

Brussels, 4 June 2019

COST 034/19

#### DECISION

Subject: Memorandum of Understanding for the implementation of the COST Action "European Network for Optimization of Veterinary Antimicrobial Treatment" (ENOVAT) CA18217

The COST Member Countries and/or the COST Cooperating State will find attached the Memorandum of Understanding for the COST Action European Network for Optimization of Veterinary Antimicrobial Treatment approved by the Committee of Senior Officials through written procedure on 4 June 2019.

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#### MEMORANDUM OF UNDERSTANDING

#### For the implementation of a COST Action designated as

#### COST Action CA18217 EUROPEAN NETWORK FOR OPTIMIZATION OF VETERINARY ANTIMICROBIAL TREATMENT (ENOVAT)

The COST Member Countries and/or the COST Cooperating State, accepting the present Memorandum of Understanding (MoU) wish to undertake joint activities of mutual interest and declare their common intention to participate in the COST Action (the Action), referred to above and described in the Technical Annex of this MoU.

The Action will be carried out in accordance with the set of COST Implementation Rules approved by the Committee of Senior Officials (CSO), or any new document amending or replacing them:

- a. "Rules for Participation in and Implementation of COST Activities" (COST 132/14 REV2);
- b. "COST Action Proposal Submission, Evaluation, Selection and Approval" (COST 133/14 REV);
- c. "COST Action Management, Monitoring and Final Assessment" (COST 134/14 REV2);
- d. "COST International Cooperation and Specific Organisations Participation" (COST 135/14 REV).

The main aim and objective of the Action is to optimise veterinary antimicrobial use with special emphasis on the development of animal- and disease-specific treatment guidelines and refinement of microbiological diagnostic procedures. Combined with diverse educational activities, the Action will contribute to build a larger critical mass of experts in veterinary antimicrobial stewardship throughout Europe. This will be achieved through the specific objectives detailed in the Technical Annex.

The economic dimension of the activities carried out under the Action has been estimated, on the basis of information available during the planning of the Action, at EUR 100 million in 2018.

The MoU will enter into force once at least seven (7) COST Member Countries and/or COST Cooperating State have accepted it, and the corresponding Management Committee Members have been appointed, as described in the CSO Decision COST 134/14 REV2.

The COST Action will start from the date of the first Management Committee meeting and shall be implemented for a period of four (4) years, unless an extension is approved by the CSO following the procedure described in the CSO Decision COST 134/14 REV2.



#### OVERVIEW

#### Summary

The global antimicrobial resistance crisis has been the driver of several international strategies on antimicrobial stewardship. Despite their good intentions, such broad strategies are only slowly being implemented into "real life". This is particularly unfortunate for veterinary medicine, which is challenged by (i) a shortage of experts in key disciplines related to antimicrobial stewardship, (ii) few antimicrobial treatment guidelines, and (iii) inferior diagnostic tests compared to human microbiology. The aim of this Action is to optimize veterinary antimicrobial use with special emphasis on the development of antimicrobial treatment guidelines and refinement of microbiological diagnostic procedures. For this purpose, the Action will first survey the state-of-the-art in terms of microbiological diagnostic practices and veterinary treatment guidelines across Europe. Secondly, tools in the form of an extensive European strain database and a standard for making antimicrobial treatment guidelines will be created. Third, Action Participants will exploit these tools for the development and refinement of microbiological methods and European treatment guidelines. Finally, the surveys, tools, diagnostic methods, and treatment guidelines will be disseminated to national and international stakeholders. Furthermore, the Action will recommend priority research areas for future optimization of antimicrobial treatment in animals, and develop a roadmap outlining how European countries can advance towards a common high level of veterinary antimicrobial stewardship. The planned investigations and the educational activities will raise the critical mass of expertise in veterinary antimicrobial stewardship in Europe, especially in less resourceful countries and among Early Career Investigators.

Areas of Expertise Relevant for the Action	Keywords
• Veterinary science: Veterinary medicine (miscellaneous)	<ul> <li>Veterinary antimicrobial stewardship</li> </ul>
<ul> <li>Animal and dairy science: Microbiology</li> </ul>	<ul> <li>Veterinary microbiology</li> </ul>
<ul> <li>Animal and dairy science: Prevention and treatment of</li> </ul>	<ul> <li>Diagnostic microbiology</li> </ul>
infection by pathogens (e.g. vaccination, antibiotics, fungicide)	<ul> <li>Antimicrobial treatment guidelines</li> </ul>
<ul> <li>Agriculture, Forestry, and Fisheries: Bacteriology</li> </ul>	<ul> <li>Antimicrobial susceptibility testing</li> </ul>
<ul> <li>Biological sciences: Microbiology</li> </ul>	

#### Specific Objectives

To achieve the main objective described in this MoU, the following specific objectives shall be accomplished:

#### Research Coordination

• To describe, compare, and review the methodologies and interpretive criteria used by diagnostic laboratories across Europe for identification and antimicrobial susceptibility testing of veterinary pathogens.

• To map and compare the availability, structure, and evidence-base of veterinary antimicrobial treatment guidelines in Europe.

• To create a European standard specifying minimum requirements for development of harmonised and evidence-based veterinary antimicrobial treatment guidelines.

• To use the standard for developing European animal- and disease-specific treatment guidelines, and supporting the adaption of these into national guidelines.

• To establish a strain database with information on veterinary pathogens stored across Europe.

• To use strains from the new database for:

1. Development of veterinary clinical breakpoints for improved antimicrobial susceptibility testing.

2. Improving the identification of veterinary pathogens by MALDI-TOF.

3. Initiating collaboration with research groups and companies developing rapid and precise methods for detection and antimicrobial susceptibility testing of veterinary pathogens.

• To identify key knowledge gaps and propose future research to tackle the current challenges of microbiological diagnostics and antimicrobial therapy in veterinary medicine.

• To set a priority list of innovative future research for optimising antimicrobial treatment in animals.

• To outline how European countries can advance to a common high level of veterinary antimicrobial

#### **TECHNICAL ANNEX**



#### stewardship.

• To disseminate knowledge, tools, research results, and the proposed solutions to a broad audience (EU agencies, national policy makers, veterinary organizations, clinical practitioners, general public, etc.) via a common website, scientific papers, conference contributions, newsletters, social media, and a white paper.

#### Capacity Building

• To build a sustainable network of European stakeholders from the fields of veterinary microbiology, clinical pharmacology, epidemiology, clinical practice, and communication collaborating within and across disciplines towards the common goal of veterinary antimicrobial stewardship.

