data sources of antimicrobial usage and resistance in livestock, people, food and the environment in UK, with the aim of mapping out data sources which could be used for benchmarking and/or monitoring. Useful datasets are being requested and barriers to accessing some industry datasets identified. A number of identified datasets will only be shared in a summarised format and individual data (e.g. from a farm) may not be possible to collect. For each useful dataset the APHA will complete a SERVAL (surveillance evaluation) form, which will provide a standardised template to describe the dataset coverage, representativeness, bias etc. AMU/AMR data from people appears to be the most comprehensive but there appears to be little data on AMR in the environment as only a small number of research projects focus on water. UoS is contacting a number of local (pig, cattle, sheep and poultry) farms and human hospitals to gather data from previous studies that may be included in ARDIG. Some farms have been identified that can provide samples over the next 18 months (pathogens and commensals).

JRP2-WP1-T2: Investigation of trends, associations and risk factors (M9-M30)
A data collection system is being developed to obtain an overview over the available data for the different participating countries. This collection system will specifically address the currently

identified differences between the systems to obtain all information required that is needed for a valid data analysis under this Task.

5.1.2.2.3.2 WP2. Longitudinal studies of persistence ESBL/AmpC/carbapenem/mcr-1 and -2/PMQR producing Enterobacteriaceae on farms or hospitals.

JRP2-WP2-T1: Assessment and selection of longitudinal data from historical studies (M1-M12)
A questionnaire has been sent to all partner participating in this Task to enquire whether they have access to longitudinal data from historical studies. Three partners have access to such collections from human origin (University of Surrey, Public Health England and Institut Pasteur). For veterinary samples, five partners have access to collections of isolates from pigs, poultry or veal calves (NVI, UCM, APHA, ANSES, WBVR). Complete information on these sample collections have been requested including data on management and antibiotic usage. Comparisons of the sample sets within each group will possibly inform on the influence of different management practices and ABU on the AMR load. The strains selection should be completed by month 9.
In addition, the Insitut Pasteur has a collection of 330 ESBL *E. coli* collected during three months in a rehabilitation hospital (i-BIRD project, Duval A. et all, Sci Rep. 2018 Jan 26;8(1):1686), which is available for this project.
The Robert Koch Institute also has isolates which may be included in the study but requires further discussion.
UoS is collecting *E. coli* isolates from human urinary tract infections and septicaemia cases in collaboration with local hospitals in the South East of England, which will provide additional information such as disease, treatment, age, and gender of source patients.

JRP2-WP2-T2: Isolation of resistant Enterobacteriaceae on farms (M1-M24)
The partners involved in veterinary monitoring have expressed through a questionnaire, in which production sectors longitudinal studies on farms are planned to take place. For the poultry, pig and veal calve/cattle sectors, at least two partners are involved for each of the sectors. The proposed experimental set up was shared between the partners and sampling will commence or has started. An assessment of available analysis methods for each of the partners has been performed and these methods will be harmonised as much as possible.

JRP2-WP2-T3: Isolation of resistant Enterobacteriaceae in hospitals and care facilities (M1-M24)
The strategy for these prospective sampling in human has been defined following responses to a questionnaire, discussion by email and finalized during the teleconference on June 11th. Given the high rate of ESBL *E. coli*, previous sampling of these bacteria and the need to analyse also strains resistant to other antibiotics, it has been decided to sample *E. coli* strains from urine samples (UTI in the hospital) without a priori on the AMR profile. The first 20 *E. coli* from UTI will be collected each month during one year. We expect therefore to collect more than 200 isolates per site. Isolates will be analysed by various methods like ST131 identification by PCR, antibiogram, MLST and WGS on a subset of isolates. The final strategy will be defined before month 9 of the project. Four partners will contribute to this sampling (University of Surrey, Public Health England and Institut Pasteur and Univ Complutense de Madrid, UCM-VISAVET)

5.1.2.2.3.3 WP3. AMR characterization, transmission of plasmids and fitness of MDR isolates

JRP2-WP3-T1: Detailed molecular characterisation of AMR genes present in human, animal, food and environment isolates from WP1 and WP2 (M6-M18)
Bacteria from WP 1 and WP2 are being collected for a harmonized analysis of genes, plasmids and fitness experiments. Each partner is also collecting meta-data on the isolates, plasmids and antimicrobial resistance determinants that they will be focusing on. In general ARDIG will be

focusing on AMR determinants for the most critically important antimicrobials following the WHO recommendations: carbapenem resistance, ESBLs, colistin resistance and resistance to new antibiotics for human health, like plazomicin.
For example, at BfR *E. coli* resistant to quinolones and fluoroquinolones from different parts of the food chain are being analysed for the genetic background of resistance using PFGE, qnr-PCRs and sequencing for isolates gathered in a national monitoring program since 2016. Furthermore, *E. coli* isolates collected since 2010 in the monitoring program are being screened for the presence of the various mcr-genes (mcr-1 to mcr-7). Isolates harbouring mcr-4 and mcr-5 are being sequenced and studies on plasmid transfer are being conducted for the plasmids harbouring these genes.
At UCM, plasmids conferring resistance to colistin are being analyzed, including sequencing using Illumina and MinION. Further, analysis of multicopy plasmids is being carried out, to identify the host and plasmid factors that elicit plasmid adaptation to different bacterial hosts. Metabolomic studies are being carried out to establish the biological basis for plasmid-host adaptation. Analysis of human, animal, environment and food enterobacteria conferring resistance to plazomicin, the newest antibiotic elicited for human use in the United States in June 2018 is under way.
At the Institut Pasteur plasmids encoding carbapenemase resistance are being characterized, including their fitness cost. IP are also investigating the phylogenetic relationships of CP-*E. coli* and strains of animal origins.
At WBVR, a collection of more than 130 colistin resistant Enterobacteriaceae have been sequenced using short-read NGS. The collection was isolated from diverse animal species between 2010 and 2017. For a more complete analysis the collection has been sequenced using long-read sequencing, ONT MinION, and data analysis is currently ongoing.
The APHA have purified ~200 isolates from pig faeces collected on the first visit to a pig farm which will be included in WP2 longitudinal study. WGS has been performed on the isolates which will be characterized for their AMR determinants next and compared with WGS data already available from pig ESBL *E.coli* isolates collected through EU surveillance.
The UoS has been collecting E. coli isolates from human urine and poultry intestinal content, phenotypically characterising antibiotic resistance of isolates, genotypically characterising AMR genes by multiplex PCR, and will sequence a subgroup. They will be setting up pig and chicken in vitro gut models(models set up and preliminary runs have taken place), check the stability of the models over time, compared to the actual gut microbiome from healthy pigs and chickens using metagenomics.
AT NVI a collection of cephalosporin resistant E. coli from broilers have been sequenced. Plasmids characterization is ongoing as well as other relevant investigations and data compilation.
Furthermore, a questionnaire is currently being prepared for WP3, in order to both optimize methodologies for sequencing of plasmids using long-read sequencing, and harmonise bioinformatics analysis. Partners will combine Illumina short-read sequencing together with different long-read platforms, like MinION or PacBio to help circularise plasmids. A workshop within WP3 is foreseen to help analyse sequencing data and improve analysis of genomic data within ARDIG.

5.1.2.2.3.4 WP4: Project coordination and management.

JRP2-WP4-T1: Steering committee quarterly meeting (M1-M36)
A teleconference meeting has been planned for every quarter and the first meeting following the face-to-face kick-off meeting in March was held on 11th June.

JRP2-WP4-T2: Consortium members annual meeting (M1-M36)
To be determined.

JRP2-WP4-T3: Reporting and communication (M1-M36)

TBD (task: A summary annual communication from each WP for distribution to relevant organisations or stakeholders such as national governments, EU, international agencies and relevant industry/health partners. It is expected that members will also publish scientific papers and other communications from the results obtained in this study).

5.1.2.2.4 List of planned tele- or video conferences, face to face meetings in the next year

A teleconference meeting has been planned for every quarter.

5.1.2.3 RaDAR

5.1.2.3.1 Summary

The RaDAR study was successfully started in January with a meeting at Schiphol airport. Immediately there was a good vibe within the group and members were eager to start working on this important topic. After the kick-off meeting several WP focused teleconferences were held in order to get the WPs starting. Subsequently this was followed-up by regular email contact. In general there is good communication and interaction between partners. In June a WP-leader TC was held. Information from the EJP management was provided by the project leader to the WP leaders (reporting, data management plan, etc). None of the partners reported financial problems (i.e. issues regarding co-funding).
Regarding the scientific work all WPs reported to be on-track. All scheduled MS are fulfilled except for one (M-JRP3-4) due to delay in appointing a PhD student. In short, WP1 (New genomic information to feed AMR transmission models) constructed a curated database of plasmid sequences which currently is the largest of its kind available. WP2 (Pharmacodynamics and transmission models) has complemented a reference database of literature which is subsequently used to draft a model framework for on-farm transmission and WP3 (Transmission through the food chain) made a start with the inventarisation of available risk assessment models and started to construct a model for ESBL transmission across the chicken production chain based on an excising model for Campylobacter. WP4 (Machine learning methods for quantification of risk and health effects) started with defining model requirements for inclusion the machine learning application. WP5 (The burden of disease caused by AMR exposure) started to develop a first framework for calculating disease burden and costs of AMR by identifying data gaps. Finally, WP6 made a descriptive overview of available Dutch data and started building up an evidence synthesis network (risk assessment and epidemiological data) for the pork chain as a multi-level bayesian model.

A physical meeting of the whole consortium is planned for October at Schiphol airport.

5.1.2.3.2 Project-specific milestones and deliverables

5.1.2.3.2.1 Deliverables

No deliverables planned before month 12

5.1.2.3.2.2 Milestones

JRP name	Milestone number	Milestone name	Delivery date from AWP	Achieved (Yes/No)	If not achieved: Forecast achievement date	Comments
RaDAR	M-JRP3-1	Kick-off meeting and report	1	yes		
RaDAR	M-JRP3-2	Identification data gaps and SEJ (Structured Expert Judgment) target questions	3	yes		
RaDAR	M-JRP3-3	Complete literature reviews of previous PK/PD and on-farm models (ANSES, APHA)	5	yes		Reference databases have been updated with recent publications
RaDAR	M-JRP3-4	Complete literature reviews of AMR transmission modelling (CVI, NCOH, RIVM)	5	no	12	Delayed due to awaiting appointment of PhD student
RaDAR	M-JRP3-5	Defined seed questions	6	yes		
RaDAR	M-JRP3-6	Database of available data	6	yes		
RaDAR	M-JRP3-7	Develop model frameworks for PK/PD and on-farm model (ANSES, APHA)	8	yes		Model frameworks have been developed. A draft report on the framework for the on-farm model is currently in internal review with APHA and our national funders VMD.

5.1.2.3.3 Description of the project activities per task

5.1.2.3.3.1 WP0: Coordination and communication

JRP3-WP0-T1: Coordination and project management
Regular mail and phone/skype contact with WP leaders; and EJP management.

JRP3-WP0-T2: Consortium meetings
JRP3-WP0-T2-ST1: Kick-off meeting
Performed in January 2018.

JRP3-WP0-T3: Annual reports
Not applicable.

5.1.2.3.3.2 WP1: New genomic information to feed AMR transmission models

JRP3-WP1-T1: Build collections of high throughput sequencing (HTS) data needed for project-specific milestones and deliverables
A curated plasmid Database consisting of 13124 Complete Plasmid Sequences from the NCBI was constructed. To our knowledge, this is currently the largest curated dataset of complete plasmids according to well-defined inclusion and exclusion criteria. The analysis of the metadata of the curated database (distribution of size, topology and taxonomy) is currently being analysed using R and graphical package ggplot.

JRP3-WP1-T2: Develop an innovative automated bioinformatic pipeline integrating de novo plasmid reconstruction and generation of chromosome scaffolds.
Artificial reads dataset was produced by ART to compare the plasmid reconstruction de novo (plasmidSPAdes) with the assembly using the BLAST algorithm (ABRIcate) https://github.com/tseemann/abricate. Preliminary results showed that plasmidSPAdes is very efficient for plasmids bigger than 6kb whereas the mass screening of contigs Blast-based (ABRicate) has a low efficiency when the search stringency is high.

5.1.2.3.3.3 WP2: Pharmacodynamics and transmission models

JRP3-WP2-T1: On-farm transmission models
JRP3-WP2-T1-ST1: PK/PD model to assess relationship between animal exposure and change in antimicrobial resistance
A reference database has been updated with recent publications which have been reviewed and used to inform the development of the PK/PD gut model. A document outlining inputs and outputs and an initial simple model framework has been shared with WP2 consortium members. This informs plans of how best to link up with the on-farm model in sub-task JRP3-WP2-T1-ST3.
JRP3-WP2-T1-ST2: Assess relative importance of AMU and clonal dissemination for resistance occurrence
In progress.
JRP3-WP2-T1-ST3: Development of on-farm transmission model
A draft model framework has been developed building on ideas from previous models identified in the literature review. The proposed model will consider ESBL *E. coli*. The literature review did identify some models that can deal with multiple resistances, but due to the added complexity in this model, it was considered that it would be a step too far to consider here. This would be a potentially useful addition to consider in the future. A document outlining the framework has been

circulated among relevant experts at APHA for feedback and discussions have been had with RaDAR partners at a WP2 teleconference.
JRP3-WP2-T1-ST4: Scenario analysis to assess hypothetical on-farm intervention measures
Work on this sub-task has not begun in earnest yet. A meeting with policy colleagues is being arranged for later in the year where practical on-farm intervention measures will be discussed.

JRP3-WP2-T2: Models for transmission between livestock and human populations
JRP3-WP2-T2-ST1: Development of mathematical models for source-attribution
Work has not begun on JRP3-WP2-T2 yet due to awaiting appointment of a PhD student to work on the project.

5.1.2.3.3.4 WP3: Transmission through the food chain

JRP3-WP3-T1: Inventory of available exposure assessment models and related data and transfer to FSK Standard
JRP3-WP3-T1-ST1: Inventory of available exposure assessment models
Members of the RaDAR team at BfR started to work with the RAKIP Project team which provides and develops the system of the model annotation scheme which will be the basis of the inventory for RaDAR. Moreover, it was important to be sure that models from EJP partners were not already used at BfR via another EJP project like ORION or COHESIVE. For this, a BfR internal meeting was organised end of June. The main concern of the meeting was to prevent people at BfR (from the EJP Projects RaDAR, ORION and COHESIVE) to potentially work with the same model or models from the EJP partners. The result of the meeting was, that nobody was working with any models from EJP partners.

JRP3-WP3-T2: Exposure assessment models for different production chains
JRP3-WP3-T2-ST1: Exposure assessment model for the chicken production chain
Work on the chicken production chain model started by adapting a model that originally simulated cross contamination of chicken carcasses in the slaughter line for Campylobacter. The aim is to adapt that model for ESBL *E.coli*. For the primary production (hatchery, transport, fattening at farm) another model should be developed. Currently ideas for its form are discussed between modellers at BfR.
JRP3-WP3-T2-ST3: Exposure assessment model for the mussel production chain
The experimental work has been planned but the lab work has not started yet as the employment of an engineer to be working with several of the EJPs including this task has been delayed.

5.1.2.3.3.5 WP4: Machine learning methods for quantification of risk and health effects

JRP3-WP4-T1: Add state of the art ML models for risk profiling to an inventory of exposure risk assessment models
JRP3-WP4-T1-ST1: Definition of the aims and requirements for literature research
Selected suitable ML benchmark data sets, simulated data sets (in silico data sets) with known effect size, variability and interdependence (correlation), and AMR data sets provided by partners within RaDAR and other EJP projects. Some of these data AMR data sets will be provided in the future. In addition, a list of requirements for real data records will be finalized which is expected to guide our partners in the selection of suitable data sets.
Evaluated the R-Package caret: The caret package (short for _C_lassification _A_nd _RE_gression _T_raining) is a set of functions that attempt to streamline the process for creating predictive models. The package contains tools for: data splitting, pre-processing, feature selection, model

tuning using resampling, variable importance estimation as well as other functionality. The caret package will be used to set up an evaluation pipeline.
Evaluation of the usability of ML for Small Data
JRP3-WP4-T1-ST2: Decision on the model inclusion criteria
Defined scores for quality assessment of ML result are under development. Evaluated ML model robustness according to e.g. data splitting is under development.
JRP3-WP4-T1-ST3: Decision on how the models are to be represented (described for the end user) and development of a template
It was decided to use the R package caret (https://topepo.github.io/caret/index.html) for the evaluation of the ML procedures. This package provides a standardized interface to a plethora of ML algorithms. For classification tasks we use all available probabilistic models (158). The chosen approach allows to remain in the known and easily accessible R environment and thus to address a wide range of users.
JRP3-WP4-T1-ST4: Repository setup including setup of a Github repository
Since all functionalities are provided by the caret package together with an elaborate manual, the implementation of a repository is obsolete. The caret library is the repository.
A wrapper is programmed and in operation, which enables a pipeline to process the special tasks of the sub-project.
All conceptual considerations and subsequent implementations were carried out by Dr Robert Opitz.
We are currently looking with our partner NVI for further sample applications (data) and would be pleased if more partners could provide data to evaluate the ML algorithms.

5.1.2.3.3.6 WP5: The burden of disease caused by AMR exposure

JRP3-WP5-T1: Identify data gaps and define target questions for SEJ (Structured Expert Judgment)
To address the burden of antimicrobial resistance, we have decided to work on a case study concerning urinary tract infections (UTI) caused by ESBL-*E. coli* at the EU level. From empirical data, we expect to be able to estimate the overall number of UTIs, identify possible health outcomes and draw health outcome trees. From empirical data, we can also estimate the overall number of ESBL (cephalosporin-resistant) *E. coli* infections. In order to reach estimates for the BoD of ESBL resistant *E. coli* UTIs, we have, therefore (so far), identified the following data gaps:

- What is the proportion of UTI infections caused by *E. coli*?
- How big a proportion of these is caused by ESBL *E. coli*?
- What is the proportion of ESBL *E. coli* UTI infections, where the used first choice of medication fails?
- And in case of failure, What is the additional average length of illness in days?
- What are the different transition probabilities in the health outcome trees for ESBL-resistant, with and without treatment failure, and non-resistant *E. coli* UTIs, respectively?

These data gaps will form the basis of our target questions in the SEJ. Besides the above quantitative data gaps, we will also ask the enrolled experts to comment on our health outcome trees to make sure that we haven't missed any important outcomes.

JRP3-WP5-T2: Defining the seed questions
We have not yet determined the final set of seed questions, but we expect to include 10-12 questions in total. Examples are:
Q1: In 2015, the total number of invasive *E. coli* isolates tested for resistance to third-generation cepahlosporins in EU/EEA (population-weighted mean) was 89,839 isolates. What percentage of these was resistance to third-generation cephalosporins? (Source: ECDC EARS-Net, 2017)
Q2: In 2015, the total number of invasive *E. coli* isolates tested for resistance to fluoroquinolones, third-generation cephalosporins and aminoglycosides in EU/EEA (population-weighted mean) was

87,798 isolates. What percentage of these was resistance to all three antimicrobial classes? (Source: ECDC EARS-Net, 2017)
Q3: What percentage of health-care associated UTI infections acquired in intensive care units is caused by *E.coli* at the EU level in 2014? (Source: ECDC, HAI-Net ICU 2017)
Q4: What percentage of all health-care associated *E. coli* infections was resistant to third-generation cephalosporins in 2014? (Source: ECDC, HAI-Net ICU 2017)

JRP3-WP5-T3: Identifying, enrolling and interviewing the experts
In progress.

5.1.2.3.3.7 WP6: Integration of information by Bayesian evidence synthesis

JRP3-WP6-T1: Collect current status data
We made a descriptive overview of available Dutch data relevant for risk assessment and epidemiological calculations. For risk assessment, this will comprise of ESBL *E. coli* prevalence data but also data that describe the human exposure intensity to ESBL *E. coli*. For epidemiology, data relate to the distribution of ESBL genes of plasmids in the human population and in the respective reservoirs. Also, risk factors and epidemiological metadata are described.

JRP3-WP6-T2: Build evidence synthesis network for current status database
We started building up our evidence synthesis network for the pork chain as a multi-level bayesian model, where parameters will have initial prior distributions whose parameters will in turn have prior distributions. This will allow to manage the level of desired uncertainty and also to find the most representatives values for some priors, e.g., uncertainty in the estimated average values on top of the spread around that estimated value. The code for carrying out the calculations is being written in R for JAGS. As first step we are constructing a network following the analysis carried out by Evers & Bouwknegt (2016) and using data there in found. By means of the QMRA analysis there presented we can estimate distributions of doses to which the population is exposed. These numbers are given as averages and for our code we are introducing a normal spread as first attempt. We will use a dose response relation model based on a Beta-Poisson function, where the function parameters will be loosely constrained. Form the epidemiology side we will employ information on duration of carriage (distributions from Teunis et al., 2018) and ESBL carriage attribution to pork (expert opinion) to estimate distributions of incidence per year and prevalence

5.1.2.3.4 List of planned tele- or video conferences, face to face meetings in the next year

A physical meeting of the whole consortium is planned for October at Schiphol airport.

