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STRATEGY REPORT

THIRD CYCLE

CALLISTO

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CALLISTO

CALLISTO PROJECT: EXECUTIVE SUMMARY

This document is the final report of the EU Framework 7-funded project entitled CALLISTO (Companion Animal multisectoriaL interprofessionaL and interdisciplinary Strategic Think tank On zoonoses), which has investigated zoonotic infectious diseases transmitted between companion animals and man and food producing animals.

The work of the CALLISTO consortium was structured as seven Expert Advisory Groups (EAGs) working within five project work packages over three cycles of one year each (2012 – 2014).

The stated objectives of the CALLISTO Project, and the cycles during which they were addressed, were:

1. To develop a detailed overview of the role of companion animals as a source of infectious diseases for man and food animals, including available information on disease incidence and geographical distribution in these host categories (cycle 1).
2. To identify knowledge and technology gaps in the management of the most important zoonoses transmitted by companion animals (cycle 2).
3. To propose targeted actions that contribute to reducing the risk for infectious disease outbreaks in man and food animals associated with keeping companion animals (cycle 3).
4. To disseminate the results of CALLISTO to relevant stakeholders to contribute to the uptake of the CALLISTO-proposed actions and to promote risk-awareness in healthy and balanced human/animal relationships (cycles 1 – 3).

WHAT IS A COMPANION ANIMAL?

Companion animals are any domesticated, domestic-bred or wild-caught animals, permanently living in a community and kept by people for company, enjoyment, work (e.g. support for blind or deaf people, police or military dogs) or psychological support – including, but not limited to dogs, cats, horses, rabbits, ferrets, guinea pigs, reptiles, birds and ornamental fish.

WHAT ARE THE DEMOGRAPHICS OF COMPANION ANIMAL OWNERSHIP IN THE EU?

CALLISTO has gathered available data on the very large and growing number of companion animals estimated to be kept within EU countries and the economic contribution made by the associated industry (e.g. breeding, sales, pet food, insurance, pharmaceutical and veterinary support). There are an estimated 66 million cats, 61 million dogs, 39 million ornamental birds, 6 million horses and 9 million aquaria in the EU and the estimated annual spend on petcare products alone is € 25.7 billion. It is also recognized that there are great challenges to obtaining accurate data of this type, particularly for other exotic animal species being kept and certain regions of Europe.

WHAT ARE THE SOCIETAL BENEFITS OF COMPANION ANIMAL OWNERSHIP?

Companion animals make crucial contributions to human society. In addition to working roles (e.g. dogs for visually or hearing impaired people), some companion animals afford profound benefits in areas as diverse as human health and childhood development. The positive influence of owning a companion animal has further benefit by reducing human healthcare spending.

WHAT IS RESPONSIBLE PET OWNERSHIP?

CALLISTO recognizes that the societal benefits of keeping pets comes with accepting responsibility for the health and welfare of these animals. Acceptance and promotion of the concept of responsible pet ownership (RPO) is required in order to reduce the risks of transmission of zoonoses from companion animals to man or production animals.

CALLISTO recommends adoption of the following definition of RPO: *Responsible Pet Ownership (RPO) is a duty of care based on the principle that animals are sentient beings having intrinsic value, are dependent on humans for their health and welfare, and are part of the ecosystem. RPO aims to maintain a good level of animal health and welfare, to maximize physical and psychological benefits to humans and to minimize the potential risk that pets may pose to the public, other animals, or the environment. This duty starts with responsible acquisition and continues with providing appropriate care and protection for pets and their offspring.*

WHAT ARE THE CHALLENGES RELATED TO COMPANION ANIMAL ZOONOSES?

Despite these unquestionable benefits, there are risks that human owners may contract zoonotic infectious diseases directly or indirectly from companion animal species. Moreover, as traditional livestock species now increasingly serve a role as companions, there are disease transmission risks from these animals to farmed animals of the same species. An increase in the keeping of exotic and wild animals as companion animals also presents a potential novel risk as sixty percent of emerging infectious diseases are zoonotic with over 70% of those originating in wildlife, presenting an increasing and significant threat to global health.

Currently within Europe there is little coordination between the numerous groups that represent the interests of pet owners, farmers or the horse-owning community. The general public has little understanding or concern about zoonotic infectious disease.

With few exceptions (e.g. canine rabies virus infection) there is little serious attempt to monitor the prevalence, emergence or re-emergence

of zoonotic pathogens arising from companion animal species (i.e. infectious disease surveillance) and this is generally limited to more traditionally kept companion animals (e.g. dogs and cats) With the exception of the EU Pet Travel scheme (again focussed on canine rabies) there is little legislative awareness of the scale or significance of companion animal zoonoses.

The monitoring and control of companion animal zoonoses is a prime example of where a 'One Health' (joint human and veterinary medical and public health) approach is essential.

WHAT ARE THE MAJOR COMPANION ANIMAL ZOONOSES?

CALLISTO has thoroughly reviewed the spectrum of companion animal zoonoses and identified 15 'paradigmatic' diseases that formed the basis for more detailed risk analyses related to those diseases and their spread between companion animals, man and farmed animals. The 15 paradigmatic diseases are listed in Table 1.