• To facilitate - through investigations, training schools, workshops, and STSMs - an expansion of the currently sparse critical mass of specialists within veterinary microbiology and clinical pharmacology in Europe. This objective is particularly important for ECIs and for countries with limited resources.

• To cooperate with non-European world-leading experts within each scientific field covered, thereby ensuring mutual benefits and the best possible platform for any research and educational activities within the Action.

• To establish cross-sectorial collaboration between stakeholders from academia, industry, stakeholder organisations, and national/international agencies, thereby facilitating broad dissemination and implementation of results, and a network with strong potential to influence political decision-making on veterinary antimicrobial stewardship.



## **TECHNICAL ANNEX**

### 1 S&T EXCELLENCE

#### 1.1 SOUNDNESS OF THE CHALLENGE

#### 1.1.1 DESCRIPTION OF THE STATE-OF-THE-ART

Antimicrobial resistance has been widely recognised as one of the major global health challenges. Specifically for Europe, the ECDC estimates that about 33000 people die each year as a consequence of an infection with antibiotic-resistant bacteria (Cassini et al., 2018). One way to tackle this challenge is through antimicrobial stewardship, which is a broad, multifaceted approach including infection control and various measures to maximise clinical efficacy of antimicrobial agents while minimising the development of antimicrobial resistance (Lloyd & Page, 2018). Antimicrobial stewardship is important in both human and veterinary medicine. As for the latter, it serves a dual purpose of protecting both animal and human health, since at least a minor part of the resistance burden in humans is known to originate from animals (Marshall et al., 2011; Wieler et al., 2011).

The level of antimicrobial stewardship practiced in veterinary medicine is difficult to assess, but antimicrobial sales figures for animals can serve as a crude indicator. The most recent report from the European Surveillance of Veterinary Antimicrobial Consumption (ESVAC) project shows that in 2016 biomass-adjusted sales of antimicrobial agents for food animals varied by up to 156-fold between countries in Europe. The sales patterns of the antimicrobial classes also varied substantially (EMA, 2018). These figures are influenced by several local factors, for example disease prevalence, availability of drugs, benchmarking, and cultural differences. Nevertheless, such a large difference in antimicrobial use between countries invariably suggests that the perception and implementation of veterinary antimicrobial stewardship vary widely across Europe, and that several opportunities exist to improve antimicrobial use practices while having no negative impacts on animal health, animal welfare and agricultural production. **Some of the main factors complicating the implementation of antimicrobial stewardship in veterinary medicine are**:

Lack of experts in veterinary microbiology and clinical pharmacology. There is a shortage of specialists in veterinary antimicrobial stewardship (Guardabassi et al., 2018), especially within the associated disciplines of microbiology and clinical pharmacology. This shortage of critical mass negatively affects the ability to develop and refine diagnostic tests of importance for antimicrobial stewardship, including those mentioned in the following paragraph. Furthermore, it hampers rational and standardised advice to veterinary practitioners about antimicrobial therapy, both *ad hoc* when treating infections, and more in general through development and implementation of antimicrobial stewardship programmes and treatment guidelines. Finally, it has negative consequences on education of veterinary undergraduate students and practitioners as well as more advanced post-graduate training of new specialists within veterinary microbiology and clinical pharmacology.

Lack of rapid and veterinary-adapted microbiological tests. The time between sampling of animals for microbiological culture and a diagnostic answer often takes 3 days or more. This period when test results are unavailable is the critical time for treatment. The lack of rapid microbiological diagnostic tests hampers evidence-based decision-making and results in a greater tendency for veterinarians to practice "defensive medicine" with likely overuse of antimicrobials in general, and higher-tier antimicrobials, specifically. Apart from the time issue, the quality of veterinary microbiological diagnostics is often questionable, partially because they are adapted from human microbiology without rigorous evaluation

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in the different animal species. One example is the widely employed method MALDI-TOF MS (matrixassisted laser desorption ionization time-of-flight mass spectrometry) for bacterial and fungal species identification. The commercially available MALDI-TOF MS systems were developed for use in human diagnostic laboratories. Despite some optimisation, the systems still regularly fail to accurately identify veterinary pathogens, in particular those that are not common or relevant in human medicine. Another example of poor diagnostics is the use of *human* clinical breakpoints (CBPs) to determine antimicrobial susceptibility of *veterinary* pathogens, or alternatively the use of CBPs for animals other than the target animal species. This is a necessary practice during antimicrobial susceptibility testing (AST) due to a relative shortage of animal species-specific CBPs (Toutain et al., 2017). However, this practice has the negative consequence that pathogens may easily be misclassified as resistant or susceptible, as pharmacokinetic drug parameters can vary substantially between humans and animals, and between animal species. Taken together, slow and imprecise diagnostic tools may lead to antimicrobial underand over-treatment, with consequences such as treatment failure and increased selection for antimicrobial resistance.

Limited insight into methodology and standards used by veterinary microbiological laboratories. Veterinary microbiological diagnostics is performed in different settings, including small in-clinic laboratories, university research laboratories, large international private laboratories, and various human microbiology laboratories occasionally processing veterinary specimens. At present, there is no central overview on the use of different methods, interpretive standards, and quality control by such laboratories. Notwithstanding the shortcomings listed in the previous paragraph, the potential lack of adherence to standards could have important consequences for diagnostic quality. This may have a large impact on a European scale, as around 90% of veterinary practitioners in a European survey reported having used culture and AST for guiding their choice of treatment (De Briyne et al., 2013).

Lack of national antimicrobial treatment guidelines and standards for making them. Some generic guidelines for antimicrobial treatment of animals exist, e.g. those developed by the International Society for Companion Animal Infectious Diseases (https://iscaid.org/). These international guidelines are valuable but cannot replace national guidelines, which take into account important local factors such as resistance patterns, availability of drugs, and national legislation. In Europe, national guidelines on responsible antimicrobial use are only available to veterinary prescribers in Scandinavia and a few other countries such as Germany, France, Switzerland, The Netherlands, and the UK. Furthermore, as pointed out by the European Medicines Agency (EMA) and the European Food Safety Authority (EFSA) recently (Murphy et al., 2017), there is no standardised approach for developing antimicrobial treatment guidelines. This means that the rationale and evidence base for treatment recommendations are often unclear, e.g. whether they are based on clinical experience, the critical importance of drugs, pharmacokinetic/pharmacodynamic (PK/PD) properties such as target site concentrations and minimum inhibitory concentration (MIC) data, or an interplay between these factors. These shortcomings are unfavourable, since veterinary treatment guidelines can have a significant impact on antimicrobial usage patterns (Jessen et al., 2017; Ungemach et al., 2006).