5.1.2.4 Tox-Detect

5.1.2.4.1 Summary

The Kick-off meeting has been organized from 28th of February to the 1st of March 2018. After the general information dedicated to architecture of the EJP, elements of reporting and budget, a focus on the work package dedicated to the selection of bacterial strains has been discussed.
The project brings together five leading institutions from EU and Norway to work together on three pathogens (ie. CPS, *Bacillus cereus* and *Clostridium perfringens*) which are responsible for a large number of food-poisoning outbreaks (FPOs) in the European Union. FPOs caused by toxigenic bacteria share a common symptomatology that makes outbreak investigation challenging. As a consequence, the proportion of "weak evidence" FPOs is particularly high in case of bacterial toxins being the causative agent. The ultimate goal of this project is to fill the dramatic gaps of lacking methodologies to detect bacterial toxins, moreover characterize foodborne toxigenic bacteria, consequently contributing to an increased consumer health protection. Proteomics approaches based on liquid chromatography coupled to mass spectrometry (LC-MS/MS), Matrix-assisted laser desorption/ionization coupled to time-of-flight detectors (MALDI-ToF), and immune-enzymatic methods will be developed and implemented in this Tox-Detect project in view of their possible use for toxins/virulence factors detection and characterization. Ring trials between partners and collaborators will be organized for evaluation purposes, to assess, and to optimize the performance of the developed methods.
The aim of the KO meeting was to select 30 strains for each species studied in the Tox-Detect project (CPS, Bc and Cp). A previously designed table has been prepared by the WPL in agreement with the partners. This table contained relevant data including origin, characterisation, vigilance factors. Partners had to complete this table by suggesting strains from the collections available in their institutions. A total of 80 CPS, 90 Bc and 54 Cp strains have been proposed.
From this proposal, about 30 reference strains that will be used for further studies in Tox-Detect project had to be selected according to different criteria with agreement of partners (origin, virulence factors…).
For CPS, the aim was to develop Ab against SEG and SEH toxins. However, recently, partners not involved in EJP projects implemented the ELSA method dedicated to the detection of toxins type SEG and SEH. In order to avoid overlapping the EU projects, EJP Tox-Detect project and WP4 coordinators decided to develop Ab against SEM, SEN, SEO and to produce their types of toxins using cell-free system. Studies carried out using NGS techniques showed that these genes (SEM,SEN and SEO) are highly found in foodborne outbreaks that occurred in Europe. 13 strains encoding for SEM, SEN and SEO and a negative control (CIP 53.154) have been selected in the frame of WP1.
For Bc, the meeting was not able to perform a selection of relevant strains. Subsequently, it was decided to organize a dedicated meeting for this topic on 12th March 2018 at Partner 19 location [This dedicated meeting enabled to select both virulence factors to be tested and associated Bc strains].
For Cp, it was not possible to cover this topic during the Kick-of meeting. Another dedicated meeting has been planned on 22nd of March 2018. [This dedicated meeting enabled to select both virulence factors to be tested and associated Cp strains].
A consensus strain library has been dispatched on May 28, 2018 to feed other WP.

5.1.2.4.2 Project specific milestones and deliverables

5.1.2.4.2.1 Deliverables

JRP name	Project deliverable number	Deliverable name	Delivery date from AWP	Actual delivery date	If deliverable not submitted on time: Forecast delivery date	Comments
Tox-Detect	D-JRP4-0.1	Report of the kick-off meeting	3	/	7	The K-O off meeting was organized on M3. Minutes of KO will be dispatched on M7
Tox-Detect	D-JRP4-1.1	List of well characterized reference strains of *S. aureus, B. cereus* and *C. perfringens*	3	5	/	done
Tox-Detect	D-JRP4-1.2	Libraries of MALDI-ToF reference spectra	3	/	11	It was proposed to postpone this deliverable until the analysis of reference strains selected in D1.1. Analyses will be performed during summer 2018.

5.1.2.4.2.2 Milestones

JRP name	Milestone number	Milestone name	Delivery date from AWP	Achieved (Yes/No)	If not achieved: Forecast achievement date	Comments
Tox-Detect	M-JRP4-01	General decision on criteria to select strains	3	Yes		Discussed during TC conference 17th January 2018
Tox-Detect	M-JRP4-02	General discussion on interlaboratory trial scheme	3	Yes		Discussed during KO meeting on 1st March 2018
Tox-Detect	M-JRP4-03	Construction of the reference strains of S. *aureus, B. cereus* and *C. perfringens*	3	Yes		Diffused by email to partners on 28/05/2018
Tox-Detect	M-JRP4-04	Exchange of libraries of MALDI-ToF reference spectra	3	No	12	Additional analysis by Maldi-TOF is necessary before exchange of libraries. TC organized with coordinators and WP Leader on 16th May 2018 Protocol extraction and experiments are in progress
Tox-Detect	M-JRP4-05	Reference materials available	5	Yes		Reference strains are available for WPs

5.1.2.4.3 Description of the project activities per task

5.1.2.4.3.1 WP0. Coordination, management and communication

JRP4-WP0-T1: General coordination and management of the project (administrative and financial)
The overall purpose of the management structure is to ensure the timely implementation of the tasks and the smooth running of the project as a whole. Its primary goal is to identify arising opportunities and detect the occurrence of obstacles as early as possible, hence maximise the outcome of the project while preventing delays in its implementation. This will ensure that all tasks and research objectives are performed in due time.

JRP4-WP0-T2 to JRP4-WP0-T5: Organisation of four face-to-face meetings with all partners.
Only Task JRP4-WP0-T2 on "The kick-off meeting. Discussion of criteria to select bacterial strains. Discussion of organization of inter-laboratory trials was planned on year 1.
The Tox-Detect kick-off meeting was held in Maisons-Alfort (France) from 28th of February to the 1st of March 2018 (M3). 16 participants representing all Tox-Detect partners were present during the kick-off meeting. All participants presented their institutions, activities and involvement in the Tox-Detect project. The kick-off-meeting was the first meeting of all project partners. The meeting was split into two half days.
The aims of the Tox-Detect Project kick-off-meeting were:

- to introduce all project members;
- to get information on administrative and financial issues by representatives of EJP coordination team;
- to give an overview of the aims of the project and provide detailed information on all work packages;
- to discuss open questions on the selection of the reference strains that should be used in this project
- to vote the logo of the project

The Kick of meeting report is in progress and expected in M9.

JRP4-WP0-T6: mandatory reports on network activities: interim activity report, final report
Not relevant yet.

5.1.2.4.3.2 WP1. Constitution of a reference strain collection for *S. aureus, B. cereus* and *C. perfringens*

The constitution of a reference strain collection for *S. aureus, B. cereus* and *C. perfringens* was launched during the first tele-conference on 17 January 2018. The selection criteria were discussed and the WP1 leader drafted corresponding table. Partners had to complete this table by suggesting strains from the collections available in their institutions representing the food, clinical and environmental categories.
All partners implemented the table by available well characterized strains until 27 February. Partners have to choice the most relevant strains for the Tox-Detect Project.

JRP4-WP1-T1: Constitution of *S. aureus* strains collection
80 *S. aureus* strains have been proposed by Tox-Detect partners, representing human and food categories. The major part was issued from food poisoning outbreaks. For CPS, the aim was to develop Ab against SEG and SEI toxins. 13 strains encoding for SEG and SEI and a negative control (CIP 53.154) have been selected.

JRP4-WP1-T2: Constitution of B. cereus strains collection
90 Bacillus (Bc) strains have been proposed by Tox-Detect partners, representing human and food categories. This meeting was not able to perform a selection of relevant strains; it was decided to organize a dedicated meeting for this topic on 12th March 2018. This dedicated meeting enables to select both virulence factors to be tested and associated Bc strains. Therefore, 21 strains were selected.

JRP4-WP1-T3: Constitution of C. perfringens strains collection
54 C. perfringens (Cp) strains have been proposed by Tox-Detect partners, representing human and food categories. For Cp, it was not possible to cover this topic during the Kick-of meeting. Another dedicated meeting has been planned on 22nd of March 2018. This dedicated meeting enabled to select both virulence factors to be tested and associated Cp strains. Therefore, 40 strains were selected representing human, food and environmental categories. All strains were selected on the base of the production or not of CPE.

JRP4-WP1-T4: Transfer of libraries of MALDI-ToF reference spectra
This task was launched on M3, TC meeting was organized on 16th May 2017. The extraction protocol was discussed and will be dispatched to involved partners. After analysis of the selected reference strains, MALDI-TOF libraries will be established and dispatched to TOX-Detect partners. Deliverable is expected by the end of 2018.

5.1.2.4.3.3 WP2 Characterization of toxins/virulence factors

JRP4-WP2-T1: Characterization of candidate toxin and/or virulence genes using toxicity tests
Toxicity experiments on human intestinal Caco2 cells have been performed after 2, 24 and 48h treatment with the media used for vegetative and sporulation cultures of C*. perfringens*. The cytotoxicity was tested by the MTT assay and the release of interleukin 8 (a mediator of inflammation) was measures by ELISA. A selection of *C. perfringens* strains (extracts from both exponential and stationary phases of vegetative cultures) from Anses was tested using these two assays.

JRP4-WP2-T2: Assessment of virulence and toxin gene expression using RT-PCR and transcriptomic assays
JRP4-WP2-T2-ST1: Optimization of growth conditions to be used for gene expression analysis
This task was launched on M5 for *B. cereus*. The protocol of bacterial growth and RNA extraction was optimized for *B. cereus*. After analysis of the selected reference strains, various growth conditions will be tested.

5.1.2.4.3.4 WP3: Development of Mass Spectrometry-based proteomics procedures for detection of bacterial toxins and virulence factors

General strategy of WP3 has been discussed with all partners during KO meeting.
WP3 dedicated TC have been organized on 22nd February and 29th March 2018. Partners started to implement the discussed strategy.

JRP4-WP3-T1: development of Mass Spectrometry-based methods for the detection of new enterotoxins (eg SEG, SEH, SEI) from S. aureus
Work on task 3.1 will begin in M9.

JRP4-WP3-T2: development of Mass Spectrometry-based methods for the detection of toxins and/or virulence factors from B. cereus
TBD

JRP4-WP3-T3: Development of Mass Spectrometry-based methods for the detection of toxins and/or virulence factors from *C. perfringens*
TBD

5.1.2.4.3.5 WP4: Development of new immuno-enzymatic assays for detection of *S. aureus* and *B. cereus toxins* and virulence determinants

JRP4-WP4-T1: Development of quantitative immunoassays for five known *S. aureus* and *B. cereus* toxins and virulence factors
JRP4-WP4-T1-ST1: Selection of 5 target genes and construction of genetic tools for proteins overexpression
For *B. cereus*, 3 toxins have been selected as targets for the development of quantitative immunoassays. These toxins are NheA, CytK2 and Smase. Construction of the genetic tools for the overproduction of these proteins is expected to start at M10, upon availability of the reference strains and of their genomic sequences.
For *S. aureus*, 6 CPS strains have been selected for cloning the genes encoding SEM, SEN and SEO. Evaluation and comparisons between the coding sequences as well as the cloning are still in progress. The results are expected for M10.
JRP4-WP4-T1-ST2: Proteins production
For *B. cereus*, protein production will start after completion of the genetic tools construction, which is expected to occur by M14.
For *S. aureus*, the preliminary works for protein production, in order to raise antibodies, is in progress. The expected time for the beginning of this Sub-task is M10.
Meeting between Tox-Detect coordination and WP4 was organised on 4th and 6th September at Berlin on SE types selection, sequences analysis, protein production was

5.1.2.4.3.6 WP6. Dissemination, protection and exploitation of results

JRP4-WP6-T1: dissemination of information within the partners
WP0 prepared various documents including contact list, logo, ppt template to promote Tox-Detect activities. All these documents will be joined as annexes to the minutes of the KO meeting (M9).

JRP4-WP6-T2: dissemination of information to the outside
An overview of the ToxDetect project has been presented during the annual workshop of the NRL for CPS which took place in Maisons-Alfort from May 30 to June 2, 2018.
Another presentation of this project has been performed during a tri lateral meeting involving Germany (RKI, Berlin), Switzerland (Agroscope, Speiz Lab, Bern) and France (CEA and Anses). This meeting took place at Agroscope (Bern, Switzerland) on May 24, 2018.
Finally, a slide presenting the overview of the ToxDetect project has been presented during Food Micro conference (Berlin, Germany) on September 3, 2018.

5.1.2.4.4 List of planned tele- or video conferences, face to face meetings in the next year

Depending on the needs, WPL will organize dedicated TC.
WP0 will organize a general coordination meeting expected to take place at Maisons-Alfort on January 2019.

5.1.2.5 MAD-Vir

5.1.2.5.1 Summary

The MAD-Vir project is progressing as planned. The project started with a Kick-off meeting held at SSI in Copenhagen (the 2nd of February). At this meeting every participant presented themselves and their institutes. In the initial project proposal the microarray technology was only to be implemented at INIA and APHA, however PIWET was very interested in learning the technology and because they already had all the microarray equipment and were able to finance the technology transfer without any additional costs to the project, it was decided to expand the technology transfer to PIWET also.

It was also decided that each partner in the project should select different samples from their biobanks to be tested at SSI with the PanVirus microarray (1st round). A common sample pre-treatment/inactivation protocol was presented by SSI and it was decided that all participant should follow this protocol. So far, SSI has received 14 samples from PIWET, 5 samples from INIA, 10 samples from IZSAM, 16 samples from OIK, 8 samples from ANSES, 3 samples from VRI and 10 samples from IZSLER to be tested for virus with the PanVirus microarray. University of Surrey and APHA has still not sent any samples to be tested in the 1st round.

5.1.2.5.2 Progress of the research project: milestones and deliverables

5.1.2.5.2.1 Deliverables

JRP name	Project deliverable number	Deliverable name	Delivery date from AWP	Actual delivery date	If deliverable not submitted on time: Forecast delivery date	Comments
MAD-Vir	D-JRP5-1.1	Kick-off meeting	6	29th of June 2018		
MAD-Vir	D-JRP5-3.1	Implementation of MAD-VIR to INIA and APHA	6	29th of June 2018		

5.1.2.5.2.2 Milestones

No Milestones before month 12.

5.1.2.5.3 Progress of the research project

5.1.2.5.3.1 WP1: Coordination and management

Project management and coordination of the project is proceeding according to the plan.

5.1.2.5.3.2 WP2: Sample collection

Each partner in the project has selected different samples from their biobanks to be tested with the PanVirus microarray in the 1st round at SSI.
A pre-treatments protocol for the samples (depending on the type of sample material) has previously been published (Erlandsson et al., 2011) and all partners follow this sample pre-treatment protocol if possible. The pre-treated samples have been shipped to SSI either as extracted NA or as non-purified inactivated samples. Inactivation was performed using MPLB-buffer (Rosenstierne et al., 2016, Vinner et al., 2007) (1:1 volumen) before shipment. SSI has to this date received samples from 14 samples from PIWET, 5 samples from INIA, 10 samples from IZSAM, 16 samples from OIK, 8 samples from ANSES, 3 samples from VRI and 10 samples from IZSLER. University of Surrey and APHA has still not sent any samples to SSI to be tested in the 1st round. SSI has contributed with 41 samples for the 1st round and 12 samples for the initial ring-testing. The samples are from wild life, human, aedes and ticks.

Ref:
Rosenstierne MW et al., 2016, Journal of Clinical Microniology, 54: 2521-2529
Vinner L & Fomsgaard A., 2007, Journal of Virological Methods 146:401–404

5.1.2.5.3.3 WP3: Diagnostic and surveillance

JRP5-WP3-T1: Technology transfer
SSI has made arrangements with Agilent Technologies so that INIA, APHA and PIWET can order the non-commercial custom made SSI PanVirus microarray v2 design.
All Standard operating procedures (S.O.Ps), microarray files for scanning and data subtraction has been distributed to INIA, APHA and PIWET.
MWR (SSI) has visited the three Institutes and implemented the PanVirus microarray technology (INIA; 15th to 25th of April, PIWET; 10th to 20th of June, APHA; 25th to 26th of June). Training in sample preparation, microarray technology and data-analysis has been performed at each Institute. The visit at APHA was shorter because APHA already knew the microarray technology and did not find it necessary to be trained in the technology.

JRP5-WP3-T2: QA-validation
SSI has sent 12 virus positive samples (purified or non-purified inactivated samples) to INIA, PIWET and APHA for ring-testing. During the training of the microarray technology some of these samples were used as positive controls. So far INIA has tested and verified the correct virus in 12/12 samples, PIWET has tested and verified the correct virus in 6/12 samples. APHA has not yet tested any of the positive samples 0/12.

JRP5-WP3-T3: Analysis of samples
SSI has started analyzing the 1st round of sample. One hundred and seven samples has been included in the 1st round of testing (see Table 1) and to this date 97 of the samples has been analyzed using the PanVirus array v2 microarray (see Table 1). Of the 97 samples tested 65 of the samples was expected to contain a known virus and 32 of the samples had an unknown viral

content. The PanVirus array v2 identified the correct virus in 48 of the samples with known viral content and in the samples with unknown content 8 samples were found positive for virus.

The microarray did not detect 8 samples expected to be positive for WNV (sample no. 2, 3, 15, 16, 17, 35, 37, 38), 2 samples expected to be positive for Usutu virus, 1 sample expected to be positive for Meaban virus (sampl no. 4), 1 sample expected to be positive for Blue tongue virus 4 (sample no. 20), 1 sample expected to be positive for Avian laringotracheitis (sample no. 31), 1 sample expected to be positive for Lassa virus (sample no. 85), 1 sample expected to be positive for Sin Nombre virus (sample no. 87), 1 sample expected to be positive for Seoul virus (sample no. 88), 1 sample expected to be positive for Puumala virus (sample no. 89) and 1 sample expected to be positive for TBE virus (sample no. 92)(see Table 1).
However, PCR control analysis of these samples showed that virus could not be detected in 9 of the samples (sample no. 2, 3, 9, 14, 35, 37, 87, 88, 89) neither before nor after whole transcriptome amplification (WTA) which could indicate a degradation of the sample (poor sample quality). PCR verification could not be performed on Meaban virus (sample no. 4), Bluetongue virus 4 (sample no. 20) or Avian laringotracheitis (sample no. 31) due to the lack of PCR assays for these virus at SSI. Bluetongue virus 4 was identified with the PanVirus array v2 in another sample (sample no. 21) which could indicate a poor sample quality or very low viral content of sample 20. This is currently under investigation. Evaluation of the probes present on the PanVirus array v2 identified the lack of probes for Meaban virus. Probes for Meaban will be added to the next updated version of the PanVirus array.
Subtracting these virus negative samples from the analysis the PanVirus array v2 detected 46 samples of out 53 samples (87%).
PCR confirmed the presence of virus in the remaining 6 samples that was not detected by the PanVirus array v2. Four of these samples showed no ct or very high ct value (Ct>34) after WTA amplification (sample no. 16, 17, 85 and 92) indicating a low viral load. For some reason these samples were not amplified to the level of detection by the array and have to be re-analyzed (ongoing). Two WNV samples (sample no. 15 and 38) had a low ct-values after WTA amplification (Ct=14 and Ct=19) indicating a high viral load in these samples. These samples should be within the detection limit of the array which could indicate that the probes present for WNV virus on the PanVirus array v2 microarray need to be optimized.
A new updated version of the microarray (PanVirus microarray v3) has been designed which contain updated WNV probes and the addition of probes for Meaban virus. This version will also have probes for all new virus present in Genbank (June 2018) in addition to several specific probes for different fish virus isolates. This PanVirus microarray v3 will be ready for use in October 2018. All samples that were not detected by the PanVirus array v2, but confirmed positive by PCR, will be re-analysed by the PanVirus array v3. In the meantime, the PanVirus microarray v2 will be used to analyse more samples as planned.
Besides identifying the already know virus present in the samples the PanVirus array v2 also identified several other virus not known to be present in the samples (Table 1). For example Exogenous mouse mammary tumor virus, Murine leukemia virus, Murine type C retrovirus and Spleen focus forming virus was identified in samples from WNV and Eyach virus isolates grown in mouse brain (sample no. 8, 12 and 13). DNase treatment of these samples showed that these virus originate from the endogenous retrovirus integrated into the mouse genome (sample no. 12 and 13). Ovine enzootic nasal tumour virus, Jaagsiekte sheep retrovirus, Enzootic nasal tumour virus of goats was additionally identified in whole blood from Sheep (sample no. 19). In two samples from Insect homogenate Ngewotan virus JKT9982, Nam Dinh virus, Houston virus, Hana virus, Dak Nong virus, Alphamesonivirus 1, Cavally virus was also identified (sample no. 14 and 16). In an Astrovirus positive sample from the intestinal content from a turkey Rotavirus, Avisivirus and Gyrovirus was also identified (sample no. 25). In a HEV positive fecal sample swine pasivirus 1, posavirus 1, porcine

teschovirus, Porcine stool associated circular virus, porcine kobuvirus, porcine enterovirus, porcine astrovirus, Parechovirus like virus, wild boar astrovirus was also identified (sample no. 59). In a pool of organs from chicken (sample no. 29) and in a fecal bovine fecal sample (samples no. 30) several additional virus were identified (Table 1). PCR confirmation of these additional virus is currently ongoing.

