

**Deliverable D-4.1.3**

**Workpackage 4**

**Responsible Partner: IZSAM**

**Contributing partners:**

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DATABASES CONTAINING THE COUNTRY DATA

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## Introduction

### Short Introduction To The Project And The Deliverable

The OHEJP COHESIVE Project aims to improve efficiency on outbreak management, surveillance and risk assessments in a One-Health approach at Member State level.

The goal can be achieved by integrating information on pathogens from the human and veterinarian side, present at Member State level.

Information under consideration in COHESIVE are:

* **WGS data** produced by analysis of pathogens by the Member State laboratories
* **Metadata**, such as the minimum epi-data associated with a pathogen.

Moreover, additional useful metadata sources will be considered.

At Member State level each system will be analyzed in order to understand:

* which WGS data contains (e.g., results of bioinformatics approach/pipelines/tool),
* which metadata contains (e.g., epi-data),
* which interoperability (data import/export) possibilities are present,
* how harmonization can be performed and so on.

In this deliverablewehave filled the three DB of this project (WGS, metadata and classicalepidemiology) with the data available from three participating countries, such as:

* Italy;
* Norway;
* The Netherlands.

For the collection of metadata we have sent to all Member States a template to be filled with the metadata of interest in order to identify the minimal set of metadata needed in an outbreak. Italy and The Netherlands provided information to fill the relative COHESIVE Information System (CIS). Norway activity is still on going.

### Application URL of CIS by Member States

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| **Member State** | **URL** |
| **Italy** | <https://cohesive.izs.it/cis_italy/> |
| **Norway** | <https://cohesive.izs.it/cis_norway/> |
| **The Netherlands** | <https://cohesive.izs.it/cis_holland/> |

## Informations On Member State Italy

The Member State Italy has chosen to investigate the pathogen “*Listeria monocytogenes*”.

### Listeria monocytogenes.

Information of this pathogen is managed in Italy by two organizations: **LNR Listeria monocytogenes** and **ISS**.

LNR Listeria monocytogenesuses the information system of the National Reference Center for Genomic Sequences of pathogenic microorganisms: bioinformatics database and analysis (CNR GENPAT).

ISS uses an information system based on IRIDA for the collection of sequence data and associated descriptive data.

In Italy this two organizations are already working together to develop a platform for the collection and sharing of genomic sequences of zoonotic pathogenic microorganisms and epidemiological data relating to human and veterinary cases. This tool is strategic for carrying out surveillance activities and allowing the study of epidemic outbreaks.

The main objective of this collaboration is the definition and sharing of protocols for the analysis of clusters starting from genomic and epidemiological data with the aim of improving the surveillance and study of epidemic outbreaks of food-borne diseases; pathogens under consideration are STEC, *Listeria monocytogenes* and *Campylobacter* spp

## Informations On Member State Norway

The Member State Norway has chosen to investigate the pathogen “*Listeria monocytogenes*”.

### Listeria monocytogenes.

Information of this pathogen is managed by two organizations: **The Norwegian Veterinary Institute** and **NIPH**.

We are waiting for the final review of the data by the two organizations.

## Informations On Member State The Netherlands

The Member State The Netherlands has chosen to investigate the pathogens “*Listeria monocytogenes*” and “Hepatitis E”.

### *Listeria monocytogenes*

Information of this pathogen is managed by two organizations: **RIVM** and **NVWA**.

The RIVM (National Institute for Public Health and the Environment) and the NVWA (Netherlands Food and Consumer Product Safety Authority) have a shared database with WGS data from humans and food for Listeria monocytogenes.

At RIVM the human isolates data are available with associated metadata. There is a system (the internal LIMS) which stores all data and links the WGS data. It is easy to retrieve data from there.

Both institutes exchange routinely the raw data for performing separately a clustering analysis in order to find interesting clusters. This happens without exchanging metadata. In case of an interesting situation, details are exchanged between the agencies. The institutes use different clustering methods: SNPs based at NVWA and cgMLST at RIVM.

The raw data are stored locally at both institutes (each institute stores own data) and exchanged in the shared database (on the ftp-server at RIVM) on regular basis. This database includes only sequences and both institutes analyze them with their own pipelines. Metadata is shared on request.

For the CIS of The Netherlands (https://cohesive.izs.it/cis\_holland/management.jsp) we have collected the informations on metadata by filling in a template for the Listeria monocytogenes database.

In detail, we have inserted the following data per Listeria monocytogenes:

* in the "Laboratory" and "Source Databases" menus we have inserted the entries with "NVWA" code and "NVWA - Netherlands Food and Consumer Product Safety Authority" description that is the institute involved on the feasibility study;
* in the "Species" menu we have inserted the entry Listeria monocytogenes;
* in the "Materials" menu we have inserted the entries Human Materials, Animal, Food and Environment;
* for the "Host" values in the "Species" menu we have inserted the entries Chicken, Cattle, Pig, Turkey, Other (for Animal); Patient (for Human). This metadata is important for Animals and Human. Could be 'Not Applicable' for Food and Environment;
* for the "Matrix" values in the "Materials" menu we have inserted the entries Specimen, Faeces, Serum, Plasma, CSF, Biopsy, Other (for Specimen); Meat, Meat Product, Fish, Shellfish, Vegetables/Fruit/Herbs, Ready to eat Products, Other (for Food);
* the format of the dates stored in the archives must be DD/MM/YYYY;
* in the “Sample Points” menu will be inserted 6 digit Postal Code of Netherlands (postal code from farms, supermarket, slaughterhouses Netherlands).