Taken together, there is an urgent need for European and international experts to join forces and address these issues, and a need for educating a new generation of specialists to ensure sustainability of new initiatives promoting antimicrobial stewardship in veterinary medicine.

#### 1.1.2 DESCRIPTION OF THE CHALLENGE (MAIN AIM)

The **overall aim of this Action** is to optimise veterinary antimicrobial use with special emphasis on the development of animal- and disease-specific treatment guidelines and refinement of microbiological diagnostic procedures. Combined with diverse educational activities, the Action will contribute to build a larger critical mass of experts in veterinary antimicrobial stewardship throughout Europe, thereby facilitating sustainability of the Action initiatives. Importantly, a white paper will be produced summarising the Action outcomes, proposing a future veterinary-specific European research agenda to close knowledge gaps, and outlining how European countries, through a coordinated effort, can approach a common high level of veterinary antimicrobial stewardship. Widespread dissemination of this white paper and other deliverables, and close interaction with political stakeholders, are expected to promote strong and targeted European goals and initiatives to optimise veterinary antimicrobial use. This would be a valuable addition to the official, but fairly general, European Commission (EC) guideline describing how Member States may develop and implement strategies to promote responsible use of antimicrobial agents in veterinary medicine (EC, 2015).



The Action is relevant and timely due to the increasing antimicrobial resistance levels encountered in both human and veterinary medicine (EFSA, 2018). Moreover, it falls perfectly in line with implementation of several international recommendations and strategies aiming to reduce the antimicrobial resistance problem. Already in 2001, it was agreed in an EU conference report that coordinated multi-disciplinary efforts were needed to tackle the resistance threat, both in the human and veterinary field (Visby Report, 2001). In 2011, the EC published a 5-year action plan to tackle antimicrobial resistance (EC, 2011), and a recent One Health action plan from the EC emphasises the need for cross-sectorial and coordinated actions at several levels to promote rational use of antimicrobials in humans and animals (EC, 2017). Internationally, the World Health Organization (WHO) has developed a Global Action Plan highlighting optimisation of antimicrobial treatment in humans and animals as one of five focus points (WHO, 2015). The World Organisation for Animal Health (OIE) supports this initiative and has launched its own strategy describing several possible ways to rationalise antimicrobial use in the veterinary sector (OIE, 2016).

#### 1.2 PROGRESS BEYOND THE STATE-OF-THE-ART

#### 1.2.1 APPROACH TO THE CHALLENGE AND PROGRESS BEYOND THE STATE-OF-THE-ART

**Overall**, the challenge will be approached by establishing a unique European network of experts and Early Career Investigators (ECIs) within the disciplines of veterinary microbiology, clinical pharmacology, clinical medicine, epidemiology, and communication. These experts and ECIs, representing academia, industry and Specific Organisations, will collaborate with human health scientists towards a common goal of veterinary antimicrobial stewardship. This approach is innovative in itself, as the described tools cannot be realised, disseminated, and implemented properly without a strong European network.

**More specifically**, the Action will advance the state-of-the-art in the following ways:

<u>More European experts in veterinary microbiology and clinical pharmacology.</u> The critical mass of European expertise in these two fields in particular, and more broadly in veterinary antimicrobial stewardship, will expand during the lifetime of the Action through targeted involvement of ECIs in all investigations. ECIs, and other stakeholders within and outside the Action, will also benefit from the planned training schools, workshops, and Short-Term Scientific Missions (STSMs), and from collaboration with human health scientists and established European and international communities specialised in one or more of the disciplines covered by the Action.

<u>Overview of practices used by veterinary microbiological laboratories.</u> The methods and interpretive criteria used by veterinary diagnostic laboratories across Europe for pathogen identification and AST will be mapped and evaluated. The outcome may guide diagnostic laboratories to improve their services per se. It may also inspire interlaboratory trials where the performance of laboratories is evaluated after sending known reference isolates for identification and AST. Finally, it will serve as an invaluable data source for future development of European quality standards for veterinary diagnostic laboratories.

<u>Better microbiological diagnostic tests.</u> the Action will establish the largest European online database of veterinary pathogens stored by Action Participants and collaborators representing academia and industry (e.g. diagnostic laboratories). This database will include information on already established strain collections as well as pathogens collected prospectively based on research needs, and it will serve as a unique toolbox for refinement and innovation of diagnostics in veterinary microbiology. As a proof of concept, the new database will be exploited during the Action for optimisation of the MALDI-TOF MS technique and for development of new animal- and infection-specific CBPs. This will lead to more precise pathogen identification and AST, respectively. Concurrently, the database and associated MIC data, produced during the Action, will be presented to research groups and companies developing novel techniques for rapid and precise detection and AST of veterinary pathogens, with the aim to facilitate their work and initiate new collaborative networks.

<u>New veterinary antimicrobial treatment guidelines.</u> The Action will establish an overview on the availability, structure, and evidence-base of veterinary antimicrobial treatment guidelines in Europe. This knowledge will serve as a basis for the development of a new standard describing minimum requirements for treatment guidelines. The standard will be used to create European animal- and disease-specific treatment guidelines. Ultimately, experts representing the Action will support national stakeholders in adapting European guidelines to national levels.



<u>New veterinary-specific research agenda and roadmap to raise stewardship awareness and implementation across Europe</u>. The Action will highlight knowledge gaps and create a priority list of future research needs for optimising antimicrobial treatment in companion and food animal species. The intention is to help politicians and funding agencies to prioritise resources for future activities on veterinary antimicrobial stewardship. Along with this list will follow a roadmap suggesting how European countries, with the EC as a coordinating stakeholder, can approach a common high level of knowledge and dedication when it comes to implementing veterinary antimicrobial stewardship practices locally.

#### 1.2.2 OBJECTIVES

#### 1.2.2.1 Research Coordination Objectives

#### A. Mapping methodologies and guidelines

- To describe, compare, and review the methodologies and interpretive criteria used by diagnostic laboratories across Europe for identification and AST of veterinary pathogens.
- To map and compare the availability, structure, and evidence-base of veterinary antimicrobial treatment guidelines in Europe.

#### B. Development of new tools

- To establish a strain database with information on veterinary pathogens stored across Europe.
- To create a European standard specifying minimum requirements for development of harmonised and evidence-based veterinary antimicrobial treatment guidelines.

