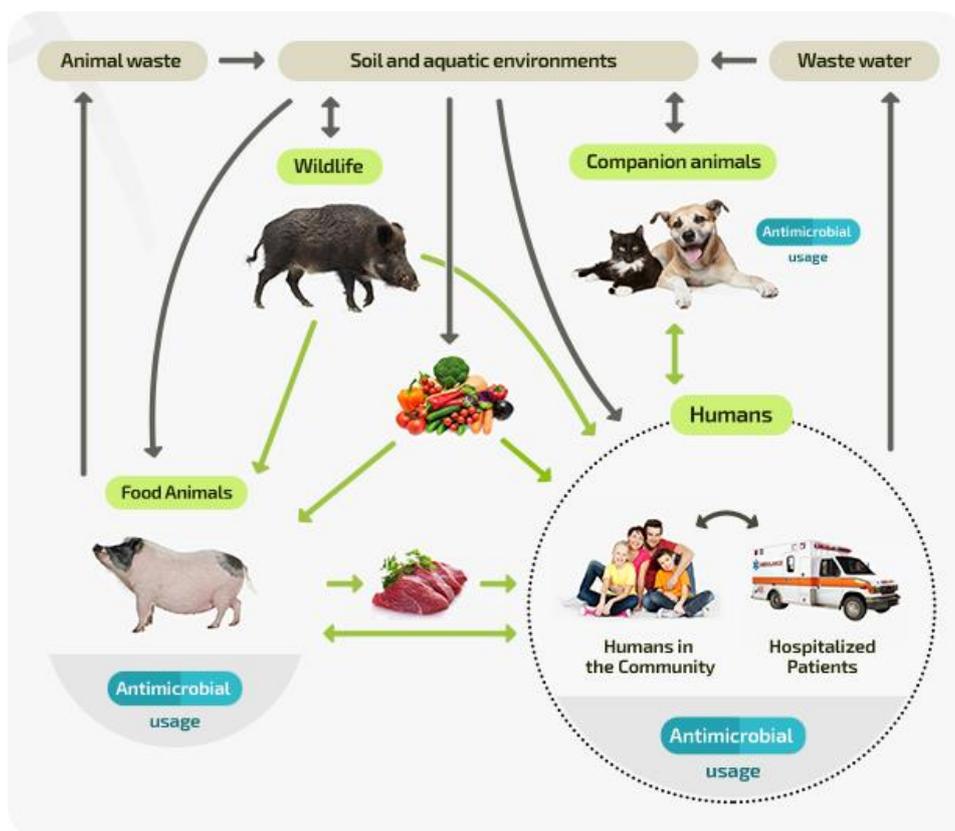


# EFFORT Publishable summary – P1

## Project context and objectives

The EFFORT project is studying the complex epidemiology and ecology of antimicrobial resistance and the interactions between bacterial communities, commensals and pathogens in animals, the food chain and the environment.

This will be conducted by a combination of epidemiological and ecological studies using newly developed molecular and bio-informatics technologies. EFFORT will include an exposure assessment of humans from animal and environmental sources. The ecological studies on isolates will be verified by *in vitro* and *in vivo* studies. Moreover, real-life intervention studies will be conducted with the aim to reduce the use of antimicrobials in veterinary practice. Focus will be on understanding the eco-epidemiology of antimicrobial resistance from animal origin and based on this, predicting and limiting the future evolution and exposure to humans of the most clinically important resistance by synthesising different sources of information in our prediction models.



Schematic drawing of antimicrobial resistance gene movements across the food chain.

Through its results, the EFFORT research will provide scientific evidence and high quality data that will inform decision makers, the scientific community and other stakeholders about the consequences of AMR in the food chain, in relation to animal health and welfare, food safety and

economic aspects. These results can be used to support political decisions and to prioritise risk management options along the food chain.