Thirty two samples with unknown content were also analyzed with the PanVirus array v2 and virus was identified in 8 of the samples. Porcine Kobuvirus, Porcine enterovirus and Porcine circovirus was identified in a blood sample from a wild boar (sample no. 50), Avian hepatitis B virus was identified in homogenates from internal organs from a stork (sample no. 54 and 55). Human parainfluenza virus 3 and JC virus was identified in a human patient (sample no. 75-77) and Uukuniemi virus and Blacklegged tick virus was identified in a homogenized pool of ticks (sample no. 71 and 73). PCR confirmation of these virus is currently ongoing.
These preliminary results show a great potential for using microarray as a screenings tool for the presence of virus. However, the initial experiments also show that an update to the current PanVirus array v2 is needed.

5.1.2.5.3.4 WP4: Data Sharing

The common EJP website (https://onehealthejp.eu) is used for the MAD-Vir project. A private MAD-Vir group has been generated and all microarray data files and sample descriptions will be uploaded to this group and shared between the MAD-Vir partners. Not all MAD-Vir partners has joined the EJP website or the MAD-Vir group yet due to summer holiday delays.

5.1.2.6 NOVA

5.1.2.6.1 Summary

The project has been in a start-up phase with continued planning and collaboration within all work packages. A kick-off meeting was held in Rome, February 28th – March 1st, 2018. At this meeting researchers working in all work packages, and from all but two partners, where present. Some of the researchers have had previous collaborations but many of us has not met in person before and it was a good opportunity to get to know each other and understand how we can make the best use of each other's competences. We also spent time within the WP groups to discuss details within each WP.

After the kick-off contact within WPs has continued through e-mail and video conferences. Each month (since October 2017), the coordinator has had online meetings with the WP leaders. Access to an online folder has been shared among the partners to make notes from meetings, presentations, templates, and other documents available to all.

The work is now ongoing within the first tasks and the very first deliverables have been completed. In several WPs (1, 2, 3, and 4), the first tasks include mapping of different aspects of surveillance and available data sources. To avoid overlap and to enable synergies across projects, mapping strategies and content have been discussed with experts in the ORION and the COHESIVE projects. WP1 also includes work on surveillance terminology that can be linked to work in ORION, and a dialogue is kept between experts in the two projects.

During the first half of the year, several partners have recruited staff that will work part time or full time in the project.

5.1.2.6.2 Project-specific milestones and deliverables

5.1.2.6.2.1 Deliverables

JRP name	Project deliverable number	Deliverable name	Delivery date from AWP	Actual delivery date	If deliverable not submitted on time: Forecast delivery date	Comments
NOVA	D-JRP6-0.1	Documentation of consortium assembly and steering committee meeting	3	2018-06-21		Documentation completed in Month 3 but deliverance was postponed because we wanted to use the right template.
NOVA	D-JRP6-2.3	Structured review of the field.	5	2018-05-31		
NOVA	D-JRP6-3.1	Full mapping of the chain process for three main productions in E.U	8	2018-08-31		

5.1.2.6.2.2 Milestones

JRP name	Milestone number	Milestone name	Delivery date from AWP	Achieved (Yes/No)	If not achieved: Forecast achievement date	Comments
NOVA	M-JRP6-1	Consortium assembly and steering committee meeting	2	Yes		
NOVA	M-JRP6-2	Meeting for information exchange (data, literature, data bases) exchange on exposure assessment, DALY's, consumption data and food handling at home	6	No	10	Meeting postponed to await recruitment of staff, and thereby enabling these new co-workers to participate.
NOVA	M-JRP6-3	Food Chain mapping completed, data sources identification advanced, and ready to start developing the SS components	7	Yes		

5.1.2.6.3 Description of the project activities per task

5.1.2.6.3.1 WP0: Coordination and project management

JRP6-WP0-T1: Project management
Monthly meetings with WP leaders has been held. The coordinator has also attended information meetings with the other coordinators within the One Health EJP (face-to-face and via video conferences). She also presented the project at the official kick-off of the whole EJP in January in Paris. Apart from these meetings, project management has included finding platforms for sharing of information and documents and to summarise information about the project e.g. for the web pages of the One Health EJP and our institutes.

JRP6-WP0-T2: Organise annual assemblies
An annual assembly (kick-off meeting) was organised and held in Rome, February 28th to March 1st.

JRP6-WP0-T3: Economic reporting and financial management
No major tasks to report.

5.1.2.6.3.2 WP1: Food chain surveillance mapping

JRP6-WP1-T1: Definition of a joint food borne zoonosis surveillance terminology
In collaboration with ORION project, an inventory of glossaries developed by international and Europeans organizations, including previous EU projects, was developed. Additionally, generic and specific terms on food chain surveillance are discussed by domain of expertise, i.e. animal health, food safety, and public health. Building up on the glossary developed by ORION, terms specific to NOVA will be addressed in close collaboration with other work packages.

JRP6-WP1-T2: Mapping of surveillance: data, regulatory framework, key stakeholders, opportunities and barriers
The output of RiskSur, a previous European project on animal health surveillance, was assessed for its suitability as framework in the public domain. A core mapping of the food chain components is under development with the animal domain being designed. Additionally, identification of key players for food chain surveillance has been started. The mapping will be further developed in finer resolution, in collaboration with WP3 and OHEJP national mirror groups, to identify unused data and stakeholders.

5.1.2.6.3.3 WP2: Analysis of food purchase data

JRP6-WP2-T1: Data availability and barriers
Investigations of data availability and barriers have been initiated.

JRP6-WP2-T2: Food purchase data for outbreak investigations
Investigations have been initiated and a structured review of existing use of purchase data for outbreak investigation has been performed.

JRP6-WP2-T3: Big data analysis of risk factors for sporadic disease
No major tasks to report.

JRP6-WP2-T4: Food distribution data for hospital outbreaks
No major tasks to report.

JRP6-WP2-T5: Trace back and food risk mapping
No major tasks to report.

5.1.2.6.3.4 WP3. Syndromic surveillance

JRP6-WP3-T1: Identify the opportunities for SyS of FBD
JRP6-WP3-T1-ST1: Food chain mapping
A preliminary food chain mapping has been performed by the WP leaders, as per project schedule, and a diagram circulated in the WP for feedback. with input from the WP. This preliminary diagram will be now reviewed in collaboration with WP1, and with other EJP projects.
JRP6-WP3-T1-ST2: Data source screening: availability, quality and suitability for SyS
The main project partners in this WP (Sweden, France and Norway) have performed an inventory of data sources currently used, and potentially useful for syndromic surveillance. This inventory will serve as a base for future tasks, in which assessments will be performed to score the data availability and quality to support traditional, event-based surveillance.

5.1.2.6.3.5 WP4: Spatial risk mapping

JRP6-WP4-T1: Identification of spatial relationships and patterns in Salmonella prevalence
JRP6-WP4-T1-ST1: Surveillance in high prevalence regions to detect introduction and changes in prevalence.
Data on salmonella, pig industry and human population are being explored to accomplish the D-4.1 (month 12). The high prevalence region chosen is Spain and therefore Salmonella surveillance in Spain has been reviewed, e.g. by using information in the legislation and in EFSA's annual summary reports (EU and for Spain). From this, databases with the information retrieved have been created, and descriptions of Salmonella surveillance "from-farm-to-fork" (from pig source), as well as salmonella surveillance in suspect patients in Spain (from ingestion of contaminated product), have been performed. Work to publish the results in a scientific paper is ongoing.
JRP6-WP4-T1-ST2: Surveillance in low prevalence regions to reduce prevalence.
The low prevalence region chosen is Sweden and since the salmonella prevalence in Swedish pigs is negligible, the focus for this subtask is salmonella in Swedish cattle. A spatial module has been developed and added to the SimInf framework, in order to address this task. SimInf is a data-driven disease spread modelling framework suitable for this type of research question. A first version of the salmonella model has been completed but further work with parameterization will be needed.

JRP6-WP4-T2: Risk of introduction of Salmonella in pig farms through animal feed.
Not yet initiated

JRP6-WP4-T3: Role of the environment in the occurrence and maintenance of Salmonella infection in extensive farming.
Data on salmonella and pig industry are being explored to accomplish the D-4.7 (month 12).

5.1.2.6.3.6 WP5: Evaluation of surveillance programs & cost efficiency

JRP6-WP5-T1: Adapt infectious disease models for assessing the effect of surveillance programs in primary animal production on consumer exposure to foodborne pathogens.
Existing models and potential development and combination of models have been discussed. A decision has been made to include several different models in the investigations, to enable potential ensemble modelling and make use of the strength of each methodology.

JRP6-WP5-T1-ST1
Adaptation of existing models has been initiated.
JRP6-WP5-T1-ST2
Codes are being developed for investigation of surveillance strategies in the primary production within a disease spread model. The disease spread model is currently parameterised for paratuberculosis in cattle and has been based on the SimInf disease spread model framework.

JRP6-WP5-T2: Assessing the effect of using metagenomics in surveillance of foodborne zoonoses
Not yet initiated

JRP6-WP5-T3: Modelling the effect of surveillance programs in the food production on human health.
Potential outcomes are being discussed. Based on the choice of outcomes, the most proper models and data will be decided.

5.1.2.6.4 List of planned tele- or video conferences, face to face meetings in the next year

The coordinator and WP leaders will have monthly one-hour (or longer, if needed) video conferences. The planned dates for these are:

January 15
February 12
March 12
April 9
May 14
June 11
August 27
September 17
October 15
November 12
December 10

An annual assembly with an opportunity for face-to-face meetings across and within WPs will also be held. The preliminary plan is to have this meeting in Berlin in May 2019.

5.1.2.7 LISTADAPT

5.1.2.7.1 Summary

The LISTADAPT JRP project has officially started in January 2018. The kick-off meeting and a workshop held in Maisons-Alfort in March. The workshop has permitted to select the statistical tools and bio-informatics approaches that will be used in the project.
Partners of LISTADAPT have concentrated their efforts on strain selection and characterization of their existing collection. LISTADAPT partners also took contact with other research laboratories to increase the diversity of the sampling at EU level.
An original algorithm for selecting strains according to metadata available has been developed and has been applied. The first batch of DNA extraction and sequencing has been carried out at month 9. Partners in charge of phenotypic characterization (adhesion, biocides, …) have received 100 strains (out of the 200 strains).

5.1.2.7.2 Progress of the research project: milestones and deliverables

5.1.2.7.2.1 Deliverables

JRP name	Project deliverable number	Deliverable name	Delivery date from AWP	Actual delivery date	If deliverable not submitted on time: Forecast delivery date	Comments
LISTADAPT	D-JRP7-1.1	Consortium agreement	1		10	Discussion on content of Consortium Agreement initiated. Official signature will probably not be achieved before month 10
LISTADAPT	D-JRP7-1.2	Description of the panel of strains already sequenced	1	1		Sequenced strains were mainly isolated from food industry/ready-to-eat food. These strains further described with metadata
LISTADAPT	D-JRP7-5.1	"LISTADAPT" workshop program	2	2		
LISTADAPT	D-JRP7-1.3	Description of the first panel of strains available to sequence	3	6		
LISTADAPT	D-JRP7-2.1	Internal reporting templates	3	3		The reporting template has been established based on template provided by EJPOH coordination team
LISTADAPT	D-JRP7-2.2	Annotation of Lm genomes already sequenced (genomes available before the start of the project)	6	6		Assemblies and annotations of Lm genomes already sequenced (genomes available before the start of the project) were carried out with different tools by different LISTADAPT partners.

5.1.2.7.2.2 Milestones

JRP name	Milestone number	Milestone name	Delivery date from AWP	Achieved (Yes/No)	If not achieved: Forecast achievement date	Comments
LISTADAPT	M-JRP7-1	Kick off meeting	2	Yes		
LISTADAPT	M-JRP7-2	Selection of the 200 strains of Listeria monocytogenes from genomic analyses in WP2	3	Yes/No	10	100 strains have been selected based on their genomic characteristic and context of isolation. These strains correspond to strains isolated along the food production chain. For the left 100, partners wait for the strains collected during the first sampling campaigns programmed (see. Tasks 1.2.1 and 1.2.2)
LISTADAPT	M-JRP7-3	Workshop done	3	Yes		The workshop on statistical and bioinformatics methods was completed with additional exchanges between EJP LISTADAPT members
LISTADAPT	M-JRP7-4	DNA prepared for 1st batch WGS	4	Yes	9	The first DNA were prepared in September.
LISTADAPT	M-JRP7-5	Strategy for selection of strains for sequencing in place	5	Yes		An original algorithm was developed for selecting strain based on meta-data describing the context of isolation of the strains

JRP name	Milestone number	Milestone name	Delivery date from AWP	Achieved (Yes/No)	If not achieved: Forecast achievement date	Comments
LISTADAPT	M-JRP7-6	WGS raw data produced	6	No	9	The sequencing was reported of 2 months (related to report of M.2.2)
LISTADAPT	M-JRP7-7	Face-to face meeting -2018	8	No	10	
LISTADAPT	M-JRP7-8	First batch Lm genomes assembly completed	8	No	10	Anticipated as report written at month 9 (Should be delivered at month 10)

5.1.2.7.3 Description of the project activities per task

5.1.2.7.3.1 WP0: Coordination

Kick-off meeting and workshop have been organized in Maisons-Alfort in March. The coordinator assisted most meeting organized by the OHEJP coordination.
The communication (e.g. exchange of documents) between partners is facilitated since website/intranet is available (opened in August).

5.1.2.7.3.2 WP1: Constitution of a strain collection representative of the different reservoirs of Listeria monocytogenes

JRP7-WP1-T1: Strain collection
All partners have selected strains from their own collections which were established before the LISTADAPT project started. After LISTADAPT started, the strains were characterized with molecular serotype, PFGE, MLST and or WGS typing in order to identify the CC group. These activities were sufficient to collect the target number of strains from foods, but more isolates were needed from other niches.

JRP7-WP1-T2: Campaigns to collect additional animal and environmental strains
JRP7-WP1-T2-ST1: External collaborations
Before the beginning of the project, external participants have already agreed to provide animal and natural environment isolates from their own strain collections: National Veterinary Institute of Ljubljana (SI); ISAE (Agronomic institute) (FR); IFIP The French pork institute (FR), Veterinary Faculty of Skopie (MK).
Several other research scientific teams were approached to collect strains form animal and environment. The list of new contacts is reported in Table 1. These collaborations will increase the representativeness/diversity of the LISTADAPT strain collection (more country at EU-level, more partners at country level).
The algorithm of strain selection (see Task 1.3) was used to select strains according to the metadata (region, period, subtype…) provided by partners.

Table 1. List of newly established external collaborations for increasing diversity of LISTADAPT strain collection

Partners	Country	Contact	Strain collection panel	Number of selected strains*
University of Helsinky	Finland	Dr Miia Lindstrorm	animal sector (cattle and farm strains)	180 strains
BIOR The Institute of Food Safety, Animal Health and Environment	Latvia	Dr Zanete Steingolde	animal sector (cattle and farm strains)	36 strains
Faculty of Food Science and Fisheries - West Pomeranian University of Technology	Poland	Dr Barbara Szymczak	Environment (soil, fruits, vegetables)	80 strains
PIWET	Poland	Dr Wasyl Dariusz	Environment/farm/animal	Discussion in progress
ONCFS	France	Dr. Anouk Decors	Wild animal	Discussion in progress

University of Munich	Germany	Dr Verena Hohenester	Wild animal	32 strains
Neiker Tecnalia	Spain	Dr Ana Hurtado	Farm animal (cattle, sheep)	38 strains
Teagasc	Ireland	Dr Kieran Jordan	animal sector (milk strains)	Selection in progress
PHE	UK	Dr Corinne Amar	Wild animal	5 strains
INIAV Animal Pathology Laboratory	Portugal	Dr Leonor Orge	Farm animal (cattle, sheep)	Selection in progress
Slovenian LNR for Lm	Slovenia	Dr Bojan Papic	Farm animal (cattle, sheep)	25 strains

* Selection procedure based on method described in task 1.3

JRP7-WP1-T2-ST1: Sampling campaigns

The strain collection established on existing isolates at the beginning of the project consisted mostly isolates from food, production environments and humans. The niches most underrepresented were wild life and nature. Several sampling campaigns have been organized during the nine first month of the project to fill this gap. Table 2 gave a list of the planned and ongoing campaigns. A specific protocol has been proposed for every partners of the project. A video has been created (the video will be shared through the website when available). The sampling has to be made either at farm (manure, soil), in the pasture (mud, soil) or in the forest (soil). For each sample, GPS coordinate (GPS coordinate are reported (in decimal format provided by google maps), as well as a picture of the sampling place with a brief description of the sampling environment.

The analyses of the samples have so far lead to less few new isolates of Listeria (e.g only 10 isolates were found from 1200 wild animals), but more samples are available and will be analysed. In order to limit resources, the analyses of pooled samples are done.

Table 2. List of sampling campaigns already realized or planned

Partners	Country	Region	Period	Type of samples	Number of samples
ANSES	France	Burgundy/Morvan	May	Meadow/forest	25
ANSES	France	Brittany	June	Meadow/forest	10
INRA	France	Burgundy	July-September	Farm/Meadow	>50
ANSES	France	Burgundy/Auxois	July	Meadow/forest	5
ANSES	France	Burgundy/Auxois	October-December	Meadow/forest/wild animal	50
VRI	Czech Republic	Various regions	September-October	Meadow/forest/farm	**50**
ANSES	Slovenia	Various regions	October	Meadow/farm	**50**
SVA	Sweden	Various regions	June-October	Meadow/forest/farm	**50**
NVI	Norway	Various regions	July-October	Soil and grass from forest, mountain areas and nature	**200**[1]
NVI	Norway	Various regions	Analyses of samples from 2015-2018	Feces from deer and other wild animals, no symptoms of listeriosis	**1200**[1]

JRP7-WP1-T3: Strategy for sequencing

We developed a sampling strategy never used before (to our knowledge) in the field on animal health or public health. The clustering process was applied on categorical metadata describing the strains (regions, season, subtype, breed,…). It contains 3 distinctive steps: (i) Calculating

dissimilarity matrix, (ii) choosing the clustering method and (iii) assess the clustering. More precisely, Gower distance was chosen for assessing dissimilarity of metadata, complete hierarchical clustering for building cluster, and "silhouette" method for assessing the optimal number of clusters (that is the optimal number of strains to select in a dataset).
The figure below illustrates the application of developed algorithm for the selection of strains from a collection provided by one partner of subtask JRP7-WP1-T2-ST1 The optimal number of cluster to sample is close to 20 (from a set of 54 strains). The 54 strains were split in 20 groups. One strain per group was then chosen randomly.

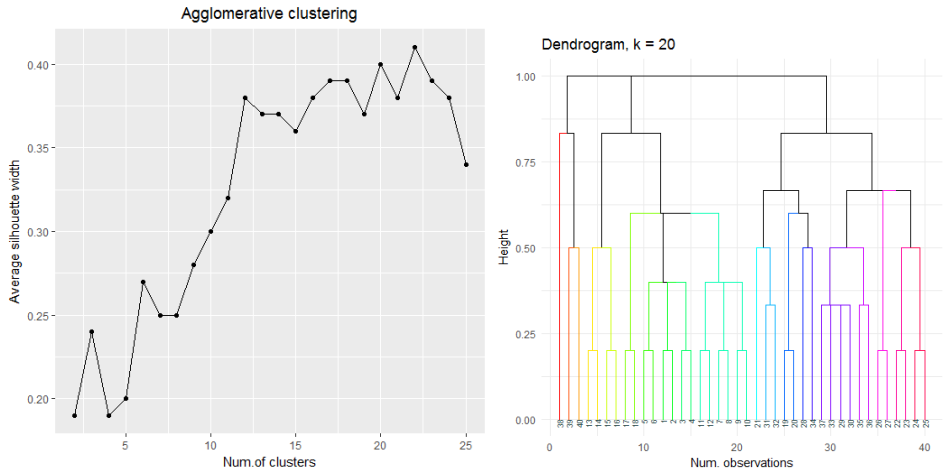

Figure 1. Results from the sampling algorithm develop in LISTADAPT to select strains based on categorical metadata describing strains.