#### C. Exploitation of new tools

- To use strains from the database for:
  - Development of CBPs for improved AST of veterinary pathogens.
  - Improving the identification of veterinary pathogens by MALDI-TOF MS.
  - Initiating collaboration with research groups and companies developing rapid and precise methods for detection and AST of veterinary pathogens.
- To use the standard for developing European animal- and disease-specific treatment guidelines, and supporting the adaption of these into national guidelines.

#### D. Proposing future solutions

- To identify key knowledge gaps that should be addressed to tackle the current challenges of microbiological diagnostics and antimicrobial therapy in veterinary medicine.
- To set a priority list of innovative future research for optimising antimicrobial treatment in animals.
- To outline how European countries can advance towards a common high level of veterinary antimicrobial stewardship.

#### E. Dissemination of Action activities

• To disseminate knowledge, tools, research results, and the proposed solutions to a broad audience (EU agencies, national policy makers, veterinary organizations, clinical practitioners, general public, etc.) via a common website, scientific papers, conference contributions, newsletters, social media, and a white paper.

#### 1.2.2.2 Capacity-building Objectives

- To build a sustainable network of European stakeholders from the fields of veterinary microbiology, clinical pharmacology, epidemiology, clinical practice, and communication collaborating within and across disciplines towards the common goal of veterinary antimicrobial stewardship.
- To facilitate through investigations, training schools, workshops, and STSMs an expansion of the currently sparse critical mass of specialists within veterinary microbiology and clinical pharmacology in Europe. This objective is particularly important for ECIs and for countries with limited resources.



- To cooperate with non-European world-leading experts within each scientific field covered, thereby ensuring mutual benefits and the best possible platform for any research and educational activities within the Action.
- To establish cross-sectorial collaboration between stakeholders from academia, industry, stakeholder organisations, and national/international agencies, thereby facilitating broad dissemination and implementation of results, and a network with strong potential to influence political decision-making on veterinary antimicrobial stewardship.

## 2 NETWORKING EXCELLENCE

#### 2.1 ADDED VALUE OF NETWORKING IN S&T EXCELLENCE

# 2.1.1 ADDED VALUE IN RELATION TO EXISTING EFFORTS AT EUROPEAN AND/OR INTERNATIONAL LEVEL

There are a number of European and international activities on veterinary antimicrobial stewardship within research groups and more broadly under the frame of agencies, communities and specialist colleges. The added benefit of networking in relation to those activities are highlighted in the following:

Stronger platform for external communication. The multidisciplinary and cross-sectorial nature of the Action and its dedicated target of veterinary antimicrobial stewardship is unique in comparison to other communities that are generally rooted in fewer disciplines, or have a broader scope in veterinary science. The large network of Action Participants from different disciplines and sectors working towards a single goal will ensure high quality output and a strong voice for communication of results and opinions.

<u>One Health approach with specialists and end-users from the human and animal health sectors.</u> One Health initiatives, such as conferences, targeting stakeholders from both the human and animal health sectors are often biased towards one or the other, and rarely engage people involved in clinical decision-making and prescribing. This Action includes not only academic specialists but also clinical practitioners representing the end-users of antimicrobial stewardship practices. Furthermore, the Action includes representatives from both the veterinary and human medical sectors, as veterinary initiatives in this area will undoubtedly benefit from the long-standing experience of diagnostic development, stewardship programmes and guideline-making in the human health sector.

<u>Closer contact to political decision makers</u>. Most research on antimicrobial stewardship is disseminated via traditional routes, such as peer-reviewed publications, without active involvement of politicians. The Action will disseminate results in a similar way, but also more broadly with the intention to increase awareness among political decision makers influencing interventions and funding in this field. This is facilitated by the represention of the Federation of Veterinarians of Europe (FVE), an umbrella organisation of veterinary organisations from 38 European countries. FVE is committed to veterinary antimicrobial stewardship and has close contact to political decision-makers influencing this field. This for veterinary antimicrobial stewardship, both at European (EC) and at national level.

<u>Benefits of larger geographical width</u>. The Action will represent different countries and hence it will reach geographically further than most ongoing activities in veterinary antimicrobial stewardship. The network of Action Participants in their home countries will facilitate identification of local stakeholders including contributors of the large pool of data needed for the Action, in particular for the Working Group (WG) 1 surveys and the WG2 strain database (see section 4.1.1.). Furthermore, knowledge of local infrastructure is crucial for national communication and implementation of results.

<u>Better education of PhD students and ECIs</u>. ECIs will be involved in all tasks of the Action and work closely together with established experts, both during investigations and as part of mentor-based careerplanning (see section 3.2.1.). This approach is different from many ongoing educational activities such as specialist colleges where PhD students and ECIs are exposed to a high degree of self-study and exams. Combined with the planned training schools, workshops, and STSMs, this networking and collaboration between experts and ECIs provides the best possible frame for education of new specialists in veterinary antimicrobial stewardship and associated disciplines.

<u>Better internal communication</u>. The Action will have a higher frequency of physical meetings than other international activities on veterinary antimicrobial stewardship. Physical meetings allow for a higher



degree of cooperation, discussion, and networking than is possible via any other means of communication, e.g. Skype meetings or teleconferences.

#### 2.2 ADDED VALUE OF NETWORKING IN IMPACT

#### 2.2.1 SECURING THE CRITICAL MASS AND EXPERTISE

The Action will be represented by experts in all disciplines required to fulfill the objectives listed in section 1.2.2:

- Epidemiologists: important for the cross-European WG1 surveys on microbiological diagnostic procedures and availability of treatment guidelines.
- Microbiologists: important for most activities in WG1, WG2, WG3, and WG4.
- Clinical pharmacologists: important for WG3 on CBPs and for WG4 on treatment guidelines.
- Clinical practitioners: Important for WG1 activities focusing on in-practice microbiological diagnostics, for WG3 when CBPs are determined, and for WG4 on treatment guidelines.
- Communication specialists: Important for dissemination to ensure maximum impact and implementation of the Action outcomes through the most appropriate communication channels.

Despite this broad representation, time will be dedicated during all WG- and Management Committee (MC) meetings for discussing potential needs and recruitment strategies for additional experts and ECIs, e.g. to meet specific or unexpected scientific challenges. One example could be the development of CBPs for an antimicrobial agent to be used against pathogens in sheep. Even though the Action has microbiologists and pharmacologists to establish all relevant PK and PD data, defining CBPs benefits from information about clinical efficacy of drugs in the field situation. For this purpose, it would be relevant to recruit an additional clinical practitioner with expertise in antimicrobial treatment of sheep.