### Hepatitis E.

Information of this pathogen is managed by two organizations: **RIVM** and **WBVR**.

Hepatitis E data are gathered in HEVNet platform that stands for a One Health, collaborative, interdisciplinary network and sequence data repository for enhanced hepatitis E virus molecular typing, characterization and epidemiological investigations. It was established in April 2017 and functions as a database for sharing Hepatitis E sequences and accompanying metadata. The members of this network include 46 institutes from various domains that originate from 20 countries (status September 2019), mostly from Europe. The number of members is growing continuously.

In the Netherlands the following institutes are involved:

* Public Health and Environment: RIVM (National Institute for Public Health and the Environment)
* Veterinary: WBVR (WageningenBioveterinary Research)
* Food: NVWA (Netherlands Food and Consumer Product Safety Authority)
* Blood donors: Sanquin

The above mention institutions apply sequences of an agreed genomic region to the HEVNet, i.e. minimum length of 300 nt within ORF2. Desired metadata accompanying the sequences include origin of the sample (i.e. human, animal, food, environmental), year of sampling, sequence method, region of sampling. These are however not available for all sequences. In the veterinary field the geographical locations are scare. With respect to sequences of human origin the additional metadata as follows are reported: patient sex, patient year of birth, year of sampling, hospitalization (yes/no), symptoms, mortality (yes/no) and region of sampling.

Currently (September 2019) there are 2065 sequences from 1919 cases in the HEVNet. The majority originate from blood donors. With respect to the data obtained from the Netherlands there are 818 sequences, from 688 cases, of which 80% originate from humans and 20% from both food and animals. No sequences from the environment are uploaded from the Netherlands.

HEVNet functions as a repository of sequences after their analysis done by researchers, no raw but analyzed sequences are uploaded. The data can be queried, analyzed, visualized including pie charts, geographical maps and phylogenetic trees. Members can retrieve whole or selection of sequences in a FastA format for phylogenetic analyses. Furthermore they can download excel file with metadata related to particular sequences. The HEVNet data are stored at RIVM server, which is an open source system.

The HEVNet is used for surveillance and the available data in the Netherlands can be used to validate the Cohesive Information System (CIS) and indicate if the system works as expected.

For the CIS of The Netherlands (<https://cohesive.izs.it/cis_holland/management.jsp>) we have collected the informations on metadata by filling in a template for the hepatitis E database.

In detail, we have inserted the following data per Hepatitis E virus:

* in the "Laboratory" and "Source Databases" menus we have inserted the entries with "WBVR" and "RIVM" code and "Wageningen Bioveterinary Research" and "National Institute for Public Health and the Environment" description that are the two institutes involved on the feasibility study;
* in the "Species" menu we have inserted the entry Hepatitis E virus;
* in the "Materials" menu we have inserted the entries Human Materials, Animal, Food and Environment;
* for the "Host" values in the "Species" menu we have inserted the entries Human, Animal, Pig, Wild boar, Deer, Moose, Rat, Mouse, Camel, Rabbit, Other (for Animal); Donor, Patient (for Human);
* for the "Matrix" values in the "Materials" menu we have inserted the entries Specimen, Faeces, Serum, Plasma, CSF, Biopsy, Other (for Specimen); Waste water, Animal waste, Agricultural water, Other (for Environment); Meat,; Meat product,; Shellfish,; Vegetables / Fruit,; Other (for Food); Transplantation,; Solid organ transplant, Haematological disorder (for Transplantation);
* the format of the dates stored in the archives must be YYYY;
* we have inserted as “Sample Points”all European States although for the feasibility study only data collected in the Netherlands could be used.

## Glossary

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| **CIS** | Cohesive Information System |
| **WGS** | Whole Genome Sequencing |
| **LNR** | Laboratorio Nazionale di Riferimento |
| **ISS** | IstitutoSuperioreSanità  <http://www.iss.it/> |
| **RIVM** | National Institute for Public Health and the Environment  <https://www.rivm.nl/en> |
| **NVWA** | Netherlands Food and Consumer Product Safety Authority  <https://www.nvwa.nl/> |
| **WBVR** | WageningenBioveterinary Research  <https://www.wur.nl/en/Research-Results/Research-Institutes/Bioveterinary-Research.htm?gclid=Cj0KCQjwz8bsBRC6ARIsAEyNnvoxh9f6lR48IeOC3PBo5JDt60A37DnnYaGhU21GSUIFird7RxU6oRYaAqvlEALw_wcB> |
| **Norwegian Veterinary Institute** | The Norwegian Veterinary Institute  <https://www.vetinst.no/> |
| **NIPH** | Norwegian Institute of Public Health  <https://www.fhi.no/en/> |
| **IRIDA** | Integrated Rapid Infectious Disease Analysis  <https://www.irida.ca/> |
| **AMR** | Antimicrobial Resistance |