5.1.2.7.3.3 WP2: Whole genome sequencing of Listeria monocytogenes strains

JRP7-WP2-T1: Purification of Lm DNA from 2000 Lm strains
JRP7-WP2-T1-ST1: First batch Purification of DNA from Lm strains available
The first batch of strains has been produced at month 9. At the month 9 the number of purification carried out is 96.
JRP7-WP2-T1-ST3: Purification of DNA from routine surveillance systems at IZSAM, DTU, AGES
Ages, DTU and IZSAM carried out since the beginning of the project. The final number of strain extracted will be established at the end of year 1

JRP7-WP2-T2: Whole Genome Sequencing
JRP7-WP2-T2-ST1: First batch Whole genome sequencing for available Lm strains
The first batch will be proposed at month 9
JRP7-WP2-T2-ST3: Ad hoc Whole genome sequencing
It is too soon for determining if the total amount of sequenced strain available at the end of the task JRP7-WP2-T2-ST2 will not reach the number of Lm genomes expected for the project. Partners of that tasks will be informed of this potential situation at month 12.

JRP7-WP2-T3: Genome Assembling and Annotation
LISTADAPT partners planned at the beginning of the project to use outputs from H2020 COMPARE projects. The cogwheel meeting in April 28th (three LISTADAPT partners ANSES, NVI and IZSAM assisted) between JRP/JIP leaders and COMPARE members permits to reveal that no SOP are yet available from COMPARE projects. Partners look for alternative solutions like tools proposed by Innuendo project (http://www.innuendoweb.org/)

5.1.2.7.3.4 WP3 Phenotypic characterisation of Listeria monocytogenes strains

JRP7-WP3-T1: Strategy for selection of strains for phenotypical characterization
A balanced sampling strategy has been selected for partitioning the 200 strains between food (100) and environmental/animal strains (100). Within the two categories, subcategories were proposed (see. Figure 2). Within each category, selection of strains was carried out based on the described CC diversity. Strains from the top three CCs of each subcategories were selected . For this reason selection of 100 strains from environmental/animal reservoir. We would like to have CC information in some sub-categories for having an homogenous selection procedure.

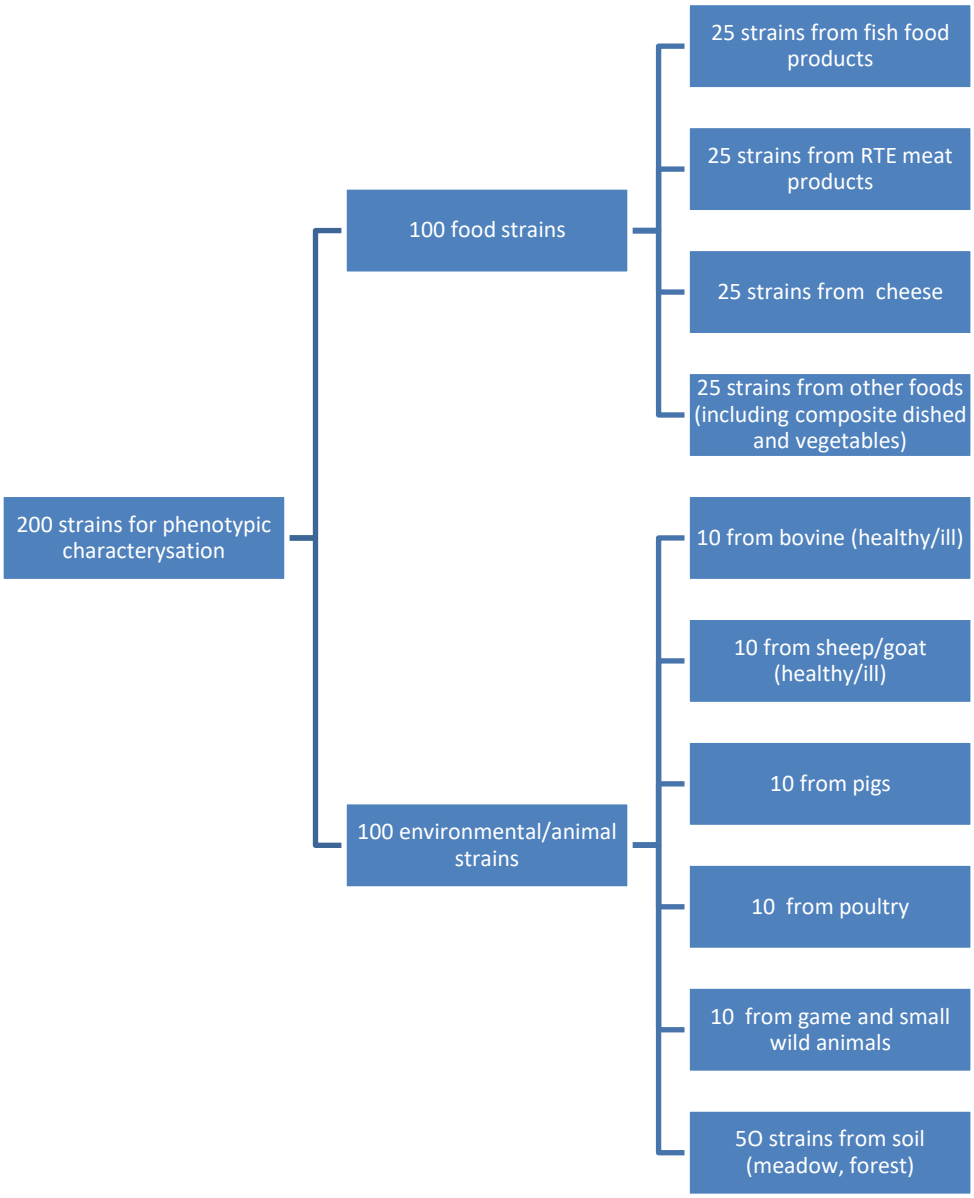

Figure 2. Partitioning of the 200 strains

JRP7-WP3-T2: The effects of biocides on *Listeria monocytogenes* strains adaptation
JRP7-WP3-T2-ST1: Antibiotics and biocides resistance profiles of *Listeria monocytogenes* strains
The starting date of experiments has been postponed of 2 months due to a report a strain reception. The determination of the final list antimicrobials (biocides and antibiotics) for determining the

susceptibility profiles of *L. monoctytogenes* has been established. Exchange with Dr Sophie Granier (from IMPART EJP project) has helped to determine the list. The resistance profile has begun in September with 100 strains.

JRP7-WP3-T3: Bacterial adhesion and biofilm formation of *Listeria monocytogenes* strains

The starting date of experiments has been postponed of 2 months due to a delay of strain reception. The experiments on adhesion and biofilm formation have begun in July with the first 100 strains from the food sector. The experiments focus first on adhesion with Biofilm Ring Test and stage biofilm with staining with crystal violet.

JRP7-WP3-T4: Survival and persistence of *Listeria monocytogenes* strains in different ecological niches

JRP7-WP3-T4-ST1: Survival of *L. monocytogenes* in food products and gastro-intestinal environment

JRP7-WP3-T4-ST2: Survival of *L. monocytogenes* in soil microcosm

For both experiments in food related conditions and medium mimicking gastro-intestinal environment, the starting date of experiments has been postponed of 2 months due to a delay in strain reception.

5.1.2.7.3.5 WP4: Identification of genetic traits in Listeria monocytogenes underlying adaptation to the ecological niches

JRP7-WP4-T1: Analyze the distribution / prevalence of clonal complexes among the reservoirs

The repartition of CC was carried for already sequenced strains for the different RTE food categories. Figure 3 illustrates the repartition for the three main RTE categories.

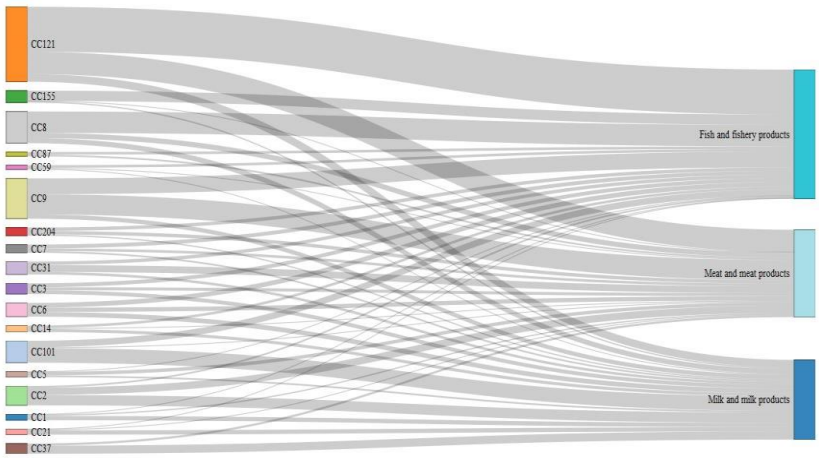

Figure 3. Sankey diagram of the repartition of the CC of already sequenced strain in the three main RTE food categories.

The analysis of reparation was also done along the farm to fork.

JRP7-WP4-T3: Biostatistic analysis of annotated genomes

JRP7-WP4-T3-ST1: Identification of statistically relevant methods and development of analysis

During the workshop (task 5.1), a list of relevant tools for identifying markers of adaptation to niches (environment, food industry) was established (see Table 4). ANSES partner has already tested most of these tools on a small dataset of 51 strains.

Table 3. List of tools to be used for GWAS (as defined in the workshop)

Publication	Year	Tool	Unit of genetic variation studied	Tested
Earle et al.	2016	----------	Genes, k-mer, SNP	X
Brynildsrud et al.	2016	Scoary	Genes (Pan-genome)	X
Lees et al.	2016	SEER	K-mer	
Marinier et al.	2017	Neptune	K-mer	X
Collins and Didelot	2017	TreeWAS	SNP	X
Thorpe et al.	2017	Piggy	Intergenic Regions	X

5.1.2.7.3.6 WP5 : Trainings and dissemination

JRP7-WP5-T1: Implementation of a workshop
The workshop related to statistical and bio-informatics tools useful for the project were discussed in the workshop the 6th of March. The resulting choice for sampling are reported in task 1.3 and 3.1. For marker identification the group have listed the tools

JRP7-WP5-T2: Trainings
Two training sessions were organized in April-May 2018 in ANSES Maisons-Alfort for LNRs of Slovenia (Dr Bojan Papic) and Czech Republic (Dr Tereza Gelbicova).

JRP7-WP5-T4: Dissemination
A poster related to description of the diversity has been presented in IAFP 2018 in Sweden in April: Felix B, Feurer C, Maillet A, Guillier L, Boscher E, Kerouanton A, Denis M, Roussel S. 2018. Population genetic structure of *Listeria monocytogenes* strains isolated from the pig and pork production chain in France. Poster presented at IAFP EU Stockholm 25-27th April.
An oral communication on the same topics will be given in FoodMicro conference in Berlin (September 2018)

5.1.2.7.4 List of planned tele- or video conferences, face to face meetings in the next year

List of future tele- or video conferences, face to face meetings are listed in Table 5.

Table 5. List of planned meeting of LISTADPATMeeting	Date	Theme	Partners invited
Face-to-face	November 2018	General meeting of LISTADAPT	all

Table 5. List of planned meeting of LISTADPATMeeting	Date	Theme	Partners invited
Tele-conference	September (first two weeks) 2018	Phenotypic characteryzation	ANSES coord, INRA, ANSES Fougères
Tele-conference	October (first two weeks) 2018	Bioinformatics tools	ANSES coord, AGES, IZSAM, NVI, DTU

5.1.2.8 Metastava

5.1.2.8.1 Summary

The Metastava project started officially on 01.01.2018. A kickoff meeting was organized in Brussels on 21.02.2018. The activities during the first months focused largely on WP1 (Collect reference data from other metagenomic projects select the metagenomic methods to be used for the project, and provide guidance data for informed metagenomic workflow design), where we organized several questionnaires , phone calls, live meetings and teleconferences in order to document and standardize the methodologies available in our consortium for metagenomics data generation as well as analysis. Publicly available datasets relevant for the sample types treated in our project were prospected (SRA). In WP2 (Quality assurance tools for the validation and interpretation of metagenomics), the first evaluation experiment of potential exogenous controls for metagenomics experiments were realized (data generation + preliminary analysis). WP4 (Concertation with ongoing efforts and dissemination), focusing on integration with other ongoing efforts saw the participation in a cogwheel workshop with COMPARE, participation in GMI and relevant ISO norm meetings, as well as direct interaction with COMPARE partners. Moreover, the majority (3/5) of Metastava partners will participate in the next proficiency test on metagenomics that will be organized by COMPARE.
One due deadline (panels of spiked samples D-JRP8-3.1, M6) is delayed until m11 in view of the shifted attention to WP1: we first need complete documentation of data generation and analysis strategies to be finalized, which will directly be tailored to the selected sample matrices types per model disease.

5.1.2.8.2 Progress of the research project: milestones and deliverables

5.1.2.8.2.1 Deliverables

JRP name	Project deliverable number	Deliverable name	Delivery date from AWP	Actual delivery date	If deliverable not submitted on time: Forecast delivery date	Comments
METASTAVA	D-JRP8-3.1	Spiked sample panels ready for analysis	6	no	10	Ongoing. M6 may be too early due to attention shift to protocol standardization in WP1
METASTAVA	D-JRP8-5.1	Consortium agreement	6	27.09.2017		The OHEJP grant agreement contains all necessary details in the integrated Metastava work plan, and details interaction rules between partners. It hence replaces the consortium agreement
METASTAVA	D-JRP8-4.1	Report of meeting with ongoing initiatives to assure input in WP1	7	9.05.2018 Cogwheel workshop report		Cogwheel workshop report =EJP deliverable 4.3. The interaction with other initiatives will continue throughout the project.

5.1.2.8.2.2 Milestones

JRP name	Milestone number	Milestone name	Delivery date from AWP	Achieved (Yes/No)	If not achieved: Forecast achievement date	Comments
METASTAVA	M-JRP8-M1	Concertation meeting with ongoing initiatives	6	y		Cogwheel workshop with COMPARE. Additional contacts are ongoing. And will be detailed in the Y1 report under WP4
METASTAVA	M-JRP8-M2	Public and own dataset identified	8	No	10	Ongoing. M8 may be too early due to attention shift to protocol standardization in WP1

5.1.2.8.3 Progress of the research project (reported until 15.06)

5.1.2.8.3.1 WP1. Collect reference data from other metagenomic projects select the metagenomic methods to be used for the project, and provide guidance data for informed metagenomic workflow design.

JRP8-WP1-T1: broad survey to collect information about sample selection and data generation methods for metagenomics.
Initiated during the kickoff meeting, these surveys were finalized in m6 and conclusions about methodological standardization options for data generation were drawn during a TC (held on 19.06.2018) . Protocol sharing initiated.

JRP8-WP1-T2: broad survey to collect information about data analysis methods for metagenomics.
Initiated. Survey finalized by 15.06.2018. A TC was held on 28.06.2018 to discuss the results. After additional discussions in M8&9, we will draw conclusions and suggest standardization options.

JRP8-WP1-T3: identifying available sequence datasets.
The NCBI Short Read Archive was mined for publicly available high throughput sequencing data for a preliminary shortlist of sample matrices as discussed during the kickoff meeting. Accession lists including SRA data summary information were extracted and provided to the project team. Updates and refinements may be necessary as soon as final sample matrix lists are decided.

5.1.2.8.3.2 WP2. Quality assurance tools for the validation and interpretation of metagenomics.

JRP8-WP2-T1: The development of quality metrics to evaluate the significance of the outcome of a metagenomics experiment**.**
To be initiated when all sample matrices and methodology standardization is decided (M7-9).

JRP8-WP2-T2: development and evaluation of external controls for metagenomics.
Initiated: Initial evaluation experiment of two potential exogenous controls. Data generated and preliminary analysis concluded. ErasmusMC presented additional data on the use and reproducibility of external controls for metagenomics during the TC on 19.07.2018.

JRP8-WP2-T3: reproducibility and batch effect evaluation
Yet to be initiated

5.1.2.8.3.3 WP3. evaluation of the analytical properties of metagenomics workflows

JRP8-WP3-T1: takes place over the first and the second annual period of the EJP
To be initiated. Awaiting final decisions of WP1

JRP8-WP3-T2: analytical sensitivity, norovirus
To be initiated. Awaiting final decisions of WP1

JRP8-WP3-T3: analytical sensitivity, large DNA viruses
To be initiated. Awaiting final decisions of WP1

JRP8-WP3-T4: analytical sensitivity, STEC

To be initiated. Awaiting final decisions of WP1

JRP8-WP3-T5: analytical sensitivity, detection of ABR genes**.**
To be initiated. Awaiting final decisions of WP1

JRP8-WP3-T6: bioinformatics and statistical analysis of analytical performance experiments
To be initiated. Awaiting final decisions of WP1. Personnel selection initiated at partner Sciensano.

5.1.2.8.3.4 WP4: Concertation with ongoing efforts and dissemination.

JRP8-WP4-T1: concertation with ongoing initiatives.
Bilateral meetings with Compare were held prior to the project launch. Good integration with compare via shared participation (FLI, ErasmusMC, ANSES). Participation in cogwheel workshop between Compare and OHEJP (12.04.2018).
3 out of 5 metastava partners will participate in the next Compare proficiency test for metagenomics.
Sigrid Dekeersmaecker participated to several ISO WG meetings, including the F2F in Lausanne; and she also attended the GMI 11 meeting (http://www.globalmicrobialidentifier.org/News-and-Events/11th-Meeting-on-Global-Microbial-Identifier-in-Geneva-Switzerland).

JRP8-WP4-T2: formal dissemination.
To be initiated

JRP8-WP4-T3: dissemination of recommendations to stakeholders
To be initiated

5.1.2.8.3.5 WP5: Project management

JRP8-WP5-T1: consortium agreement
The grant agreement of the entire Onehealth EJP covers all necessary agreements between partners and includes the work plan of our project as it was submitted. There is no need for a joint research project – level consortium agreement.

JRP8-WP5-T2: internal communication.
Pre-kickoff meeting phone calls with workpackage leaders. Kickoff meeting (21.02.2018, Brussels). WP1 phone calls (coordinator- WPL) about standardization. General Assembly 1 (22.03.2018) to decide on WPL role changes. Questionnaires on data generation and data analysis, including follow-up teleconferences. Mailings to all collaborators or partner contacts about general EJP-OH information. Teleconference on WP1 standardisation (end of M6).

5.1.2.8.4 List of planned tele- or video conferences, face to face meetings in the next year

- M6-7: teleconference WP1: conclusions on methodological standardization. + WP3 finalisation of sample matrix list per target pathogen. + General progress & planning of project.
- M9-10: WP2 teleconference: results & planning
- M9-10: WP3 teleconference: results & planning
- M12-13: First annual meeting (face to face).
- M15: Intermediate progress teleconference with focus on WP2 and WP3
- M18: Intermediate progress teleconference with focus on WP1; WP2; WP3

5.1.2.9 AIR Sample

5.1.2.9.1 Summary

The project is proceeding according to the plan, there is a good sense of collaboration and there is an active dialogue through email, exchange of protocols, Skype meetings and phone calls. So far, eight newsletters have been circulated to stimulate the internal communication (Appendix 1).
The project has entered an official agreement with Sartorius (Germany) to provide us with equipment (AirPort 8) and air filters for poultry farm sampling this summer. All partners have been in contact with their local Sartorius office and have obtained the equipment and implemented the protocol.
Overall, the project will move through the following four phases:

Harmonization -> Implementation -> Evaluation -> Validation.

We have completed the method harmonization and implementation phases. The summer time was focused on sampling, sample analysis and data generation. All protocols have been implemented by partners during April-June 2018 (Appendix 2). The results of sampling will be discussed during the next project meeting on Sept 27-28 in Teramo, Italy.
It was agreed to use one pair (one per foot) of sock samples according to national practice. However, the socks were weighed in advance, wetted and then enriched in a broth according to the ISO protocol in the ratio of 1:10 (or 1+9). Campylobacter colony confirmation were done by colony PCR or colony-MALDI-TOF, in the case the biochemical testing is too tedious.
DTU has carried out extensive spiking experiments on the filter system, which needs further optimization if it is to be used for DNA purification and PCR. In addition, the presence of blood in Bolton broth has inhibited the PCR. Hence, it was decided at this stage to drop the harmonization of PCR testing on the samples from this summer, until these technical issues have been solved. Nevertheless, some partners have setup their own PCR to analyse the filters and sock swabs by their own in-house PCR protocol.