Importantly, WG and MC meetings will also be used to address the involvement of persons from European countries not represented from the beginning, and persons with experience from the human health sector, as these are underrepresented relative to veterinary specialists. The advantages of representation from the human health sector and of a broad geographical representation are elaborated in section 2.1.1. Depending on the role to be filled, additional stakeholders may be enrolled *ad hoc* for specific tasks (e.g. as speakers at workshops), or more permanently as Action Participants.

#### 2.2.2 INVOLVEMENT OF STAKEHOLDERS

Overall, stakeholders working on veterinary antimicrobial stewardship will be invited to participate when their specific expertise is needed or desired. This will bridge the Action with other related efforts in the area, prevent duplication of activities, and create possibilities for synergistic collaboration, e.g. joint training schools, joint investigations, or joint campaigns promoting antimicrobial stewardship. Involvement of more specific stakeholders is elaborated in the next paragraphs.

Most experts that will be involved in the Action will represent academia and will be employed at **universities**. Furthermore, these universities contribute to the Action with ECIs. Vice versa, education of ECIs through Action activities is of benefit to the universities, as ECIs return with an expanded network and increased knowledge of importance for both research and teaching activities. On a more practical front, the Action MC will seek opportunities to use university facilities for meetings, workshops and other activities in order to minimise costs.

From the beginning, stakeholders from **private and public veterinary diagnostic laboratories** will be involved in the Action to facilitate the WG1 survey and the collection of pathogens for the strain database of WG2. Apart from contributing actively, they will help to identify and attract stakeholders from other diagnostic laboratories to ensure the widest possible geographical representation. Stakeholders from the **diagnostics industry** will also be part of the Action from the start. They will take a leading role in optimising pathogen identification methodology once the strain database has been established. They will also be asked to contribute to one or more training schools. Importantly, other European stakeholders developing rapid and precise methods for detection and AST of veterinary pathogens will be identified and introduced to the novel strain database and associated MIC data produced during the Action. The aim of this activity is to initiate new collaborative networks accelerating diagnostic development within veterinary microbiology through further exploitation of the strain database.



**EC members** and representatives of **Specific Organisations** with international strategies for veterinary antimicrobial stewardship will be invited to participate in an advisory board for the Action. Getting regular advice and sharing ideas with these stakeholders will function as inspiration and quality control for Action activities. Furthermore, the final white paper with recommendations for future research and for implementation of veterinary antimicrobial stewardship across Europe, will likely have a higher political impact if developed in some sort of cooperation with EC members.

**National veterinary organisations** will be identified with the help of FVE and contacted when assistance is needed, e.g. for provision of national treatment guidelines on veterinary antimicrobial use. They will also be involved when communicating results at national level, as they can (i) help identify the most appropriate local communication channels, and (ii) officially support recommendations by the Action, thereby maximising local recognition and impact. In that regard, results and recommendations of the Action will be presented to and discussed with **national politicians** influencing local politics on veterinary antimicrobial stewardship.

# 2.2.3 MUTUAL BENEFITS OF THE INVOLVEMENT OF SECONDARY PROPOSERS FROM NEAR NEIGHBOUR OR INTERNATIONAL PARTNER COUNTRIES OR INTERNATIONAL ORGANISATIONS

Reaching beyond Europe is a priority of the Action as veterinary antimicrobial stewardship is of global interest. The mutual benefits from collaborating with partners outside Europe are highlighted in the following:

- Two Near Neighbour Country (NNC) Institutions are included, namely Institut Agronomique et Vétérinaire Hassan II (Morocco) represented by Nassik Saadia who is an expert in antimicrobial resistance, and Lebanese University (Lebanon) represented by Dalia Khachman who is an expert in veterinary pharmacology. Apart from their expertises, the Action will benefit from a larger network facilitating access to local diagnostic laboratories and strain collections. This will be of value to the Action, as pathogens may easily cross borders and very little is known about veterinary pathogens, their resistance, diagnostic microbiology practices, and antimicrobial stewardship programmes in countries near Europe. This collaboration will also be of benefit to NNC participants who will learn and be inspired from participation in the WG tasks, and from the educational activities of the Action.
- Two International Partner Country (IPC) Institutions are included, namely University of Adelaide (Australia) represented by John Turnidge who is an expert in pharmacology and antimicrobial stewardship in human medicine, and University of Guelph (Canada) represented by Scott Weese who is in the board of ISCAID (see next paragraph) and an expert in veterinary microbiology, infectious diseases, and antimicrobial stewardship. Both are world-leading experts within their respective fields and will thus contribute significantly to the Action with their knowledge and experience from the human and veterinary fields. Meanwhile, they will benefit from an increased network, and they may transfer the tools and other outcomes of the Action into local stewardship programmes.

**ISCAID** is a Specific Organisation supporting and developing initiatives to improve diagnostics and treatment of infections in companion animals. A key activity of ISCAID is to involve world-leading researchers in the production of international antimicrobial treatment guidelines. Therefore, the Action will benefit tremendously from the expertise and experience within ISCAID when working on such guidelines. Meanwhile, ISCAID will benefit from, and help with the dissemination of, the knowledge created in the Action, both concerning diagnostics and treatment guidelines. **FVE** is another Specific Organisation. The benefits of having FVE represented in the Action are described in section 2.1.1., namely close contact to national veterinary organisations and political decision makers that may help promote and implement Action activities. Since promotion of antimicrobial stewardship is a key activity of FVE, this organisation will also benefit from collaborating with the Action.



## 3 IMPACT

# 3.1 IMPACT TO SCIENCE, SOCIETY AND COMPETITIVENESS, AND POTENTIAL FOR INNOVATION/BREAK-THROUGHS

# 3.1.1 SCIENTIFIC, TECHNOLOGICAL, AND/OR SOCIOECONOMIC IMPACTS (INCLUDING POTENTIAL INNOVATIONS AND/OR BREAKTHROUGHS)

<u>Short-term impacts.</u> The Action will maintain current international focus on veterinary antimicrobial stewardship by engaging a broad range of stakeholders in the subject and by turning *words* of the many political visions and strategies (section 1.1.2) into real-life *activities*. This focus is important to ensure future funding options and a general interest in the topic by stakeholders ranging from politicians to scientists and veterinary practitioners.

The tools developed during the Action will be used immediately: (i) the European strain database created by WG2 from stored and prospectively collected veterinary pathogens will be used for improving MALDI-TOF MS pathogen identification and for the development of new CBPs, as described in section 4.1.1 Such updated interpretive criteria can be readily implemented in laboratories and contribute to more precise diagnostics; (ii) the new European animal- and disease-specific treatment guidelines developed during the Action can be readily used by veterinary practitioners. Together, the tools developed during this Action will therefore have a short-term impact contributing to antimicrobial stewardship.