## Main objectives

Main objectives and important innovative aspects of EFFORT are:

- ✓ The characterization of the resistome of production animals as determined by metagenomics and assessing the added value of genomic analysis of isolates and metagenomic analysis of bacterial communities in comparison with the conventional used method for EU based surveillance of antimicrobial resistance using indicator organisms.
- ✓ The comprehensive and multinational/multispecies datasets that will be collected and built will allow determination of the complex associations between risk factors including antimicrobial usage, and the occurrence of resistance (resistome and conventional data).
- ✓ An estimation of the relative contribution of different sources and various transmission routes on antimicrobial resistance in humans in the general population as well as in selected occupational risk groups. This will also allow for an estimation of the effect of reduced antimicrobial use and other specific interventions on human exposure
- ✓ The determination of genetic characteristics involved in success of high-risk clones and mobile genetic elements in the epidemiology of AMR and the estimation of the relative impact on human infection risks caused by transfer of antimicrobial resistance determinants between commensals and pathogenic organisms.
- ✓ The implementation of on-farm interventions (e.g. restricted usage of antimicrobials) in multiple European countries and animal species following a common approach, including an analysis of the economic effects, animal welfare consequences and resistance levels.
- ✓ The use of novel statistical analytical approaches for rich meta-genomic data to obtain a “fingerprint” of resistance patterns for different populations (humans, animals) and the environment. Simultaneously these fingerprint patterns will be associated to determinants of antimicrobial resistance of relevance for human and animal health.

## Work performed since the beginning of the project

During the first 18 months of the EFFORT project, efforts have been focused on the preparation of the lab and study protocols, receiving ethical approval for the descriptive study, and – eventually - starting the descriptive studies and collecting data in nine countries.

Progress is as follows:

### WP1 “Integrated evidence base for the food chain”

A full sampling plan (for both descriptive and in-depth study) including lab- and study protocols and questionnaires for different animal species (pig, poultry, veal calves, turkey, companion animals, fish and wildlife) has been established. Sampling has started in all nine countries from September 2014, M9 of the project, onward. The deadline to finish sampling will be October 1<sup>st</sup> 2015. For the questionnaires gathered in both the descriptive and in-depth studies, a joint protocol for data

storage (with the use EpiData software) has been developed, including the preparation of templates for data storage in dedicated software.



Sampling of pig faeces.

## **WP2 “Molecular approaches for determining the molecular ecology and epidemiology of AMR genes”**

A protocol for DNA extraction from faecal samples for metagenomic analysis has been prepared and distributed to the project partners. Since the quality of the DNA is crucial for the outcome of the study, a DNA extraction proficiency test was designed. This test allows comparing DNA extractions performed by different partners, to ensure that equal quality is obtained from all participating countries.

Furthermore, the metagenomic sequencing strategy was identified and a pipeline for analysis of the sequence data has been developed by Intomics. This pipeline will enable identification of resistance genes and associated genetic information.

## **WP3 “Ecology and transfer of resistance mechanisms”**

WP3 has compiled knowledge regarding the most widely used food processing regimes, in order to determine the biophysical conditions bacteria encounter throughout the food chain. Food industry personnel were consulted to catalogue and describe the different processes. Furthermore, a literature search was conducted. Based on the collated information and taking into account the relative strength of the studies, WP3 members evaluated available evidence and ranked biophysical parameters considered priority parameters for study.

## **WP4 “Epidemiological analysis of antimicrobial resistance patterns in humans and the environment”**

For WP4, the main task in this period was to streamline field work and data collection. An infrastructure for effective data processing was created and is ready to be taken into use when data becomes available later in 2015. In addition, the literature has been explored for analysis of meta-

genomic data using data reduction techniques and analytical pipelines have been set up using multidimensional preference analysis in R software to reduce the dimensionality of gene data.

### **WP5 “Relationship between farming practices, antimicrobial usage, animal health and resistance”**

The aim of WP5 is to study the relationship between farming practices (including biosecurity), antimicrobial usage, animal health and antimicrobial resistance. The bulk of the work of WP5 will only start when the data collection of WP1 is completed. As preparation for an accurate data description and analysis, we have performed an exhaustive literature study of all methods described in literature to quantify antimicrobial usage both in human and veterinary medicine. This information will be used to select the most appropriate quantification systems to be used in the project. In the mean-time also some preliminary data analysis to describe and analyse data on biosecurity in pig production in four European countries was performed to get a feeling with data and to understand the potential linkages.



Pig farming.

### **WP6 “Intervention studies aiming at reducing AM usage and resistance in pig and poultry production”**

The literature has been explored on available knowledge about interventions along the food chain. Additionally an assessment and decision support (ADS) tool for a multi-level intervention on pig and poultry farms has been developed. In the frame of the WP6 study assay, antimicrobial resistance patterns of *E coli* from control and intervention farms will be monitored to assess time trends along the study. A protocol for sampling, storage and bacterial methods has been developed.