5.1.2.9.2 Progress of the research project: milestones and deliverables

5.1.2.9.2.1 Deliverables

JRP name	Project deliverable number	Deliverable name	Delivery date from AWP	Actual delivery date	If deliverable not submitted on time: Forecast delivery date	Comments
AIR SAMPLE	D-JRP9-1.1.	Prototype laboratory method to detect and enumerate *Campylobacter* in air samples.	9	3 August 2018		

5.1.2.9.2.2 Milestones

JRP name	Milestone number	Milestone name	Delivery date from AWP	Achieved (Yes/No)	If not achieved: Forecast achievement date	Comments
AIR SAMPLE	M-JRP9-1	Sample bank is established	9	Yes		A decentralized sample bank at partner organizations involved.
AIR SAMPLE	M-JRP9-2	Sample preparation method is selected	9	Yes		QiaAMP Tissue&Blood kit

5.1.2.9.3 Description of the project activities per task

JRP9-WP1-T1: Creation of a sample bank (air and boot-swab samples) from different regions.
The sample bank has been created decentralized by each partner during the summer of 2018. The partners have selected at least two poultry producers per country for paired sampling, one by the sock swab method and the other by air sampling. The samples were cultivated for Campylobacter according to a harmonized ISO method agreed upon by all the partners (Appendix 2).

JRP9-WP1-T2: Development of a protocol for non-complex DNA extraction for diagnostic qPCR and metagenomics analysis from gelatin-filter samples.
A number of DNA extraction methods have been assessed in-house at DTU and two other partner labs (Appendix 3). The Qiagen Tissue&Blood column, with some modifications, has resulted in a good performance (Appendix 4). Since this method is commercially available to all labs, and the price is reasonable, this method has been selected for metagenomics and real-time PCR testing. During the final quarter of 2018, the protocol will be validated (decentral) on the farm samples collected during this summer.
The plan for the validation of metagneomic detection on air filters will be finalized during the Teramo meeting. The work will be carried out during October-December 2018 in Copenhagen, Oslo and Teramo.

5.1.2.9.4 List of planned tele- or video conferences, face to face meetings in the next year

Two workshops and 5-8 Skype meetings are envisaged for 2019.

5.1.2.10 MoMIR-PPC

5.1.2.10.1 Summary

This project is based on the recent studies, which have uncovered the importance of host heterogeneity in the most important zoonotic infections. In particular, it has been shown that a minority of the infected individuals (Super-shedders) are responsible for the majority of the transmissions and thus infections. To improve the microbial safety of food and to develop new preventive measures for controlling zoonosis, we have to take into account this heterogeneity of infection and target the interventions to the super-shedders. Moreover, it seems important to determine why some animals are super-shedders and other are low-shedders. Preliminary data suggested the role of gut microbiota in addition to variability of the host immune response. In this project, we will develop new approaches to predict, identify and prevent the appearance of animal super-shedders based on immune response and gut microbiota composition and to identify the risk factors to be human carriers. Moreover, developing new mathematical models of pathogen transmission within a population taking into account the heterogeneity of infection and the role of gut microbiota will help to test several intervention strategies in order to optimize husbandry and feeding practices, but also decrease the use of antimicrobials and block the spread of antimicrobials resistance genes.

The start of the project has been in part delayed due to the withdrawal of few partners. Indeed, SAIM is no longer member of the EJP consortium, Vet-DTU has been closed by Danish government, A.L. Wester left the NIPH. Consequently, the project proposed by NIPH has been modified and is now supervised by AC Stüken, works devoted to SAIM will be in part performed by Partner 18 and H. Dashalov group (NDRVMI) entered within the consortium to performed the Vet-DTU works. Beside these difficulties, the majority of the management tasks have been finalized for this period. Numerous informal exchanges allowed us to coordinate our animal experiments and defined the compounds that will be tested in the project.

The chicken experiments planned to identify predictive immunological and microbiota markers have been performed. Immune parameters are under study. Preliminary results suggested that we already identified predictive microbiota markers of resistance to *Salmonella* colonization. The majority of pig experiments have been delayed and will be performed from month 9. The protocols to identify in human the risk factors associated with prolonged convalescent *Salmonella* shedding, and virulence of *Salmonella* strains recovered from human and animals are defined.

Lactobacillus strains, which will be used by other partners in experimental infections and in farm conditions are under purification and characterization. Several experiments have been conducted to test nutraceuticals and prebiotics. Preliminary results are encouraging but the majority of the results are under investigation.

Partners involved in WP3 started formulating and analyzing a generic mathematical model of the dynamic interplay between the gut microbiota, the pathogen and the host's immune response, based on recent literature. The chicken and pig in vitro gut models, developed by Partner 22, will be used to validate some parts of the mathematical model, in addition to the experimental infection models performed by the other partners.

5.1.2.10.2 Progress of the research project: milestones and deliverables

5.1.2.10.2.1 Deliverables

JRP name	Project deliverable number	Deliverable name	Delivery date from AWP	Actual delivery date	If deliverable not submitted on time: Forecast delivery date	Comments
MoMIR-PPC	D-JRP10-0.1	Project initiation, Kick off meeting, Project-planning and management documentation	2	2		
MoMIR-PPC	D-JRP10-0.3	Minutes of project meetings (Kick off meeting)	2	2		
MoMIR-PPC	D-JRP10-4.3	Creation of a database of each animal group included in the study (age, conformation, diet, clinical status, previous antibiotic treatments, infectious status, etc.)	2		12	Some partners have left the consortium. NDRVMI has join the consortium in June (month 6). He supplant Vet-DTU Partners
MoMIR-PPC	D-JRP10-1.1	Panel of immunological markers to assess in pig and chicken	3	6		Each partner has defined its markers. A general discussion will be done to harmonize these markers
MoMIR-PPC	D-JRP10-4.1	Development and production of MoMIR-PPC website	4		?	We are waiting the EJP website to develop ours
MoMIR-PPC	D-JRP10-4.2	Data management policy and strategies	4	6		
MoMIR-PPC	D-JRP10-0.2	Approved and signed Consortium Agreement	6	1		This has been done at the EJP level

5.1.2.10.2.2 Milestones

JRP name	Milestone number	Milestone name	Delivery date from AWP	Achieved (Yes/No)	If not achieved: Forecast achievement date	Comments
MoMIR-PPC	M-JRP10-1	Organization of the consortium kick off meeting	1	y		
MoMIR-PPC	M-JRP10-2	Protocols and ethical committee requests for the different experiments	1	y		The ethical clearance from the Norwegian Committee for Medical and Health Ethics has been received for the human part of the MoMir-PCC project (granted 15.05.2018)
MoMIR-PPC	M-JRP10-3	Update of the members of the steering committee and of the leader and deputy leader for the WPs and tasks	2	y		Discussions with NDRVMI, which has join the consortium
MoMIR-PPC	M-JRP10-4	Define the panel of probiotics for use in pigs and chickens	2	y		
MoMIR-PPC	M-JRP10-5	Define the panel of pre-biotics and feed for use in pigs, chickens and humans	2	y		
MoMIR-PPC	M-JRP10-6	Identification and selection of farms	4	y		
MoMIR-PPC	M-JRP10-7	Recovery of samples from the first round of experimentally infected animals	8	N	8-12	Some experiments have been delayed due to the modification of the partners

JRP name	Milestone number	Milestone name	Delivery date from AWP	Achieved (Yes/No)	If not achieved: Forecast achievement date	Comments
MoMIR-PPC	M-JRP10-8	Recovery of samples from selected farms ; Identification of super- shedders and low-shedders in poultry and pig farms	8	N	8-12	Some experiments have been delayed due to the modification of the partners
MoMIR-PPC	M-JRP10-9	Four sets of NGS derived 105 mimotope sequences – positively and negatively enriched in IgM and IgA	8	N		Resulting from the left of SAIM (A. Pashov), this task has been deleted in the new version of the project
MoMIR-PPC	M-JRP10-10	Recovery of samples from experimentally infected animals and from farms, pretreated with pre-biotics or neutraceuticals	8	N	8-12	Some experiments have been delayed due to the modification of the partners

5.1.2.10.3 Progress of the research project

5.1.2.10.3.1 WP0: Management

JRP10-WP0-T1: Draft and agree Consortium Agreement
As consortium agreement was signed between the EJP coordinator ANSES and the EJP beneficiaries, we considered at the first MoMIR-PPC meeting that it was unnecessary to sign a particular consortium agreement at the MoMIR-PPC level.

JRP10-WP0-T2: Produce project-planning, control documentation and Data Management Plan.
The project planning has been modified several times due to the left of SAIM from the EJP consortium, the Vet-DTU, which has been closed by its Government. We also modified the project planning of the Norwegian Institute of Public Health because Astrid Louise Wester left her institute. The final project planning was decided in June (month 6). The Data Management Plan has been performed in relation with the EJP board.

JRP10-WP0-T3: Control and manage activity progresses, the timely delivery of project tasks and outputs
Numerous exchanges have been performed to coordinate the work performed by the members, especially concerning the pro and prebiotics, which will be tested in farms. We discussed also how to store and exchange the strains recovered from low and super-shedders. Informal meeting will be organized to exchange information required for the mathematical models and to define who will test what.

5.1.2.10.3.2 WP1. Risk prediction for Super-shedder animals and human asymptomatic carriers through the use of gut microbiota and immune status analyses.

JRP10-WP1-T1: Predictive immunological markers associated to the high and low shedders in chickens and pigs
Concerning the experimental infection of pigs, they have been delayed. They will be performed months 9-11. In these conditions, the immunological markers will not be tested before month 12. Several exchanges between partners allowed us to define the best conditions to define both immunological and microbiota markers. Bilateral discussions will improve technical cooperation and protocol exchanges. A set of immune markers to be tested has been defined by partners and especially by P 27 and 29 after a review of the literature. The data obtained, concerning the immunological markers (before and after infection) will be compared with the microbiological ones (elimination and colonization in the organs of S. Typhimurium 14028) to study the existing correlations.
As a preliminary and ancillary approach, an experimental infection of mice were conducted by partner 27. In this experiment, 28 CD1 mice were inoculated, by intraperitoneal route, with 107 CFU of an attenuated mutant strain of Salmonella Typhimirium, named STMΔznuABC, which allowed us to obtain a sub-lethal infection in susceptible mouse model. All samplings were performed and results are in progress.
Regarding the experimental infection of chicken, they have been performed month 4 and 6. We are testing the immune response by flow cytometry. Transcriptional response and level of immunoglobulins will be tested months 9-11. For this task, a Post doc who has carried out her PhD in Partner 27's (ISS) labs, has been recruited by Partners 18 (INRA-Tours). She will manage part of the work devoted to SAIM.

JRP10-WP1-T2: Predictive microbiota markers associated to the high and low shedders in chickens and pigs

Because the same experiments will be used to develop predictive immunological and microbiota markers, all the work planned on pigs has been delayed. The requirements of the microbiota analysis are now in the final stages of finalization by Partner 22 and discussion is now ongoing between partners to arrange shipping and analysis of the microbiota samples.
Concerning experimental infection of chicken, they have been performed at month 4 and 6 by partner 18. Gut microbiota of chicks was sequenced by partner 8 and analysed by both partners. Some bacterial genus, identified in fecal samples before infection, have been correlated to the low shedders phenotypes, determined after Salmonella infection. Their use as predictive microbiota markers of "resistance" to Salmonella colonization will be tested in future experiments. We also tested their putative protective activity against Salmonella colonization but without success. Presence of few bacterial genus, just after infection, have been correlated to the low-shedder phenotype.
Similar experiments will be tested by Partners 22 (Surrey) and 27 (ISS) on pig and or chicken model of infection. Chicken and pig faeces from animals with known Salmonella shedding levels (confirmed by culture at time of collection) will be collected and DNA extracted. All samples will be sent for 16S sequencing in order to determine the community structure and differences between birds or pigs with no, low and high shedding of Salmonella. A detailed analysis of the pan genome present within the samples will be carried out using a subsection of the samples and shotgun whole genome sequencing of the community.

JRP10-WP1-T3: Risk factors associated with prolonged convalescent Salmonella shedding in humans
The protocols has been finalized. Partner 32 applied for and received ethical clearance from the Norwegian Committee for Medical and Health Ethics for the human part of the project (granted 15.05.2018). Due to the implementation of the EU General Data Protection Regulation (GDPR) on May 23rd, 2018, unforeseen delays occurred. GDPR requires a higher level of security to collect and store personal and medical data. NIPH has applied for the use of these systems and was granted access on 20.08.2018. NIPH also had to apply for permission to use patient contact data for research purposes and is currently waiting for the decision from the Norwegian tax authorities (expected in mid-September). Design of information letters and questionnaires for study participants, as well as a Norwegian project website hosted at NIPH were done. Materials for sample collection were procured. Participant recruitment is delayed. It will start as soon as possible after the decision of the Norwegian tax authorities has been received.

JRP10-WP1-T4: Virulence of Salmonella strains originated from high and low shedders
This task is expected to be performed based upon what was achieved during the first annual period of the EJP. So far, the Salmonella strains to be tested were not provided yet. The when and how the strains will be recovered was defined. Meanwhile, the experiments to investigate the bacterial adhesion and invasion to epithelial and phagocytic cells as well as the induced immune response were set-up using bacteria strains available in P18 laboratory.

5.1.2.10.3.3 WP2. Prevention of the appearance of Super-shedder animals and asymptomatic carriage in humans and animals by modifying feed and/or microbiota

JRP10-WP2-T1: Use of probiotics in chicken and pig
This task is in progress. No formal results have been obtained yet. Partner 22 (Surrey) is using chicken caecal and pig faecal samples for the isolation of *Lactobacillus spp*. Both chicken caeca and pig feces have now been collected for Lactobacillus isolation. To date 67 chicken, 18 turkey and 43

pig *Lactobacillus sp.* isolates have been obtained and are currently undergoing characterization and genetic testing to ensure their uniqueness. Partner 22 will continue to collect isolates over the next 12 months in order to build a comprehensive library for use in both in vivo and in vitro studies. These isolates are currently undergoing genetic screening to ensure they are members of the *Lactobacillus* genus and have a unique Random Amplification of Polymorphic DNA (RAPD) profile. Following this initial screening, the isolates will be tested for survival of low pH, bile, lack of antimicrobial resistance to key antibiotics, and inhibition of key bacterial species. Cell cytotoxicity assays will also be carried out and competition assays to confirm that Lactobacillus species are suitable for use in vivo. Finally, successful candidates will be fully sequenced. All screening will be compatible with EFSA guidance.
In parallel a chicken probiotic library from previous research at UoS is being investigated for suitable targets to take forward to the in vivo studies, which will be carried out by NDRVMI. Four isolates have now been identified from this library for in vivo use and the transfer of these isolates and the development of a study protocol has recently been initiated.

JRP10-WP2-T2: Use of pre-biotics and nutraceutical already defined by the consortium partners in chicken and pig
For experiment with chickens, Partner 8 (VRI) introduced a protocol based on specific supplementation of nutrient broths to identify bacterial species, which are dependent on particular supplements or growth substrates. At the beginning of the experiment, caecal contents of adult hen are decimally diluted and inoculated to nutrient broth. Nutrient broths are then anaerobically incubated and after 3 days, microbiota composition is determined by 16S rRNA sequencing. WCHA agar and BHI medium supplemented with lactate, glucose, starch, cellulose, mucin, bile salts, panthenol, biotin, vitamin B12 or whole vitamin B complex have been tested. Samples from both these experiments have been already sequenced and biological meaning and relevance is currently evaluated. In addition, in the last experiment we inoculated BHI supplemented with sodium acetate, propionate, lactate, succinate, pyruvate, fumarate, ascorbate, glucose, maltose, saccharose, trehalose, fucose, rhamnose, pectin and inulin. These samples have been collected, DNA purified and sequencing is planned for July. These experiments allows to i) determine metabolic potential of individual gut microbiota members, ii) define conditions under which it will be possible to enrich target gut anaerobes and obtain them in pure cultures and iii) map characteristics of different supplements which can be used as prebiotics.
To measure the effect of nutraceuticals in chicken and pigs, Partner 16 (VISAVET-UCM) has finished the previous studies in hens with “alperujo”. In this experiment, two groups were defined (control and treated), having tested several percentages of inclusion in the diet (1%, 2%, 4%, 5% and 6%). Production parameters were analyzed from 12 samplings performed between week 2 and week 90 of life. Faeces for microbiological studies and tissues for pathological exams were collected. No abnormal visual signs were observed in any of the animals tested, without any signs of rejection to the food even in higher inclusion percentages.
Very slight variations of weights were observed between the animals. However, considering the average of the weighing, a higher value was obtained in the animals treated compared with the animals of the control group. During the experiment, the treated batch presented a higher percentage of eggs production and lower feed consumption per bird that has resulted in an increase of 1.3% of the profit of sale of eggs and a decrease of 1.7% in the cost of the feed consumed, comparing with the control one. Significant differences ($p < 0.05$) in the distribution and percentage of eggs that were eliminated (broken or cracked) have been observed. These results indicate that the “alperujo” provided an improvement of the intestinal health, since not only influenced the digestibility of nutrients, but also the composition of the shell and quality of the eggs, reducing the loss due to broken or cracked eggs.

Macroscopic measurements of various portions of the digestive tract of the animals showed that in the treated animals there was a greater number of intestinal villi at the level of the small intestine, having a higher height. The depth of the intestinal crypts of the anterior portion of the digestive tract and of the caecal mucosa was higher in the treated animals than in the control one. In the large intestine, the number of crypts observed per visual field is superior in the control animals, however, depth of crypts was higher in the treated animals.
A microbiological study performed in a selection of samples have shown differences between the proportion of Bifidobacterium, Lactic Acid bacteria and Bacteroidetes in each of the groups. In the coming months, they will depth in these analysis in order to stablish which percentage was able to better modulated the microbiota, reducing the number of Enterobacteria and resistant microorganisms.
The start of the experimental test with broilers which will be carried out in a BSL3 boxer has been delayed due to the availability of BSL3 boxers and authorization by the Community of Madrid to use experimental animals in projects (RD 53/2013). Initial date of this study will be at the beginning of January. The animals after a week of adaptation and 35 days of feeding with "alperujo" and short-chain fatty acids, will be challenged with a pathogenic strain of avian Salmonella. The objective of these approaches will be to analyze the modification of the microbiota before and after the challenging, comparing treated and control groups. At this time, Partner 16 are also collecting data from a pig farm and a fishery whose animals are being fed with these nutraceuticals. These results, together with metagenomics analysis of "alperujo" experience, will help to design the BSL3 assay, trying to obtain more accurate and representative data.

JRP10-WP2-T3: Use of pre-biotics in human travelers to high-risk areas for contracting salmonellosis and AMR
Due to the left of Astrid Louise Wester, from the Norwegian Institute of Public Health (NIPH), this task has been deleted from the new version.

5.1.2.10.3.4 WP3. Modelling the transmission of zoonotic agents to improve intervention strategies on livestock farms

JRP10-WP3-T1: Transmission modelling at within-host and between-host scales
JRP10-WP3-T1-ST1: Within-host scale: modelling individual responses and shedding
A set of data analyses is aiming to link gut microbiota composition and immune response parameters to shedding status. The implementation of the corresponding scripts and the analyses of existing data on chicken (with P18-Tours and P8) is in good progress.
A second set of analyses consists in inferring interactions between the pathogen (here Salmonella) and the resident microbiota, based on time series of gut microbiota composition. We are currently developing a computer code for the model used for inference of such interactions, that we plan to achieve within this first nine-month period.
In parallel, Partners 30, 41 and 18 started formulating and analyzing a generic mathematical model of the dynamic interplay between the gut microbiota, the pathogen and the host's immune response, based on recent literature (Byndloss et al., 2017). Our objectives are (i) to qualitatively mimic heterogeneity in Salmonella level in the gut, (ii) to keep the model simple so that it can be later embedded in population scale epidemic models. Based on this ongoing modelling work, we have proposed a work session at the CEMRACS 2018 summer school in Marseille (16th july-24th August).
Partner 22 (Surrey) will inform experimental modelling of the gut using both chicken and pig in vitro gut models to validate some parts of the mathematical model. Faecal and caecal contents will be used to 'seed' the models with whole microbial communities followed by inoculation with Salmonella and/or probiotics. Modelling will highlight not only how Salmonella infection may

progress in response to various gut community compositions but also how the probiotic species might influence the progression of infection in vivo.
JRP10-WP3-T1-ST2: Between-host scale: modelling transmission, linked to within-host results
As a first step towards this sub-task, an experiment studying the indirect transmission of Campylobacter between broilers, has been performed in the experimental animal facilities of Wageningen Bioveterinary Research. This experiment serves to validate and refine an existing model for transmission of bacteria between spatially separated animals, and to do so consisted of three different spatial setups that were each studied in two repeat animal rooms. A PhD student has been selected from international applicants and was appointed on 1 August 2018. This PhD student will carry out the modelling analyses of the outcomes of this experiment and of other relevant historical and new data. The between-animal transmission model under development is formulated such that it can both be linked to between-stable transmission models as well as to the within-host modelling of subtask 3.1.1.