Long-term impacts. The strain database should be further exploited for optimising veterinary microbiological diagnostics. This includes refinement of existing methods but also development of new methodology. In order to speed up such innovation, one of the tasks of WG2 is to present the strain database, and associated MIC data, to academia- and industry-based research groups developing novel microbiological diagnostic methods, e.g. using whole genome sequence-based technology, flow cytometry, or selective agar plates. Such active search for collaborators will increase the chances of improving future quality and speed of diagnostics through innovation. In addition to optimising microbiological diagnostics, the new strain database may be used for several other purposes, e.g. surveillance of clonal types spreading across Europe, and evaluating the spectrum of activity of novel antimicrobial agents.

The new standard for evidence-based treatment guidelines, the new European animal- and diseasespecific treatment guidelines, and the overall increased European expertise in veterinary antimicrobial stewardship will drive the development and refinement of national treatment guidelines. In some countries, this process is expected to start during the Action with assistance from Action Participants. In other countries, it may take a while before political will and national funding accelerate this process. More in general, the increased critical mass of expertise in veterinary microbiology and clinical pharmacology will strengthen the quality of research and teaching in these disciplines, especially in participating countries where these fields are currently small and/or down-prioritised.

The white paper summarising results, highlighting knowledge gaps, and providing ideas for future research and a roadmap to advance veterinary antimicrobial stewardship in Europe, will support the EC and national policy makers in prioritising future initiatives within this field. This is expected to impact funding opportunities and thereby the possibility to impact further veterinary antimicrobial stewardship through research.

Taken together, it is without a doubt that these initiatives - individually and collectively - will have an impact optimising veterinary antimicrobial usage in Europe. The extent of this and the timeline are however difficult to predict, since future trends of antimicrobial usage are also influenced by several other factors, such as availability and price of drugs.

<u>Innovative aspects.</u> The main innovative aspect of the Action is the cross-sectorial and interdisciplinary networking approach to optimise veterinary antimicrobial use through new tools. Individually, these tools may not be considered as technological breakthroughs, but the potential for them to collectively advance veterinary antimicrobial stewardship in different ways is immense. For example, the European strain database will be a gold mine for several purposes, including innovation of novel technology for pathogen identification and AST. As mentioned above, the Action will facilitate such innovation through active promotion of the database and search for research collaborators in academia and industry.



#### 3.2 MEASURES TO MAXIMISE IMPACT

#### 3.2.1 KNOWLEDGE CREATION, TRANSFER OF KNOWLEDGE AND CAREER DEVELOPMENT

<u>Knowledge creation</u>. The composition of the Action with participants from several different disciplines, sectors and countries provides a unique opportunity to plan and perform research that would otherwise be cumbersome or impossible to conduct. For example, the planned WG1 survey on availability, evidence base, and structure of antimicrobial treatment guidelines in Europe benefits from the joint expertise of epidemiologists, microbiologists, clinical pharmacologists, and veterinary practitioners. Presence of Action Participants from across Europe, and access to national veterinary organisations through FVE facilitate dissemination of the survey to relevant stakeholders in many countries. This gives the possibility to obtain more broadly representative data on available guidelines than otherwise possible. All other tasks described are also designed to benefit maximally from the large network of the Action. Most of the knowledge created will be readily applicable by veterinarians, diagnostic laboratories and policy makers, but - as mentioned in section 3.1.1 - there will also be long-term impacts and the potential for more basic research during and after the Action, e.g. rooting from the opportunities of the new strain database.

Knowledge transfer. A very important goal of the Action is to expand the critical mass on veterinary antimicrobial stewardship in Europe. Both existing knowledge of the participants and new knowledge generated during the Action should therefore be transferred as broadly as possible. This is possible through the planned investigations, training schools, workshops, and STSMs, all of which are described in section 4.1.1. Importantly, the Action remains open to new participants, and a strategy for recruiting persons (especially ECIs), who may both contribute to and benefit from the Action, will be made by the MC and individual WGs from the beginning. Furthermore, knowledge created during the Action will be transferred broadly through the dissemination channels described in section 3.2.2.

<u>Career development.</u> The Action will promote career development of ECIs in different ways. First, ECIs will be encouraged to participate in all activities together with more established experts. This close interaction will automatically strengthen the network of ECIs, and thereby create opportunities for future collaboration and jobs. Secondly, each ECI could be affiliated to a mentor from the Action outside his/her home institution. The role of these "Action mentors" will be to assist ECIs with career planning. Third, whenever possible for each WG, an ECI Vice-Leader will be appointed. These ECIs that should have some experience in the WG discipline, would benefit from increased leadership experience.

## 3.2.2 PLAN FOR DISSEMINATION AND/OR EXPLOITATION AND DIALOGUE WITH THE GENERAL PUBLIC OR POLICY

Dissemination of results will be coordinated by WG5, a group that could be composed by communication specialists, a member of the MC, and representatives from the other four WGs. Having a WG dedicated to this task ensures that all Action results are discussed centrally with the aim to help identify the most appropriate communication channels and reach the highest possible impact. Another advantage is that WG5 members will get a good overview of Action activities, which will equip them as a central organ for regular external communication of Action activities, for example via newsletters. Finally, keeping track of results will facilitate the WG5 work towards the final white paper (see section 4.1.1.). The following channels will be used for external dissemination and communication:

- <u>International peer-reviewed scientific journals</u>: This platform will be used to communicate deliverables such as surveys, standards, and guidelines, as well as opinions and reviews on subjects pertaining to veterinary antimicrobial stewardship. Importantly, articles should preferably be open-access to ensure broad dissemination and uptake of results by stakeholders ranging from policy makers to veterinary practitioners.
- <u>National scientific communication fora (e.g. local veterinary journals)</u>: Synopses of planned or ongoing activities and results will be prepared by WG5, and later translated and disseminated nationally by local Action Participants. This will be done to ensure that the Action is broadly known by national stakeholders and to recruit new Action Participants with an interest and/or expertise in veterinary antimicrobial stewardship. It is also a way to promote deliverables that may be exploited or implemented nationally, such as the WG4 standard for making antimicrobial treatment guidelines.</u>



- <u>Action website:</u> A dedicated website will be developed for communication of ongoing activities of the Action, publications, conference contributions, minutes of meetings, etc. The website will also have links to other relevant sites on antimicrobial stewardship, and educational sections could be added explaining principles of antimicrobial stewardship to the general public and to veterinarians, respectively. The ambition is to make it the "go-to website" for anyone seeking information on veterinary antimicrobial stewardship.
- <u>Conferences:</u> Results will be disseminated at relevant conferences, and a final Action conference will be arranged at the end of the Action.