### **WP7 “Quantification of exposure to AMR through different transmission routes from animals to humans”**

The work in WP7 relies on mainly on data collected in other WPs and was therefore limited during this first project period. However, careful monitoring of data collection methods and tools installed

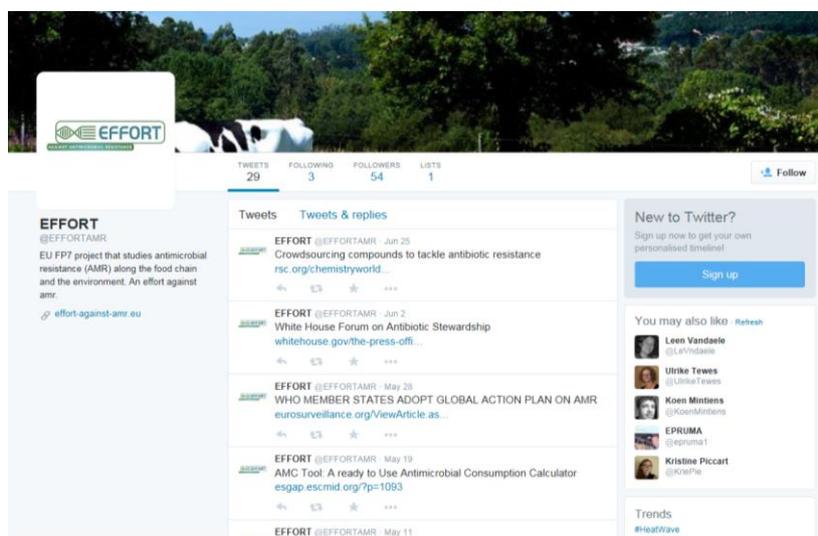
by the sampling partners was performed, to ensure that the data collected is relevant. In parallel, several analyses using data from external sources have been initiated.

### WP8 “Economic impact analysis”

A consortium-wide questionnaire with regard to Animal Welfare issues was delivered, and preparations for data analyses and future collaboration between TiHo and BEC were made. A slight deviation from the original plan had to be made, since collection of slaughterhouse data was not possible in all countries. A conceptual framework on the economic decision making regarding AM and AMR issues was developed. Moreover, collaboration was initiated with WP6 and resulted in the development of protocols and analysis approaches for the upcoming intervention studies.

### WP9 “Project dissemination and training”

WP9, responsible for dissemination activities, is taking care of disseminating widely news and outputs which have been produced within the EFFORT project. To ensure consistency and quality of this process, a project dissemination plan has been implemented and is followed for all dissemination actions. A strong online presence can be expected, via the EFFORT public website ([www.effort-against-amr.eu](http://www.effort-against-amr.eu)), the Twitter account (@effortamr) and a LinkedIn group ([EFFORT: Ecology from Farm to Fork of microbial drug resistance and transmission](#)). To inform relevant stakeholders and to obtain feedback on the project’s workplan, a series of online policy round tables have been organised. Members of the EFFORT consortium have also attended scientific conferences and meetings with particularly relevant stakeholders such as the European Medical Agency (EMA).



EFFORT's twitter feed.

## The expected final results and their potential impact and use

The EFFORT research will provide scientific evidence and high quality data that will inform decision makers, the scientific community and other stakeholders about the consequences of AMR in the food chain, in relation to animal health and welfare, food safety and economic aspects. The project’s research will also contribute to the reduction of the transfer and spread of antimicrobial resistance by using evaluated intervention strategies that are targeting a range of possible intervention points along the food chain.

Specifically, EFFORT will strive to answer the following fundamental, but complex questions demanded by risk managers:

- ▶ What is the impact of antimicrobial usage in food-producing animals on human exposure to AMR determinants?
- ▶ What are the most important transmission routes and sources of human exposure to AMR determinants?
- ▶ What is the impact on human health of transfer of AMR determinants between commensals and pathogenic microorganisms?
- ▶ How can human exposure to AMR determinants through food-producing animals be reduced?
- ▶ What is the most cost-effective way of monitoring antimicrobial resistance occurrence in food-producing animals and in the food chain?

The answers are expected to support political decisions and to prioritise risk management options along the food chain both on the short and long term horizon. In addition, the results can inspire and guide future research initiatives.

More info available at: [www.effort-against-amr.eu](http://www.effort-against-amr.eu)