JRP10-WP3-T2: Interventions strategies: Identification and evaluation tools
JRP10-WP3-T2-ST1: Systematic inventory of relevant intervention measures
The research for this sub-task is being started during the summer of 2018, through involving MSc students in literature studies of relevant intervention measures.
JRP10-WP3-T2-ST3: Development of economic analysis tools
The start of the detailed work for this sub-task is planned at a later stage.

5.1.2.10.3.5 WP4: Communication and Dissemination for Impact

JRP10-WP4-T1: Dissemination of data within the project and management of data
Some works have been already presented in congresses

Publications

- Ugarte-Ruiz M., Dominguez L., Corcionivoschi N., Brendan WW., Dorrell N. and Gundogdu O. Exploring the oxidative, antimicrobial and genomic properties of *Campylobacter jejuni* strains isolated from poultry. Research in Veterinary Science, 119(2018)170-175. 2018. (A). DOI: 10.1016/j.rvsc.2018.06.016.

- Moreno MA., Florez-Cuadrado D., Ugarte-Ruiz M. and Dominguez L. *Veterinarios y antibióticos: destinados a entenderse. Profesión Veterinaria.* ISBN: 2253-7244. 2018.

- Florez-Cuadrado D., Moreno MA., Ugarte-Ruiz M. and Dominguez L. Antimicrobial Resistance in the Food Chain in the European Union. Advances in Food and Nutrition Research. Elsevier, 2018.

Invited conferences:

- Velge P. CIAG Prévenir et guérir les maladies infectieuses dans le concept One Health. (2018) June 21, Tours (FRA). « L'approche microbiote : Stratégies pour prédire et prévenir les infections à *Salmonella* chez le poulet »
- Velge P. Animal Microbiome congress (2018) June 20-21, Paris. « Faecal gut microbiota composition of chicks can predict the super-shedder phenotype of *Salmonella* Enteritidis"

Presentations in congresses:

- Miguela-Villoldo P., Iglesias MR., Quijada NM., Rodriguez-Lazaro D., Quesada A., Dominguez L. and Ugarte-Ruiz M. *Identificación y caracterización de bacterias resistentes a la colistina.*

Evaluación de su persistencia y posible diseminación. IV VETINDOC PhDay, *Facultad de Veterinaria*. Universidad Complutense, Spain, Madrid. 27/06/2018 - Poster communication.

- Herrera-Leon L., Hernandez A., Monzon S., Llorente M., Ugarte-Ruiz M., Sanchez S., Cuesta de la Plaza I., Dominguez L. and Herrera-Leon S. Whole genome sequencing analysis of *Salmonella enterica* serotype Choleraesuis isolates in Spain provides insight into possible transmission chains. European Congress of Clincal Microbiology and Infectious Diseases, European Society of Clinical Microbiology and Infectious Diseases, Spain, Madrid. 22/04/2018 – Poster communication.

5.1.2.10.4 List of planned tele- or video conferences, face to face meetings in the next year

Informal face to face meetings were (or will be) arranged during the EJP meetings (June 2018) ; the international congresses like “Salmonella, salmonellosis international symposium (Sept 2018) ; the CEMRACS 2018 summer school in Marseille (July-August 2018) etc. Numerous video conferences are planned between partners for scientific and technical exchanges. The midterm MoMIR-PPC meeting is planned in December 2018 in Spain.

5.1.2.10.5 Summary

One of the first and main goals of MedVetKlebs project was the development and harmonization of detection, isolation and quantification methods of *Klebsiella pneumoniae* (Kp) from different sources. For this purpose, we have tried different culture, proteomic and molecular approaches. Regarding the culture approach, the selective SCAI medium was tested in all partners' institutions in comparison with other culture media and seems to be the best strategy. Based on the experiments performed by the different MedVetKlebs partners, SCAI showed higher recovery and specificity rates when compared to other selective media for Kp (such as BIND, or other chromogenic media tested), being easy to prepare and to identify Kp colonies from. At this moment, four partners (NUI, IZS, SSI, AGES) are optimizing the methods for the isolation of Kp using the SCAI medium by testing samples of chicken meat. Different pre-enrichment conditions are being tested upstream of plating on SCAI.

Regarding the proteomic approach, we demonstrate for the first time the potential of MALDI-TOF mass spectrometry, a fast and cost-effective technique that is well established in routine laboratories for microbial identification, to correctly identify strains of the *K. pneumoniae* complex at the phylogroup level (https://doi.org/10.1101/350579). This approach now needs to be validated using independent datasets in order to evaluate its value in clinical practice. Incorporation of reference spectra of the various *Klebsiella* species in diagnostic spectra databases, would represent an important advance for fast and simple identification of *K. pneumoniae*.

Regarding molecular approaches, we aimed to develop a real-time PCR for the identification and quantification of the Kp complex and the different phylogroups (or species) directly in the samples in order to allow a more efficient broad sampling. Two partners are involved in this task (IP, INRA). For this purpose, a pan-genome strategy was applied to a collection of reference set genomes. Candidate genes exclusive for the different phylogroups were obtained, which were filtered based on BLAST results and GC content, reducing the number of target candidates . These candidates were mapped in a large collection of genomes (n=1001), leading to define seven optimal specific target genes. qPCR primers/probes were designed and are being validated on a reference panel of strains. The qPCR strategy will be optimized by developing a 3 multiplex-qPCR strategy in order to be adopted in the broad sampling task (WP2). Sensitivity of the assays is currently being tested on spiked soil in INRA Dijon, and it will be also tested on other matrices by the different MedVetKlebs partners.

Regarding broad sampling (WP2), this task will take off at a large scale later in 2018 once the best detection/isolation methods are validated.

5.1.2.10.6 Progress of the research project: milestones and deliverables

5.1.2.10.6.1 Deliverables

JRP name	Project deliverable number	Deliverable name	Delivery date from AWP	Actual delivery date	If deliverable not submitted on time: Forecast delivery date	Comments
MedVetKlebs	D-JRP11-4.3	Consortium meetings – Review of work done/progress made and definition of priorities for next period	1	11-12 JANUARY 2018		Kick-off meeting, Paris, two days
MedVetKlebs	D-JRP11-4.3	Consortium meetings – Review of work done/progress made and definition of priorities for next period	1	29 MAY 2018		TC with all partners, 2 hours

5.1.2.10.6.2 Milestones

JRP name	Milestone number	Milestone name	Delivery date from AWP	Achieved (Yes/No)	If not achieved: Forecast achievement date	Comments
MedVetKlebs	M-JRP11-1	SCAI medium culture protocol validated on sites	3	YES		SCAI medium tested at all centers; need to still define the best enrichment steps

5.1.2.10.7 Progress of the research project

5.1.2.10.7.1 WP1. Methods for Kp detection and isolation

JRP11-WP1-T1: Evaluation and optimization of culture-based approaches
The selective SCAI medium was tested in all partners' institutions in comparison with other culture media. At this moment, four partners (NUI, IZS, SSI, AGES) are optimizing the methods for the isolation of Kp using the SCAI medium by testing samples of chicken meat.

JRP11-WP1-T2: Detection and quantification
- MALDI-TOF mass spectrometry - specific peaks for the correct identification of the Kp complex members. Independent dataset is being defined in order to validate this ID method.
- Targets for real-time PCR identification and quantification of Kp complex members were defined, primers/probes were designed and successfully tested on a reference panel of strains. Currently, the qPCR is being optimized to develop a 3 multiplex-qPCR in order to be adopted in the broad sampling task (WP2). Sensitivity of the assays is currently being tested on spiked soil. So far, plating the enrichments on SCAI medium confirmed the qPCR results in most cases.

JRP11-WP1-T3: Harmonization and alignment
Enrichment/selective procedures have been optimized by different partners of the project until the end of August 2018, in order to start the broad screening in a comparable way in fall 2018 by distributing the optimized protocol to all the partners.

5.1.2.10.7.2 WP2. Sampling

JRP11-WP2-T1: Broad sampling of potential reservoirs and sources of Kp
What concerns the broad sampling, this task will take off in a large-scale in September 2018, after optimization of isolation and detection protocols. In the meanwhile, a broad set of samples has already been tested by the partners using the SCAI medium, showing recovery of Kp from large number of sources; but the methods being incompletely standardized, this data cannot be used to compare prevalence in the different sources.

5.1.2.10.7.3 WP3. Genomics and Modeling

JRP11-WP3-T2: Modeling and source attribution
Will depend on WP2 first – therefore Not started yet.

5.1.2.10.7.4 WP4: Management, dissemination, exploitation

JRP11-WP4-T1: Implementation of the project management structure
As planned.

JRP11-WP4-T2: Administrative, legal, financial and ethical support to the consortium
As planned.

JRP11-WP4-T3: Exploitation of results and Intellectual Property rights management
The MALDI-TOF Klebsiella identification manuscript was posted on BioRxiv.

5.1.2.10.8 List of planned tele- or video conferences, face to face meetings in the next year

We have planned a face-to-face meeting in 10-11th January 2019 at Institut Pasteur (Paris, France) with all the MedVetKlebs partners, and also some invited researchers with expertise in the field of *K. pneumoniae*. WP3 leaders are welcome!

5.1.3 Task 3.3: Organisation of a second round of projects and their supervision.

Based on the expert meeting in Bilthoven, NL organized by WP2, a new list of priority topics for the joint research and integrative projects for the second internal call was proposed. In its meeting of October 2nd, 2018 in Brussels, SSB will select the priority topics and will assign a budget to these. Only afterwards the letter if intention can be sent out to the OneHealth EJP beneficiaries. This milestone (MS28), initially planned for September 2018, will be delivered as soon as possible after the SSB meeting.

5.1.4 Task 3.4: Organisation of annual scientific meetings (ASM) where results from JRP are presented.

In preparation of the protocol for the organisation of Annual Scientific Meetings, 2 videoconferences were held (16 February and 2 March 2018). The protocol (Deliverable 3.2) was prepared by a dedicated work group and validated by PMT. On 6 April 2018 an invitation to the EJP beneficiaries was sent out to ask for their interest to submit a bid to organize the first ASM in May or June 2019. Colleagues from Ireland, both Med and Vet side, proposed to hold the meeting in Dublin on 22-24 May 2019 and the PMT agreed with this. Further teleconferences were set up to detail the preparation.

5.2 Deliverables and Milestones

5.2.1 Deliverables

Del Rel No	Del no	Deliverable tittle	Submission
D3.1	D39	Guidelines for project coordinators to report (JRP&JIP)	M4
D3.2	D40	Protocol for Annual Scientific Meeting (ASM) organisation	M4
D3.3	D41	Updated guidelines for Submission and selection of project proposals (JRP&JIP)	M7
D3.4	D42	Report on the recently started projects, 1st call	M8

5.2.2 Milestones

Mil Rel No	Milestone tittle	Notification
MS25	Kick-off meeting 1st call projects	Before the start of the EJP, all project leaders from 11 JRP and 2 JIP were invited in Brussels (15 December 2017). The objectives of the meeting were to inform JRP and JIP representatives on practical issues related to the research and integrative projects, i.e. guidelines, scientific and financial reporting, ethical issues, the use of a collaborative platform and data management

MS26	Questionnaire for feedback of recently started project sent out to Proj Coord. 1st call	The questionnaire has been sent out to all scientific project leaders on the 28th of February. It is available upon request.
MS27	Questionnaire for evaluation of available guidelines submitted to partners of 1st call	The questionnaire has been sent out to the PMT and SSB members on 26 April 2018. The results served as input for the update of the original guidelines on the submission and selection of project proposals.
MS28	Letter of Intent for 2nd call sent out	Upcoming

6 WP4 - Joint integrative projects

6.1 Work carried out to date

6.1.1 Task 4.1: Development of procedures and guidelines for submission and selection of JIP proposals, and for reporting and evaluation

Task 4.1 consists of three subtasks: 1) preparation of guidelines for submission and selection of JIP proposals; 2) preparation of instructions for reporting on, and monitoring of JIP progress and; 3) preparation of guidelines for evaluation of JIPs. During the first 9-month period, there have been activities related to subtasks 1 and 2.

For subtask 4.1.1, WP4 collaborated with WP3 in preparing D3.3, *Updated guidelines for Submission and selection of project proposals (JRP&JIP)*, which was delivered in M7. A questionnaire was prepared and administered to PMT and SSB members to ask for feedback on the procedures from the 1st round (MS49). The outcome was discussed in a PMT meeting and served as input for the adapted guidelines. Some improvements as compared to the first call were identified, such as providing more time for the entire selection process – it has now been extended to almost 5 months (less than 4 months in 1st round). A broader approach in the elicitation of priority topics, involving important stakeholders such as EFSA and ECDC, was also seen as desirable.

It should be noted that to avoid conflict of interest it was not possible to have direct exchange with EFSA and ECDC in the preparation of priority topics for the 1st call. Instead, an indirect approach was used, based on the awareness and understanding of the applicants regarding EU level strategic agendas and with requirements to show (through references) in the proposal that the project was in line with EU priorities. Although this indirect approach is not as efficient as direct communication with EFSA and ECDC, it can be considered a reasonable proxy considering that OHEJP partners are all active members of EFSA and ECDC surveillance and reporting networks where strategic intentions of the EU authorities can be expected to be discussed and communicated. Once the OHEJP was granted, communication was initiated. In December 2017, WP4 represented the OHEJP at an expert workshop on One Health preparedness, and also informally shared information about the contents of the granted JRPs and JIPs with ECDC representatives to mitigate the effects of the previous information gap. Fortunately, for the 2nd call, our ability to involve EFSA and ECDC more directly in the process has been highly facilitated by the actual launch of the programme, and there is now a positive and dynamic interaction between the OHEJP, EFSA and ECDC, facilitated by WP5, and informing WP2 where the OHEJP strategic agenda is developed.

In the 2nd call there will also be more focus on inclusiveness and integration of partners that were less active in the 1st call, and it will be possible to have a more standardised evaluation process, with involvement of more external evaluators (now reimbursed). The PMT agreed to keep the 2-

step selection format, and it was proposed that more direction should be given in the first step to guide applicants that have similar proposals to merge.
For subtask 4.1.2, WP4 has produced guidelines for reporting on JIPs (D4.1, *Instructions for monitoring of and reporting on JIPs, excl final reporting*). The plans for reporting were first discussed during a pre-kick off meeting held in Brussels in 15 December 2017 (D4.2, see below) with all project representatives. The final guidelines include detailed guidance for the project leaders on all intermediate reporting; from the online startup questionnaire to get a first feedback on the newly started projects, to the input needed for 9- and 12-month periodic reports. The templates for these reports are also provided in the guidelines. The instructions were developed in collaboration with WP3, where similar guidelines were produced, but covering also the final evaluation. (For WP4, guidelines for final evaluation are due by M18). A videoconference with the project leaders was organised by WP3 and 4 on 25 April 2018 to explain the contents and expectations, and with an opportunity for the project leaders to ask for clarifications.

6.1.2 Task 4.2: Supervision of JIPs

Task 4.2 consists of three subtasks: 1) start-up support; 2) project monitoring and; 3) final evaluation of JIPs. During the first 9-month period, there have been activities related to subtasks 1 and 2.
For subtask 4.2.1, a supportive startup meeting was held in Brussels already on 15 December, in the format of a "pre-kick-off" meeting where WP3 and WP4 met with all JRP and JIP project leaders to prepare for the launch of the OHEJP (D4.2, *Report from supportive start-up meeting, 1st round*). As part of the startup support, WP4 also attended the kick-off meetings of both ORION and COHESIVE. WP4 is also responding to requests from project leaders on a regular basis. An online questionnaire (MS48) was sent to the project leaders on 28 February 2018, to get early feedback on the start of the projects (e.g. status with regards to kick-off meetings, recruitments etc), and to clarify needs and expectations from project leaders. The results of this survey were described in a document and summarised in a presentation that was communicated through videoconference with the project leaders on 1 June 2018. Comments from the project leaders and from PMT members were also included in the WP3 deliverable 3.4, *Report on the recently started projects, 1st call*.
In response to feedback from REA we would like to highlight that the deliverables of WP4, listed below, are products that reflect the administration of the WP and of the OHEJP, as well as reports from the execution of planned activities. Consequently, deliverables at WP4 level are not of the nature that they overlap work done by ECDC and EFSA. Rather, WP4 focus is to facilitate the process at the level were potential overlaps should be managed, i.e. at the JIP level. From the start of the JIPs, WP4 has made clear to the project leaders that close communication and collaboration with EFSA and ECDC is anticipated. Consequently, early initiatives were taken by both project leaders to involve the EU authorities more closely. This has been well received, and EFSA and ECDC have now appointed contact persons for both ORION and COHESIVE, who participate in the regular meetings of the JIPs.
Similarly, since the pre-kick-off meeting in December 2017 there has also been structured interaction between the granted JIPs and JRPs, where identified similarities and synergies have been discussed and accounted for.

The progress of the two JIPs is described in more detail below:

6.1.2.1 *ORION*

6.1.2.1.1 Summary of the work carried out in the EJP

The ORION project started on January 1st 2018 and performed its work according to the planned "Inventories and requirement analysis" phase. This included extensive literature reviews, surveys and expert interviews with public health institute representatives. In WP1 a literature review has been conducted to develop the ORION Glossary facilitating a joint understanding on One Health Surveillance terminology between the ORION partners. A second literature review aimed at best practices for the harmonization of One Health Surveillance data. There, advanced methodological frameworks developed and applied by the UNECE and leading statistical offices could be identified. In WP2-Epi a literature review were performed to analyze the differences between sectors (feed/food, animal health, public health), to get an overview on the definitions within the sectors and to identify available methods for the description of surveillance systems. WP2-NGS reviewed current state-of-the art NGS-based analyses for several zoonotic agents, with the aim of discovering commonalities and key decision making points that guide the analysis process. This included extensive discussions with the COMPARE project and with EFSA/ECDC. WP2-Integration organized and facilitated a workshop in January 2018 to ensure a coherent project start. It also enabled the identification of synergies between all work packages in ORION and to align work efforts and identify expertise in the project. As a key outcome WP2 Integration facilitated a common way of looking at surveillance and the different steps in the pathway.

In April the ORION project held the joint ORION "Requirement Analysis" workshop where partners took important organizational decisions, e.g. on the revision process of the ORION-Glossary. All WPs presented and discussed the status of their research accomplished so far. For example WP1 presented GSBPM as a potential framework for the One Health Surveillance Codex. For WP3 a decision was made to focus this WP on the development of an ontology for surveillance, and the construction of an architecture that allows its implementation in practice, using proof-of-concept case studies. During the workshop, the work plans of all WPs were reviewed and further detailed. This included synchronization between the WPs on planned surveys or expert interviews. For example the revision of the ORION Glossary was carried out with domain experts from the ORION consortium and will be followed by consultations with experts from other EJP Projects and stakeholders. WP2Epi carried out an internal first survey on surveillance systems that are established in the partner countries. WP2-Integration developed a conceptual framework for 'OH Surveillance Initiative' and discussed a semi-structured interview outline for efficient information collection. Initial screening questions are to be distributed to EFSA focal points, project participants and other key-surveillance people in EU to identify, who to interview in more detail.
Finally all ORION WPs started discussions on the selection of their WP-specific One Health pilot projects. The aim of these pilots is to illustrate and validate the usefulness and added value of various ORION results in year 2 and 3 of the project.

The project coordination established shared project management resources including a shared space for documents, a shared calendar, an online mailing list and on several other features. The project holds monthly web meetings for the whole ORION consortium and a monthly call for the WP leaders & deputy leaders. The project organized and performed joint web meetings with EFSA and ECDC, contributed to the EJP DMP and initiated collaborations and information exchange with other EJP projects. Members of the project presented ORION and its work at several international conferences.

6.1.2.1.2 Progress of the integrative project: milestones and deliverables

Deliverables

JIP name	Project deliverable number	Deliverable name	Delivery date from AWP	Actual delivery date	If deliverable not submitted on time: Forecast delivery date	Comments

Milestones

JIP name	Milestone number	Milestone name	Delivery date from AWP	Achieved (Yes/No)	If not achieved: Forecast achievement date	Comments

No deliverables and milestones planned before the end of month 12

6.1.2.1.3 Progress of the integrative project

WP1: "OH Surveillance Codex"

Task 1.1: Inventories and requirement analysis for "OH Surveillance Codex"

- Subtask 1.1.1: Literature review, drafting a first questionnaire

To facilitate the understanding on One Health Surveillance terminology between the ORION members (including Animal Health, Food and Public Health domains), we carried out a literature review to document definitions to develop the ORION-Glossary. The first Glossary draft was presented and discussed during the Workshop facilitated by WP2 Integration in Denmark (22-23 January 2018). A second literature review aimed at best practice for the harmonized annotation of One Health Surveillance data and metadata. The generic frameworks developed by the UNECE (the Generic Statistical Business Process Model (GSBPM) and its generalized vocabulary) and supporting standards (e.g. DDI, SDMX) were explored to assess if they can be adapted/implemented as a high-level harmonization framework for the One Health Surveillance domain.