Communication to - and potentially a dialogue with – the **general public** will be made in local languages through national veterinary organisations using their preferred communication channels, which may include press releases and social media such as Facebook. The strategy to communicate via national veterinary organisations is deliberate, as the Action has direct access to them via FVE. Furthermore, these organisations are recognised nationally and therefore more likely to impact the general public, including local veterinarians, than English messages sent centrally from the Action. Results of the Action could be combined with more general information on antimicrobial stewardship. This will provide the general public with essential basic knowledge on stewardship and provide a better basis for people to understand results of the Action.

In addition to external communication, WGs must provide annual status reports for internal evaluation by the MC. These reports should describe progress in relation to the time plan, plans for dealing with deviations, and plans for exploitation of results. The MC will discuss these reports with the WGs in order to achieve successfully all objectives of the Action.

**Exploitation of results** is outlined in section 4.1.1. for each WG, e.g. how the strain database of WG2 will be exploited for CBP determination, and for optimisation of MALDI-TOF MS. The potential for further use of the database is also introduced below and in section 3.1.1. However, final decisions on which bacteria to prioritise and which collaboration to pursue will be made during the course of the Action once it becomes clear which strains are available, what are the data gaps that are most urgent to investigate, and how strains may be exchanged between laboratories. As for the latter, rules for exchange and use of strains from the database need to be agreed upon.

### 4 IMPLEMENTATION

#### 4.1 COHERENCE AND EFFECTIVENESS OF THE WORK PLAN

#### 4.1.1 DESCRIPTION OF WORKING GROUPS, TASKS AND ACTIVITIES

A rough overview of Action activities and outcomes is provided in the PERT chart below. The objectives, tasks, and deliverables of the five WGs are described in more detail in the following text. When possible, WGs 2-4 should prioritise their tasks towards clinically important diseases and pathogens accounting for a relatively high fraction of antimicrobial use in food and companion animals, respectively. Focusing on high-use areas will maximise impact of these WGs on veterinary antimicrobial stewardship.





**WG1 (mapping microbiological diagnostics and treatment guidelines)**. The <u>first objective</u> of WG1 is to map and compare the practices and interpretive criteria used by diagnostic laboratories across Europe for isolation, identification and AST of veterinary pathogens. For this purpose, WG1 will design and submit an online questionnaire to diagnostic laboratories. Results from the survey, and from interviews with microbiologists in veterinary diagnostic laboratories conducted during STSMs, will then be used to assess microbiological practices broken down by country and type of laboratory. The <u>second objective</u> is to map and compare the availability, structure, and evidence base of veterinary antimicrobial treatment guidelines in Europe. This will be done in close collaboration with authors and distributors of guidelines, including national veterinary organisations. Generic guidelines, such as those available from ISCAID, and national guidelines from countries outside Europe will also be included in the evaluation for comparison and inspiration.

WG2 (European strain database). The first objective of WG2 is to establish a database with information on veterinary pathogens stored across Europe. Initially, WG2 will develop material and data transfer agreements (MTA/DTA) as well as a consortium agreement (CA) in which the ownership of background and foreground data is agreed upon. Concurrently, and in collaboration with WG3, a strategy will be made for prioritisation of animal pathogens. Apart from those representing important diseases and accounting for high antimicrobial use in companion and food animals, pathogens that are traditionally difficult to speciate (e.g. non-fermentative Gram-negative bacteria), completely unidentified pathogens, and pathogens for which animal-specific CBPs are lacking, could be included. Afterwards, Action Participants and diagnostic laboratories contributing to WG1 will collect target pathogens prospectively. These, and pathogens from existing European strain collections, will be kept in their original place, but information about their origin, year of isolation, method of identification, etc. will be added to the database. Later work on database isolates would also benefit from strain collections outside Europe, hence these will also be included when available from the involved NNC and IPC Institutions, and more generally through the international network of Action Participants. The second objective of WG2 is to use selected pathogens from the database for refining their identification by MALDI-TOF MS, and for determining epidemiological cut-off values (ECOFFs) based on existing MIC data and MICs produced during the Action as part of ongoing projects or STSMs. ECOFFs will subsequently be used by WG3 for development of CBPs. Furthermore, WG2 participants will actively identify and contact academia- and industry-based research groups developing alternative, precise, and rapid microbiological diagnostic methods (e.g. using flow cytometry, sequence-based methods, or selective growth media), with the purpose to initiate collaboration, share the strain collection and associated MIC data, and ultimately accelerate development of such novel methodologies.



**WG3 (clinical breakpoints)**. The <u>first objective</u> of WG3 is to make a priority list of animal- and infectionspecific CBPs that are currently lacking for veterinary pathogens. Prioritisation will be based on factors such as clinical importance and contribution of infectious diseases to overall antibiotic consumption. For example, it would be relevant to focus on tetracycline against porcine pathogens, as this drug is one the most frequently used antimicrobials in pig production. The <u>second objective</u> is to retrieve data for establishing prioritised CBPs: WG2 will be the main contributor of PD data in the form of ECOFFs, whereas PK data are expected to pose a bigger challenge. WG3 will therefore use different approaches to obtain these data, namely by (i) literature searches, (ii) requests to pharmaceutical industry and academic collaborators, and (iii) active production of data as part of ongoing *in vivo* studies. Finally, as the <u>third objective</u>, WG3 will perform mathematical modelling on collected PK and PD data, and incorporate available clinical efficacy data for creation of veterinary-specific CBPs.

**WG4 (antimicrobial treatment guidelines)**. The <u>first objective</u> of WG4 is to make the world's first standard for development of veterinary antimicrobial treatment guidelines. This standard will highlight prerequisites for making guidelines, e.g. which evidence base is needed for treatment recommendations. Action Participants representing veterinary microbiology, clinical practice, and clinical pharmacology will use their expertise and inspiration from current human standards for this task. The <u>second objective</u> is to use this new standard for making European animal- and disease-specific treatment guidelines for selected infections that are considered treatment challenges by veterinary practitioners, and which account for a relatively high fraction of antimicrobial consumption in companion animals (e.g. canine skin infection) and/or food animals (e.g. porcine enteritis). Finally, as the <u>third objective</u>, WG4 will assist countries represented in the Action with adaptation and implementation of the European guidelines into national guidelines by taking into account local factors such as prevalence of infections/pathogens, prevalence of resistance, and availability of drugs.