- Subtask 1.1.2: Joint ORION "Requirement Analysis" workshop (hosted by WP4) to synchronize questionnaires within ORION

During the workshop, we took organizational decisions for the revision process of the ORION-Glossary, starting within Animal Health, Food and Public Health-sub-groups, followed by monthly web calls. The GSBPM was presented as a theoretical framework for future mapping of One Health Surveillance processes which can build a bridge between the Animal Health, Food and Public Health domains.

- Subtask 1.1.3: Survey and/or interviews with internal / external experts

The revision process of the Glossary was carried out within ORION and will be followed by consultations with experts from EFSA and ECDC, as well as with other EJP Projects (COHESIVE). The GSBPM processes were mapped onto surveillance processes within the Animal Health (RiskSur), Food and Public Health domains and reviewed within ORION.

Task 1.3: One Health pilot

Initial discussions preparing the decision on the topic for the WP1 One Health pilot (due by month 12) were initiated within WP1 and with other EJP projects.

WP2: Epi

Task 2Epi.1: Inventories and requirement analysis for OH Knowledge Base Epi

Within Task2Epi.1 we will create a list of available surveillance systems, existing data on surveillance systems and on tools/methods. In this context, there are discussions on (1) the selection criteria for the inventories, (2) the specific target groups for the inventories (e.g. public, scientists, decision

makers), (3) the differences and similarities between the sectors (a Webinar is planned) and (4) appropriate methods (e.g. Generic Statistical Business Process Model [https://ec.europa.eu/Eurostat]) to describe statistical methods in a general and process-oriented way. Based on the discussion and on the results of the subtasks, the partners will decide on the specific content of the inventories as well as on the technical basis.

- Subtask 2Epi.1.1: Literature review, drafting a first questionnaire

To run a literature review we first have to analyze the differences between sectors. Moreover, many publications on surveillance are part of official reports and are written in the local language. We run a first literature search within google to get an idea on the diversity of the literature and to get an overview on the definitions within the different sectors (feed/food, animal health, public health). Moreover, we will run a literature review or questionnaires on available methods for the description of surveillance systems.

- Subtask 2Epi.1.2: joint ORION "Requirement Analysis" workshop (hosted by WP4) to synchronize questionnaires within ORION

WP2Epi contributed actively to the ORION "Requirement Analysis" workshop hosted by WP4 in April 2018.

- Subtask 2Epi.1.3: Survey and/or interviews with internal / external experts

We carried out a first survey of the surveillance systems that are established in the partner countries. In total, the partners reported 171 hazards with 194 different surveillance systems. Nevertheless, the survey showed that there are essential differences in the definitions of the different sectors. Hence, the survey has to be revised. Therefore, it is necessary to first define the specific terms and explain the differences between the sectors. This work will be done in cooperation with WP1 (glossary).

Task 2Epi.3: Epi - OH pilot studies

The One Health pilot studies will be carried out in year 2 and year 3. The preparations have been initiated.

- Sub-Task sT-2Epi.3.1: One Health Pilot 1: topic to be determined
- Sub-Task sT-2Epi.3.2: One Health Pilot 2: Salmonella
- Sub-Task sT-2Epi.3.3: One Health Pilot 3: topic to be determined

WP2: NGS

Task 2NGS.1: Inventories and requirement analysis for OH Knowledge Base – NGS

There are four aspects to this task: 1. Examining the infrastructural requirements for running robust and reliable analyses, 2. exploring the various analyses systems that can be set up for typing of zoonotic agents, 3. elucidating what outcomes are useful and desirable for each zoonotic agent, and 4. coordinating our outcomes with requirements from epidemiological modelling.

For this first part of the project, we have mainly focused on parts 2 and 3.

- Subtask 2Ngs.1.1: Literature review, drafting a first questionnaire

  We are in the process of reviewing current state-of-the art analyses for several zoonotic agents, with the aim of discovering commonalities and key decision making points that guide the analysis process. We are also in discussions with the COMPARE project and with EFSA/ECDC to map what work they have done within these fields. Members of this WP also presented the project at the "ASM Conference on Rapid Applied Microbial Next-Generation Sequencing and Bioinformatic Pipelines" conference in Washington DC, USA, with the goal of integrating information on current practices into the project, as well as getting feedback from the community.

- Subtask 2Ngs.1.2: joint ORION "Requirement Analysis" workshop (hosted by WP4) to synchronize questionnaires within ORION

  WP2NGS contributed actively to the ORION "Requirement Analysis" workshop hosted by WP4 in April 2018.

- Subtask 2Ngs.1.3: Survey and/or interviews with internal / external experts

  We are in the process of discussing within the consortium what the desired outcomes of such analyses are, and also what is required for running such analyses in a reliable and robust manner.

Task 2NGS.3: NGS OH pilot studies

We have just hired a person who will work jointly at the NVI and NIPH on the pilot studies, and further decisions regarding how to run the pilot will be done once that person is settled within the project.

WP2: Integration

Task 2Int.1: Inventories and requirement analysis for OH Knowledge Base - Integration

- Subtask 2Int.1.1: Literature review, drafting a first questionnaire

Literature review, knowledge gathering and drafting of the screening questionnaire are in progress.
The WP2 integration organized and facilitated a workshop for work package leaders held in Lyngby, Denmark on 22-23rd of January 2018. The aim of the workshop was to ensure a coherent start on WP 1, 2 and 3, to identify potential synergies and overlaps between all work packages in ORION and to align work efforts and identify expertise in the project. The workshop also provided an excellent opportunity to bounce work package ideas and methodologies off the other WP-leaders and the outputs were initial work documents for each WP. These documents are live project descriptions that includes the detailed aims and the work processes of each WP with room for adding details, new ideas, updating work and changing methodologies along the way. A common way of looking at surveillance and the different steps in the pathway was also developed and used as communication tool in various work packages.

- Subtask 2Int.1.2: joint ORION "Requirement Analysis" workshop (hosted by WP4) to synchronize questionnaires within ORION

WP2 integration contributed actively to the ORION "Requirement Analysis" workshop hosted by WP4 in April 2018.

- Subtask 2Int.1.3: Survey and/or interviews with internal / external experts

The integration knowledge hub was specified and inclusions and limitations defined, followed by a meeting with NOVA and COHSIVE to ensure that the three projects supported each other without significant overlaps.
A conceptual framework for 'OH surveillance initiative' was established and a semi-structured interview outline developed to ensure standardized information collection. Initial screening questions were sent out via EFSA focal points, project participants and other key-surveillance people in EU to identify, who to interview in more detail. Supplementary identification of initiatives using a literature review approach is also in progress.

Task T-2Int.3: Integration OH pilot studies

The pilot study in WP2 integration will enhance the OH input to the Danish Campylobacter Surveillance system. The pilot project design is in progress and the Campylobacter surveillance system is mapped and integrated initiatives between public health, food and vet are in the process of being identified. This will work as a stepping stone for the pilot study, which will trial various enhancements to the system.

We have also started an internal evaluation of our data processes used for collating and integrating data from different surveillance components from veterinary and food surveillance to enhance and optimize the systems in place today. This will include exchanging data with external data providers and recipients including the public health agency.

WP3: OH Surveillance Harmonisation Infrastructure

Task 3.1: Inventories and requirement analysis for OH Harmonisation Infrastructure

- Subtask 3.1.1: Literature review, drafting a first questionnaire:

The WP leaders have carried a literature review on the subject of data integration and interoperability, and a detailed review of available ontologies which could be reused for data interoperability within the surveillance domain.

- Subtask 3.1.2: joint ORION "Requirement Analysis" workshop (hosted by WP4) to synchronize questionnaires within ORION:

A decision was made to focus this WP on the development of an ontology for surveillance, and the construction of an architecture that allows its implementation in practice, using once proof-of-concept case. During this workshop, we reviewed the plan for year 1, and reviewed knowledge themes that will allow partners to contribute within specific knowledge domain areas.

- Subtask 3.1.3: Survey and/or interviews with internal / external experts.

Following the workshop, we started documenting the flow of data within one case study per partner country, with specific focus on the data exchange between institutions within the country (animal, public and food surveillance authorities).

Task T-3.3: One Health pilot

The preparations for a decision on the One Health pilot topic (due by the end of month 12) have been initiated.

WP4 : Coordination, Communication, Training and Sustainability

Task 4.1: Internal project coordination

The project coordination established shared project management resources on Google and on a Virtual Research Environment. This included a shared space for documents, a shared calendar and an online mailing list. On the VRE several other features (tickets, messaging board, wiki, data analytics tools etc.) were made available. The coordination holds monthly web meetings for the whole ORION consortium and a monthly calls for the WP leaders & deputy leaders. EFSA & ECDC representatives as well as the leads of EJP WP 4 and 5 and the coordinator of the COHESIVE project were invited to join these calls. A physical full consortium kick-off meeting was organized and held in Berlin in April that also served as joint ORION "Requirement Analysis" workshop.

Task 4.2: External project integration (synchronized with EJP WP5)

The project coordination organized and performed two joint ORION-EFSA-ECDC+EJP WP5 web-meetings (1st on June 5th 2018, 2nd on 28th June 2018), contributed to the EJP DMP, to the EJP survey and initiated collaboration and information exchange between EJP projects ORION, NOVA, COHESIVE and RaDAR.

Task 4.3: Sustainability roadmap

ORION initiated the evaluation of Virtual Research Environment infrastructure which might potentially serve as OHS Knowledge Hub and as project communication and project management resources. In case the evaluation is successful the developed ORION resources can become an integral component of the envisage European Open Science Cloud.

Task 4.4: Training and Dissemination

- Sub-Task sT-4.4.1: Internal training (sharing knowledge on currently available national solutions)

The ORION project performed the following project internal training until month 9:

- Training on VRE: 28th May 2018
- Training on WP1: 25th June 2018
- Training on WP2: 30th August 2018

- Training on WP3: September 2018

- Sub-Task sT-4.4.2: Knowledge integration (web portal, Wiki, curricula, tutorials, videos, sample data)

The ORION coordination established with support from the EU-funded project AGINFRA+ a Virtual Research Environment (VRE) as knowledge integration platform. This ORION VRE also serves as project-specific web portal with Wiki functionality, shared workspace, messaging and data publishing features. It is part of the project research to exploring if such VRE can serve as knowledge integration platform and technical foundation of the envisaged OHS Knowledge Hub.

- Sub-Task sT-.4.4.3: Training and support for other EJP projects & partners

The ORION project contributed actively to all dissemination event organized by the overarching EJP project, e.g. the EJP Kick-of meeting from 30th - 31st January in Paris, the EJP project website, the web-meeting with the COMPARE project. ORION further initiated direct collaboration with a number of other EJP projects, as e.g. COHESIVE, RaDAR and NOVA. The ORION project has further been presented at international conferences like the SVEPM in Tallinn, the FLI Junior Scientist Symposium and the ASM Conference on Rapid Applied Microbial Next-Generation Sequencing and Bioinformatic Pipelines in Washington DC.

6.1.2.1.4 List of planned tele- or video conferences, face to face meetings in the next year

The ORION project plans to pursue one physical full consortium meeting per year and monthly full consortium conference calls as well as monthly WP leader & deputy leader calls. In addition each WP organize further conference calls on their specific schedule and needs. For WP2Epi there are web-meetings planned monthly or two monthly (in summer). Furthermore there is a FTF WP2-Epi satellite meeting planned at the annual meetings. Stakeholder like EFSA, ECDC, other EJP projects as well as EJP WP leads are invited to join the monthly WP leader & deputy leader calls.

6.1.2.2 COHESIVE

6.1.2.2.1 Summary of the work carried out in the JIP

The main start of the Cohesive project was with the kick-off meeting in March in Amsterdam. The approaches of the different WPs were discussed with the participants. Also representatives of the ORION project, EFSA and the EU were present and took part in the discussions. It was decided to have several workshops parallel in November, in order to prevent too much travel. Also connecting to EFSA and ECDC was again emphasized. A meeting was held at ECDC in June as well as direct contact with EFSA specifically for WP4.
For WP2 the main goal is to develop guidelines for **national** One Health structures (such as present in for instance The Netherlands and UK) or other ways to strengthen human-veterinary collaborations, with the aim to improve signaling, risk assessment and response by better communication, (early) exchange of information, sharing of knowledge and joint forces. This is most important for (re)emerging pathogens, but also the response to notifiable pathogens will profit from better collaboration. Since countries are very different in many aspects, no blue-print can be made for such One Health structures. The guidelines should provide information, checklists and approaches to set-

up or strengthen human-veterinary collaborations taking into account the specifics of countries. In order to achieve this, an inventory via a questionnaire is being set up to gather general and specific information of the different member states (MS). The results of the inventory will be used as input for the workshop planned to be held in November 2018.
Within WP2 another goal is to develop a tool (possibly an decision tree) to help decide which tool/model best to use for the risk assessment for the specific situation in which it is needed. A literature review is performed on existing tools for risk assessment, information from other lists with such tools is used and a questionnaire is sent out, but not all data are back yet. The inventory is an open document that can be expanded during the course of the project. The inventory is input for further discussion on the decision tree (or other tool) in the November workshop.
Within WP3 is started with exploring current ways of exchanging signals between countries by contacting them directly. Also, some questions on this topic are included in the questionnaire mentioned under WP2 and will be used as input for the workshop in November. The same holds true for the task with respect to Horizon scanning. Also, a literature review is performed to determine what methods are currently used.
The main activity performed by the WP4 of COHESIVE (Data platform to facilitate risk-analysis and outbreak control) during the first 6 months of the project was to co-ordinate our activities with those of other EU projects (especially IA-1-ORION and COMPARE) to avoid duplications, and to build a strong interconnection with EFSA and ECDC. WP4 of COHESIVE is aimed at creating national structures for the analysis of WGS and epidemiological data, for the tracing of outbreaks of foodborne infections and the risk assessment. These national information systems should be harmonized with the future EU Joint Database EFSA/ECDC. Since the activities of COHESIVE are carried out in parallel with the design and implementation of the EU Joint Database, a strong interconnection with EFSA and ECDC is necessary to ensure harmonization: this requires a continuous feed-back from EFSA and ECDC to steer the development of the activities of COHESIVE. Connections with ORION, COMPARE as well as EFSA and ECDC are made.

6.1.2.2.2 Progress of the integrative project: milestones and deliverables

Deliverables

JIP name	Project deliverable number	Deliverable name	Delivery date from AWP	Actual delivery date	If deliverable not submitted on time: Forecast delivery date	Comments
COHESIVE	D-1.1	Kick-off meeting	3	3		Meeting in Amsterdam
COHESIVE	D-1.2	Website/platform operational	6	Does not apply		When the website of the overarching One Health EJP fulfils our needs we will not develop our own website
COHESIVE	D-2.1	Inventory of tools for systematic risk-assessment via questionnaire	8	8		Initial questionnaire sent out by month 8, we may need longer to allow respondents to return answers. The inventory will be an 'open' record that we can add to as more partners respond

Milestones

JIP name	Milestone number	Milestone name	Delivery date from AWP	Achieved (Yes/No)	If not achieved: Forecast achievement date	Comments
COHESIVE	M-A2. COHESIVE.4.1	Initial workshop	2	No	Month 11	Decided to postpone the workshop so it can be held

						together with the workshops of WP2 and WP3
COHESIVE	M-AI2.COHESIVE.1.1	Website/platform operational	6	Does not apply		When the website of the overarching One Health EJP fulfils our needs we will not develop our own website
COHESIVE	M-A2. COHESIVE.4.2	Prioritization of requirements for risk modeling framework	6	Yes		

6.1.2.2.3 Progress of the integrative project

WP1: Coordination, communication and sustainability

Task 1.1: Coordination

A steering group has been formed, consisting out of the WP leaders, deputy WP leaders and a secretary. Teleconferences are organized every 6 weeks to discuss the progression of the project as well as management issues.
Connecting to other organizations and activities (including projects) has been started. During the kick-off meeting ECDC and EFSA were invited and EFSA was present. On June 26th, representatives of the steering group have visited ECDC with participation of EFSA, to look for further collaboration between Cohesive and ECDC/EFSA. Cohesive took part in the cogwheel meeting with Compare to look for possible connections. A separate videoconference will be organized to exchange goals in more detail and find these possible collaborations. ORION and NOVA were identified as other EJP-projects to which Cohesive could relate. Both were invited to our kick-off meeting and ORION was present. The coordinator of Cohesive was present at the kick-off of ORION together with several people involved in both projects. Clear links were identified and it was agreed to keep each other informed on the progress within the projects and collaborate where fruitful, in first instance mainly within WP4.
Task 1.2: Communication/dissemination

The kick-off meeting took place on March 28-29 in Amsterdam.
Since a website is built for the overarching EJP-project, most likely no separate website will be built solely for Cohesive when it appears to meet our requirements. A summary and picture are offered to the overarching EPJ WP6 for the general website.

WP2. Integrated risk-analysis at the national level

Task 2.1: Development of guidelines for national One Health structures

To develop guidelines for national One Health structures an inventory is being set up to gather general and specific information of the different member states (MS). The general information will focus on geographical information such as number of inhabitants, number of domestic animals, wild life and so on. The more specific information we want retrieve is about the organization of the public health and animal sectors, already existing contacts and collaborations between the public health and veterinary public health domain as well as barriers for collaboration. The inventory will be used as input for the workshop planned to be held in November 2018.
Task 2.2: Development of structured decision making

This task has some similarities with objectives in ORION and in the EU project COMPARE and connections were made with both of these projects to identify synergies and complimentary activities. A questionnaire to collect information on risk-assessment methods has been developed and sent out. In addition, a literature search has been performed to minimize the number of questionnaires required. The results will be used as input for the workshop organized in November 2018.

WP3.Towards an EU zoonoses structure

Task 3.1: Explore current ways for exchanging signals between countries and cross disciplines – pathway analysis

Within this task is started with exploring current ways of exchanging signals between countries by contacting them directly. Also, some questions on this topic are included in the questionnaire mentioned under WP2 and will be used as input for the workshop in November.

Task 3.2: Select tools for Horizon scanning and signal detection

A literature review is performed to determine what methods are currently used. For the participants on the workshop on WP2 and WP3 a couple of questions on this topic are added to the questionnaire. The results will be used as input for the workshop in November.

Task 3.3: Retrospective systems analysis of detection of outbreaks

This task was started in month 6. Preparation of a generic overview of zoonotic pathogen detection system is underway.

WP4: Data platform to facilitate risk-analysis and outbreak control

Task 4.1: Molecular typing data and metadata – database creation

A new description of task 4.1 has been made with a more extensive explanation of the National Information Systems we are aiming to develop and their placement in the general picture. This new description in incorporated in the Annual Workplan Year 2.

Sub-Task sT4.1.1 - Workshop on data and DBs

The workshop has been postponed to November 2018 and will be held in parallel with the workshops for WP2 and WP3. In the meantime, for the purpose of this sub-task, tele-conferences have been made with COMPARE and ORION projects and a meeting has been held with EFSA (April 2018). A further meeting has been held on June 26 with ECDC to harmonize our activities and outputs with the future EU Joint Database EFSA/ECDC. Harmonization with EFSA has been discussed through repeated telephone calls and a face-to-face meeting. Refinement of Task 4.1 output is ongoing.

Sub-Task sT4.1.2: Design and implementation of DBs

So far, a preliminary logical E-R diagram is depicted, taking into consideration comments from EFSA side during kick-off meeting. An architecture of foreseen information systems interactions and information flow has been designed and discussed during EFSA/ECDC meeting of June 26.