**WG5 (dissemination)**. The <u>first objective</u> of WG5 is to coordinate and promote dissemination activities of the Action. This includes the communication channels outlined in section 3.2.2, e.g. the Action website. A <u>second objective</u> of WG5 is to produce – in collaboration with other WGs - a white paper (i) summarising the outcome of the Action, (ii) highlighting knowledge gaps compromising microbiological diagnostics and antimicrobial therapy in veterinary medicine, and (iii) proposing a new European veterinary research agenda to address these knowledge gaps. In addition, the white paper should (iv) include a roadmap outlining how European countries – through a coordinated interaction with the EC as a central player – can approach a common high level of knowledge and dedication when it comes to implementing veterinary antimicrobial stewardship practices locally. The white paper will be discussed at the final Action conference. Subsequently, it will be distributed along with minutes of discussions at the Action conference to stakeholders, including politicians from relevant ministries in European nations and in the EC.

#### In addition to the WGs, the Action will includes several networking activities as outlined below:

**Training Schools**. Potential topics of training schools include antimicrobial stewardship, development of diagnostic tools, and PK/PD concepts, Training schools will be open to all Action Participants with a focus on attracting ECIs. European stakeholders from outside the Action will also be invited when possible. One priority is to teach across disciplines and sectors. For example, microbiology practices should be taught not only to microbiologists but also to clinical practitioners, clinical pharmacologists, and epidemiologists who are less familiar with this topic. This will facilitate better collaboration and a common understanding across WGs.

**Workshops**. Workshops (WS) will be planned for in-depth discussions of central issues pertaining to the Action, e.g. prior to starting up new activities, or if unforeseen problems arise requiring intervention.

**Short-Term Scientific Missions**. STSMs will be planned *ad hoc* to solve tasks of the Action and to ensure exchange of knowledge. As for the latter, one example could be STSM candidates visiting veterinary diagnostic laboratories to learn microbiology routines and standards.

**Final Action Conference**: European and international stakeholders with an interest in veterinary antimicrobial stewardship, and politicians of the EC and national governments, will be invited to a final Action conference. At the conference, results of the Action network will be presented, and the Action white paper will be discussed.



#### 4.1.2 DESCRIPTION OF DELIVERABLES AND TIMEFRAME

Action deliverables and their timeframes are outlined below. Care has been taken to allow the required time for each deliverable.

Deliverable	Month	WG	Description
D1	3	1-5	Action website online
D2	15	3	Report with a priority list of CBPs, and strategy for obtaining required data
D3	15	4	Published standard for making antimicrobial treatment guidelines
D4	21	2	Strain database ready
D5	27	1	Publication assessing the microbiological practices in diagnostic laboratories across Europe and relating those to the respective gold standard methodologies
D6	27	1	Publication on the availability and quality of veterinary treatment guidelines across Europe
D7	39	2	Report describing new MALDI-TOF MS interpretive criteria for ≥ 20 veterinary pathogens
D8	39	2	ECOFFs published for ≥ 5 drug/pathogen combinations
D9	39	4	Publication of ≥ 2 European animal- and infection-specific treatment guidelines
D10	47	3	New CBPs published for $\geq$ 3 drug/pathogen combinations
D11	47	1-5	White paper

#### 4.1.3 RISK ANALYSIS AND CONTINGENCY PLANS

The main anticipated risks associated with the Action and contingencies are listed in the following.

<u>Risk 1 (medium): Lack of time among participants to complete tasks.</u> Several meetings and ambitious tasks are planned, and the Action therefore relies heavily on the dedication of the participants. Despite the undeniable commitment of the Action members, it will be difficult for everyone to participate in all scheduled activities due to a heavy workload. In order to meet this challenge, each Action member must appoint a local colleague from their own discipline as a stand-in when unable to attend meetings or participate in other tasks. When possible, such a colleague should be a PhD student or an ECI. Additional ECIs will add to the work force of the Action while benefitting from an expanded network and derived publications. Ultimately, this strategy contributes to the objective of increasing European critical mass within veterinary antimicrobial stewardship.

<u>Risk 2 (low/medium): Lack of funding to complete tasks.</u> The lack of funding for COST Action research could imply a risk, e.g. for establishment and maintenance of the strain database. The aim is therefore to identify other sources of funding to support the database. If this is not possible, the Action members will discuss the possibility to share expenses for this purpose. As for the other tasks, different measures have been thought of to meet financial challenges, including that projects overlap with running projects and/or are partially funded from the beginning. Another point is that most tasks require primarily manpower with little or no funding needed for consumables. This includes the WG1 surveys, the WG3 mathematical modelling of PK/PD data, the WG4 development of treatment guidelines, and the WG5 activities including preparation of the white paper. Although it can be difficult to find time for these tasks, the above-mentioned strategy of involving local colleagues should meet this challenge.

<u>Risk 3 (low/medium): Slow or absent implementation of Action outcomes locally.</u> Many countries are expected to be involved in the Action, and ultimately the hope is that all of them will contribute to, and benefit from, the Action activities. However, it will be difficult to ensure this completely, especially in



countries with a shortage of critical mass and a limited tradition for veterinary antimicrobial stewardship. It is to be expected that the Action itself over 4 years cannot lift all countries to a common high standard, but likely even countries with less resources will gain increased focus on the topic. This would give the incentment to start up initiatives like creating national treatment guidelines or implementing new diagnostic methods or CBPs locally. In order to pursue this process, the Action aims for sustainaibility of its initiatives. This is embedded in the intention of the final white paper as described for WG5.

#### 4.1.4 GANTT DIAGRAM

The diagram below illustrates in colour the time and frequency allocated for each activity, except for training schools, workshops and STSMs, which will be planned *ad hoc*.

Activities	Year 1			Year 2				Year 3				Year 4				
	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4
Meetings																
CG* meetings																
MC meetings																
WG meetings																
Action conference																
WG1																
Mapping practices in veterinary diagnostic laboratories																
Mapping veterinary antimicrobial treatment guidelines																
WG2																
Establishing strain database																
Making new MALDI-TOF MS interpretive criteria																
ECOFF determination																
WG3																
Making CBP priority list and strategy for getting required data																
Creating CBPs																
WG4																
Making standard for treatment guidelines																
Making European treatment guidelines																
Assisting participants in making national guidelines																
WG5																
Developing and updating Action website																
Action whitepaper																

\* A Core Group (CG) will meet every 3 months via teleconferences for targeted micro-management of ongoing activities.



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