Task 4.2: Development of a platform-independent tracing framework

Sub-Task sT4.2.1: Evaluation of available tracing tools:

- Initial list of available tracing tools is established and made available where possible. Questions to be answered during evaluation are fixed and the evaluation process is ongoing. Partners are requested for further tools to consider. Next, a web-conference with partners (tbd) will be organized

Sub-Task sT4.2.2: Development of the tracing platform

- Server for platform is designed and set up. A restricted area is designed and developed. A data model for data collection form and database are defined. First analyses and visualizations are realized and performance needs are identified. A first web-conference with partners (tbd) will be organized

Task 4.3: Development of a platform-independent risk modeling framework

Sub-Task sT4.3.1 Requirement analysis (M1-9)

- Typical components have been identified that support quantitative microbiological risk assessment, advanced simulation techniques, documentation and extended usability. Selection of minimal models for testing and development is ongoing. As well as the prioritization of building blocks for implementation in web application of rrisk. Currently, also the search of models and data suitable as case study (ideally with input from project partners) is ongoing

6.1.2.2.4 List of planned tele- or video conferences, face to face meetings in the next year

Every 6 weeks a teleconference is planned for the steering group. After the meeting on June 26 at ECDC the steering group has met. . During the workshop which will be held in November 2018, also a meeting of the steering group will be planned. The annual meeting for all members of the project will be planned in the beginning of 2019.

6.1.3 Task 4.3: Integrative support

Task 4.3 consists of three subtasks: 1) alignment with strategic initiatives at EU level; 2) support function for integration of additional partners in ongoing JIPs and; 3) scientific meetings to enhance and leverage integration. During the first 9-month period, there have been activities related to all subtasks.

Under subtask 4.3.1, a procedure for so called cogwheel workshops (CW) has been developed (MS47). CWs are meetings that allow partners within the EJP, typically coordinators or WP leaders of JRPs or JIPs, to meet with representatives of selected strategic initiatives or projects in order to identify synergies, joint priorities and opportunities for collaboration. The target for the first cogwheel workshop - the FP7 project COMPARE, (http://www.compare-europe.eu) - was identified already in the EJP proposal, and the CW was held on 12 April 2018. COMPARE is a 60-month EU funded project aimed to develop an analytical framework and information sharing platform that will enable identification, containment and mitigation of emerging infectious diseases and foodborne outbreaks. The project is coordinated by DTU, an OHEJP beneficiary, and ends in 2019, by the time of the 2nd internal call of the OHEJP. The purpose of selecting COMPARE as target for the first CW was to ensure that OHEJP developments are complementary and that potential synergies were identified at a stage when the OHEJP is starting and COMPARE is still active. The fact that eight of COMPAREs partners are also beneficiaries in the OHEJP is a strength in that they can also contribute to alignment between the two initiatives.

Information about the upcoming cogwheel workshop and about COMPARE was sent to all OHEJP Project leaders on 5 February 2018. The project leaders were asked to check the description of COMPARE to identify whether it contained activities of relevance to the own project; to learn more about, to avoid duplication and/or to have potential for synergies with the OHEJP. If relevant activities were identified, participation in the CW was compulsory. In all, three JRPs and both JIPs registered for the CW. The CW was held as a web meeting (Adobe Connect and Skype for business). A physical meeting had to be avoided due to a potential strike in Denmark, but a positive side effect was that this saved participants' travel time and costs, and also served to reduce the carbon footprint.

The outcome of the CW is detailed in D4.3, *1st cogwheel workshop report with COMPARE*. During the workshop, some concrete points for collaboration were identified, in particular between activities in COMPARE vs IMPART and LISTADAPT. However, from COMPAREs side, a more formal agreement between the OHEJP and COMPARE would be necessary for a closer collaboration regarding data sharing and access to infrastructure. This issue was forwarded to the PMT after the meeting. Furthermore, a couple of potential overlaps were identified between activities in COMPARE vs ORION and METASTAVA. Due to the fact that the workshop was held at an early stage during implementation, this provided an opportunity to redirect activities where needed. However, this requires access to relevant COMPARE deliverables which unfortunately are not classified as public at the time. This is unfortunately a general challenge when trying to align and complement existing research, but

hopefully the situation will change in the future when more projects adhere to the open research data principles, as is the case with many H2020 projects.
It was also noted that although DTU is indeed an OHEJP beneficiary, there is no internal coordination between COMPARE and the OHEJP. In order to achieve better alignment, partner institutes involved in the OHEJP and other strategic initiatives should, in general, be encouraged to actively facilitate exchange and communication. Planning for a 2nd CW in M10 is underway, tentatively with the EU co-funded project EFFORT (www.effort-against-amr.eu).
Under subtask 4.3.2, preparations to launch so called integrative missions have been made. In the OHEJP proposal, two specific types of integrative missions were considered – Short Term Integrative Missions (STIM) targeting individual experts, and Integrative Mentoring (IM) targeting the management level. This format has been further broadened in D4.5 whose name has been changed from *Guidelines for submission and selection of proposals for STIMs and IMs* to *Guidelines for submission and selection of proposals for integrative missions*. JIP leaders will define the exact format based on the needs and activities in the JIP. An integrative programme will be presented in M11 with missions for which non-JIP partners will be invited to apply. These activities will be offered starting in early 2019.
For subtask 4.3.3, WP4 has collaborated with WP3 in the preparation of D3.2, the *Protocol for Annual Scientific Meeting (ASM) organisation*, but is currently not part of the executive organisation team, led by WP3.

6.1.4 Task 4.4: Organisation of call for additional JIPs for the period Y3-Y5

n/a

6.1.5 Task 4.5: Open data management

Task 4.5 consists of three subtasks: 1) development of the Data Management Plan (DMP); 2) guidance and support for implementation of the DMP; and 3) open data access point. During the first 9-month period, there have been activities related only to subtask 1.
In order to develop the first version of the OHEJP *Data Management Plan*, information on the current status of data management within JRPs and JIPs was collected via an online questionnaire, to provide a basis for our understanding of the experience level across OHEJP partners with respect to structured and open research data management. Furthermore, relevant online resources were explored, such as OpenAire, DCC, JISC and similar to locate existing DMP guidance. Since existing DMP guidance is generally for individual projects, and not for multi-project programmes, contact was made with another EJP, the HBM4EU, to build on their experiences with DMP development at the programme level.
The first version of the DMP, which describes the overarching data management strategy for the OHEJP, was submitted by the end of M6 (D4.4). It outlines the step-wise process to ensure the data management adheres to the FAIR principles (Findable-Accessible-Interoperable-Reusable), and a series of actions that will be taken to further develop the granularity of the DMP. As a next step, JRP and JIP leaders will develop their project-specific DMPs by M11, that will further inform the choice of repositories and standards relevant to all specific data types. This development will be supported by the OHEJP DMP team. As part of the DMP development, the team has set up a One Health EJP sub-community on the OpenAire platform. Furthermore, DMP contact points will be identified in all partner institutes, to assist in the development of the DMPs in projects in which their institution is involved. Guidelines and training by the WP4 DMP team is being planned, to further support the development of the DMP. In general, the DMP requirements is a key opportunity to leverage capacity in open data management among OHEJP partners.

6.2 Deliverables and Milestones

6.2.2 Deliverables

Del Rel No	Del no	Deliverable title	Submission
D4.1	D59	Instructions for monitoring of and reporting on JIPs, excl final reporting	M4
D4.2	D60	Report from supportive start-up meeting, 1st round	M5
D4.3	D61	1st cogwheel workshop report with COMPARE	M5
D4.4	D62	Data management plan	M6
D4.5	D63	Guidelines for submission and selection of proposals for integrative missions	M8

6.2.3 Milestones

Mil Rel No	Deliverable title	Notification
MS47	Cogwheel workshop protocol defined	The protocol of the cogwheel workshop has been defined. The document is available upon request.
MS48	Online questionnaire administered to new coordinators	The questionnaire has been sent on the 28th of February. It is available upon request.
MS49	Questionnaire data to evaluate 1st call collected	The data from the questionnaire has been analysed and compiled.
MS50	2nd call for letters of intent issued	Upcoming in M10

7 WP5 - Science to Policy translation to stakeholders

7.1 Work carried out to date

The progress of WP5 activities followed the planned timeline, with the exception of Deliverable 5.3, which, after consulting with PMT, was submitted later than originally planned. This was done to ensure the best possible input for WP2. The objectives were met.

7.1.2 Task 5.1: Identification of the stakeholders and establishment of communication links

During the first reporting period (M1-M9), WP5 focused on EU stakeholders to establish the interaction links for the EJP, with some focus on the strategic research agenda and the second call for research and integrative projects. The stakeholders were identified and categorized, and the structures within their organisations were analysed to identify the persons who are responsible for the strategy, policy, and operational work (including training) related to foodborne zoonoses, antimicrobial resistance and emerging threats. Furthermore, persons acting as direct contact to the JIPs and JRPs (where of interest) were identified in collaboration with ECDC and EFSA. The contact lists were updated further already during this first reporting period. During the first reporting period, the stakeholders participated mainly in Task 5.2, but provided input also to the other tasks of WP5, e.g. the development of procedures for

interaction with the EJP. Deliverable 5.1, Report on the stakeholders contact list and the communication procedure established with stakeholders, was submitted in M2.

7.1.3 Task 5.2: Identification of the research needs of EU stakeholders

During the first reporting period (M1-M9), using the communication links established in Task 5.1, WP5 together with other EJP structures engaged the EU stakeholders in active dialogue on several areas. This covered the establishment of interactions for both the ongoing and the next round of JRPs and JIPs as well as research and integrative needs.
For drafting the call for the second round of projects in the EJP, research needs and integrative needs of ECDC and EFSA were identified and discussed for consideration for the strategic research agenda developed and updated in WP2. The starting point was the needs presented at the Kick-Off Meeting in January. The stakeholders added details and comments on first drafts of the listed needs as well as added new needs, and scored the listed needs regarding how relevant a One Health approach is for them. In collaboration with WP2 and PMT, the needs were evaluated for whether they were within the scope of the EJP and whether they were addressed in other activities (to avoid overlap). Feedback of the process was positive. Deliverable 5.2, Report on the procedure to identify research needs of international stakeholders, was submitted in M2, and Deliverable 5.3., Provisional report on the identified research needs of international stakeholders for the integration into the strategic research agenda, was submitted in M5. Both documents covered research and integration needs. These outputs were provided to WP2 in several formats and served as input for the Strategic Research Agenda. Task 5.2 was also the main focus in the additional Stakeholders Committee meeting WP5 organized on 21 June 2018. ECDC and EFSA were also encouraged to give input into the call descriptions under development for the next round of projects. Applicants for the second round of projects will be required to specify how their work plan will match EFSA and ECDCs needs and complement / built on their activities and repositories. Avoiding overlap with other activities will be emphasized.
For the projects started in January 2018, ECDC and EFSA representatives expressed their expectations as well as potentials for overlaps and synergies. Several activities were started in the EJP to address these comments. For example, in meetings of JIP partners with ECDC and/or EFSA, the potential synergies to ongoing work of Key EU stakeholders were discussed.
Additional procedures are under development to increase awareness on and understanding of research and integrative needs of EU stakeholders as well as their activities and aiming to ensure complementarity / to avoid duplication of work of ongoing and future activities within the EJP. These procedures envisage (formalised) interaction on several levels. It comprises interaction with ECDC and EFSA on the work planned, interim results and identification of opportunities for complementarity in the annual Stakeholders committee meeting, the regular meetings organised by WP5 with Key EU stakeholders, and the contacts between nominated contacts from ECDC and EFSA with coordinators of integrative and research projects (where relevant, as a whole or with dedicated work packages of the projects). Furthermore, experts from EFSA and ECDC are invited to participate in workshops, meetings and tele-conferences of the JIPs and the annual scientific meetings of the OHEJP.

7.1.4 Task 5.3: Linking of the scientific capacity available in the EJP with the stakeholders' identified needs: closure of knowledge gaps

The capacity map aims to support future synergistic collaborations, prepare for emergencies, identify gaps and areas of expertise and support linkage with similar expertise.
During the first reporting period (M1-M9), WP5 started to develop the concept for this capacity map. This capacity map will reflect the capacities, infrastructures, equipment and technical resources of all partner institutes involved in the OHEJP consortium in an easy to access form to support the quick identification of teams which could respond to specific needs or be involved in future activities. It will

also reflect capacities and repositories of ECDC and EFSA as well as established interactions with EJP partners in relevant fields to support collaboration and consideration throughout the EJP and in national activities.
The capacity map will include relevant aspects of ongoing integrative activities in the JIPs and JRPs and by EFSA and ECDC. Potential synergies will be identified and communication procedures will be established between WP5 and JRPs and JIPs (via WP 3 and WP 4).This will increase transparency related to complementarity of ongoing and completed activities as well as improve understanding where future approaches can build on work already performed, integrate science and close identified gaps. This capacity and activity map will increase understanding on different levels (EU, national and institutional) as well as across domains and areas. The capacity map will also be useful for providing scientific support to enhance exploitation of results, as well as to follow up on the development of the partners (capacity building, better preparedness).
After consultation within the PMT, the capacity map will be implemented as an electronic tool (exchange platform) in a way that it will complement existing databases and inventories of EU and international stakeholders. All projects within the OHEJP will be encouraged to use this platform to describe their approaches, skills, tools etc. and include links to their specific activities. This will increase transparency and complementarity of approaches.

7.1.5 Task 5.4: Dissemination of new knowledge, tools and materials

During the first reporting period (M1-M9), WP5 started to compile a dissemination strategy and ideas for targeted communication to disseminate the outcomes of the One Health EJP to the stakeholders efficiently.
The strategy for interaction will also highlight on a regular basis the ongoing integrative activities and the links between activities in JIPs, JRPs, EFSA and ECDC, the progress achieved and the potential for future development and synergies.

7.2 Deliverables and Milestones

7.2.2 Deliverables

Del Rel No	Del no	Deliverable title	Submission
D5.1	D87	Report on the stakeholders contact list and the communication procedure established with stakeholder	M2
D5.2	D88	Report on the procedure to identify research needs of international stakeholders	M2
D5.3	D89	Provisional report on the identified research needs of international stakeholders for the integration into the strategic research agenda	M5

7.2.3 Milestones

Mil Rel No	Milestone title	Notification
MS64	Communication channel with stakeholders established	Communication channel with stakeholders has been defined. Please refer to Deliverable 5.1 Report on the Stakeholders contact list and the Communication procedure

		established with stakeholders, submitted in M2.
MS65	Implementation of a communication platform and procedure to identify research needs of international stakeholders in the field established	The communication with international stakeholders and the procedure to identify research and integrative needs of international stakeholders have been established. They are described in D5.1 and D5.2 (both submitted in M2). The procedure works well, and the feedback from the stakeholders has been positive.
Additional milestone	An additional meeting with Stakeholders Committee during M6 for (1) consultation regarding the preliminary list of priority research topics and priority integrative topics for the updated Strategic Research Agenda and (2) strategic interaction with all Members of the SC	The meeting was held on June 21 in Brussels, Details can be taken from the minutes of the meeting.

In addition to the milestones planned, there was a Stakeholders Committee Meeting in M6.

8 WP6 - Education and training

8.1 Work carried out to date

8.1.2 Task 6.1: Short-Term Missions

n/a

8.1.3 Task 6.2: Workshop programme (satellite to Annual Scientific Meetings)

The first Annual Scientific Meeting (ASM) has now been confirmed to take place on 22nd – 24th May 2019 in Ireland. The lead on the first ASM is Dr Geraldine Duffy at the TEGASC institute in Ireland. WP6 leader Roberto La Ragione has been in bi-weekly TC with WP3 deputy leader Hendrik-Jan Roest at WbvR. Monthly TC with Dr Geraldine Duffy will now follow to ensure that all the necessary planning is in place. Furthermore, the MVNA project manager will engage with the process to ensure documentation and learnings from the MVNA ASM's can be utilised. As the first ASM date and location has been confirmed, the process for selecting the priority theme for the first satellite workshop is currently being developed.

8.1.4 Task 6.3: 'One health' Summer School for medical and veterinary science undergraduates

The protocol for organising the One Health summer schools has been written and is currently being validated by PMT members. The call for hosting the first summer school will be announced to the consortium at the end of September 2018.

8.1.5 Task 6.4: Doctoral Training Programme

OHEJP partners were invited to submit PhD grant proposals for the first PhD grant call. Guidelines were provided to applicants detailing the call background, the number and type of grants available, the assessment procedure, eligibility criteria, criteria for selection, and finally the budgeting details. Applicants were also provided with a Frequently Asked Questions document associated with the guidelines. The PhD proposals were screened for their eligibility in alignment with the criteria listed in the G.A. Each proposal was reviewed by 2-3 reviewers, who were provided a pre-approved scoring matrix. The scores were compiled, analysed and validated by PMT. SSB were briefed on the process, and voted for the 4 projects to be funded in this round (8 projects will be funded in the second round). The scores were compiled, and validated by PMT. The result was communicated to the OHEJP consortium, and applicants individually. These 4 PhD programmes will commence in early 2019. The second PhD call will be announced in September 2018.

8.1.6 Task 6.5: One-Health Continuing Professional Development (CPD) Module

n/a

8.1.7 Task 6.6: Communications workshop and media training

n/a

8.2 Deliverables and Milestones

8.2.2 Deliverables

n/a

8.2.3 Milestones

n/a

9 WP7 – Sustainability

9.1 Work carried out to date

9.1.2 Task 7.1: Gathering Stakeholders´ Needs and Expectations

This task received the input from WP5 which identified the stakeholders relevant for the EJP and for the SRA (report 5.1). The preliminary evaluation of the report 5.1 indicates that for the sustainability, it will be strategic to integrate the list with some other stakeholders that will be identified and approached in the following stage of the task.

9.1.3 Task 7.2: Strategic Research and Innovation Agenda (SRIA) 2021-2030 (SRIA 2021-2030).

Members of the WP7 took part in some activities related to the definition of the SRA, as facilitator in the expert meeting. The updated research topics defined will be one of the inputs for the task 7.2.

9.1.4 Task 7.3: Making the EJP sustainable through other funding and/or legal basis

According to the proposal approved by the EC, the overarching ambition of the One Health EJP is to develop a European network of research institutes, mainly reference laboratories, integrating medical, veterinary and food scientists in the field of food and feed safety. The network can provide a larger critical mass, which results in improved research on the prevention and control of mainly foodborne zoonoses, antimicrobial resistance and emerging threats, while taking into account the public health concerns of consumers and other stakeholders throughout the food chain.

The EJP can be a privileged speaker in the EU area, to promote the alignment and the harmonization of priorities and research agendas in the domains of foodborne zoonoses, antimicrobial resistance and emerging threats.
The EJP can generate knowledge and capacity beyond the state-of-the-art with regard to foodborne zoonoses, antimicrobial resistance and emerging threats.

From a purely technical point of view, EJP can considerably help the harmonization of approaches, methodologies, databases and procedures for the assessment and management of food-borne hazards, emerging threats and AMR across Europe, which will improve the quality and compatibility of information for decision making.
In principle, the abovementioned aspects of One Health EJP are the "core business" of the Program, and should be maintained beyond the project's life.
To be realistic, and considering the Med-Vet Net Association experience, a networking activity can be the minimum achievement in term of sustainability. Through the network, part of the core activities, like exchange of information, sharing of best practices, alignment of methods and approaches, training and other synergies among partners can be maintained. Also the "identity" of the EJP can be maintained, to ensure the role of "privileged speaker".

Although it is still too early to identify the strong and the weak parts of the Program, the capacity of interaction with the key stakeholders for the development of the strategic research agenda will be also in the future a valuable support for the EC and the MSs. If the One Health EJP will be appointed as "provided of services" for the European Commission (management of research calls (and possibly grants) in the remit of the EJP, identification of priorities, technical support to EC and MSs in terms of laboratory capacity, surveillance and risk assessment, training and knowledge sharing), we will have great opportunities to maintain the activities after the end of the program.

EU fundings are considered as main drivers to make the EJP sustainable. Firstly, WP7 has monitored the launch of new calls from existing tools. The JPI AMR has recently launched a string of calls aiming at building a Virtual Research Institute. JPIAMR-VRI will provide a platform to increase coordination, improve visibility of the AMR researcher base and facilitate knowledge exchange and capacity development across the globe, covering the full One Health spectrum. The last calls of Horizon 2020 also represent a mean to ensure the sustainability of the EJP like *SC1-BHC-13-2019: Mining big data for early detection of infectious diseases threats driven by climate change and other factors.* Even if the EJP cannot apply as a whole as it doesn't have any legal basis, its members do. Finally, the WP7 follows carefully the negotiations around the next Framework Programme. As Horizon Europe will be based on several missions, the EJP could serve as a model. A sound analysis has been conducted taking into account the valuable documents like the Mazzucato's report on "Mission Oriented Research and Innovation in the EU" or the EC's proposal on Horizon Europe.

Considering that EU could not continue to fund the EJP as whole, there is the opportunity at least for a number of partners of the network, to apply to other EU funding, and the possibilities are many, including e.g. the Marie Curie Fellowship.
Taking into account the stakeholders' needs, legal basis will be investigated (e.g. art. 185).

9.1.5 Task 7.4: Making the bridges between EJP's beneficiaries and stakeholders sustainable

n/a

9.2 Deliverables and Milestones

9.2.2 Deliverables

n/a

9.2.3 Milestones

n/a

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