Of the 15 CALLISTO paradigmatic diseases, seven are currently notifiable to OIE; nine are notifiable to ECDC and three to both OIE and ECDC. Two paradigmatic diseases are not notifiable to ECDC or OIE (those caused by Toxocara canis/cati and Bartonella henselae).

Campylobacteriosis and salmonellosis were the most commonly reported zoonosis with 220,209 and 95,548 confirmed human cases, respectively, but the role of companion animals in the transmission of these pathogens to food-producing animals and people is not clear and needs further investigation. Most of the 15 paradigmatic pathogens are linked to the more commonly kept companion animal species of cats and dogs. Only eight of the pathogens are also relevant to other species.

Table 1
CALLISTO Paradigmatic Pathogens

VIRAL PATHOGENS
Crimean-Congo haemorrhagic fever virus
West-Nile virus
Foot-and-mouth disease virus (non-zoonotic)
Rabies virus
Bluetongue virus (non-zoonotic)
PARASITIC PATHOGENS
Echinococcus granulosus sensu lato
Leishmania infantum
Toxoplasma gondii
Giardia species
Toxocara canis/cati
BACTERIAL PATHOGENS
Campylobacter jejuni
Leptospira interrogans sensu lato
Salmonella enterica
Bartonella henselae
Extended Spectrum Beta-Lactamase (ESBL) producing organisms
BITE WOUND INFECTIONS
Bite wound infections are included in the priority list.

WHAT ARE THE CALLISTO PARADIGMATIC VIRUS INFECTIONS?

The viral pathogens that were ranked most important for human health risk were rabies virus, Crimean-Congo haemorrhagic fever virus (CCHFV), cowpox virus, hantavirus and lymphocytic choriomeningitis virus (LCMV). The human case fatality rates of these viral infections range from very low (cowpox) to nearly 100% (rabies). However, prompt postexposure prophylaxis will almost always prevent disease from rabies.

Route of transmission, companion animals involved and occurrence in Europe differ between these viruses. Rabies virus is transmitted mainly by the bites of infected carnivores. The main reservoir in Europe is the red fox, but domestic dogs and cats are the primary source of human infections. Although rabies in foxes is largely under control in Europe through oral vaccination, recent reports of rabid foxes in southern Europe highlight the risk of re-emergence of rabies in Europe.

CCHFV is transmitted to humans by infected ticks, mainly of the genus Hyalomma. CCHFV may infect many different species of wild and domestic birds and mammals, including domestic dogs. CCHFV is not present in most of western Europe; however, it is considered as emerging based on its occurrence in 2002 in Turkey with an increasing number of cases thereafter, specific foci in the Balkan region, and the detection of the virus in ticks in Spain. Importation of CCHFV-infected animals is a potential route of introduction into CCHFV-free countries.

Cowpox virus, hantavirus and LCMV are transmitted to humans by contact with infected animals, or contact/inhalation of infected faeces/urine. Wild rodents, including house mice and voles, are commonly infected, and act as the main source of human infection in Europe. Companion animals (e.g. domestic cats, hamsters, guinea pigs and pet rats) may become infected by wild rodents, putting their owners at risk.

The viral pathogens that were ranked most important for livestock production risk were bluetongue virus, African swine fever virus, foot-and-mouth disease virus and influenza virus. The livestock in large parts of Europe are currently free of these important pathogens and incursion would have major impacts on the livestock industry and international trade. For these viruses, ruminants, pigs and poultry kept as companion animals may be relevant. The main concern regarding companion animals is introduction into countries that are currently free of these viruses, either by importation of infected animals kept as pets or feeding of infected food waste to pet pigs. Rabies virus was

also considered important for livestock production, because it infects a variety of domestic animals, including cattle, sheep and goats.

The viral pathogens that were ranked most important for fish production risk were cyprinid herpesvirus-3 (Koi herpesvirus), viral haemorrhagic septicaemia virus, infectious pancreatic necrosis virus, spring viraemia of carp virus and grass carp haemorrhagic virus. These viruses are transmitted mainly through water and typically occur in multiple fresh water and marine fish species, although cyprinid herpesvirus-3 and grass carp haemorrhagic virus appear restricted to carp species. The main concern is that these viruses can cause epidemics with high mortality in both farmed fish and wild fish populations. There is little to no information on the prevalence of these viruses in ornamental fish, which therefore form a potential weak spot in control measures against these viruses.

WHAT ARE THE CALLISTO PARADIGMATIC BACTERIAL INFECTIONS?

The bacterial pathogens that received the overall highest score for human health risks were *Campylobacter jejuni, Leptospira interrogans, Salmonella enterica, Bartonella henselae, Chlamydophila psittaci* and *Escherichia coli* producing extended spectrum beta-lactamase (ESBL). The diseases associated with these six selected zoonotic pathogens are all endemic in EU Member States and have been associated with specific companion animal species. Dogs and cats appear to be the main companion animal sources of campylobacteriosis; *B. henselae* infection (e.g. cat scratch disease) has been traditionally associated with cats, although dogs have recently been recognized as reservoirs of other *Bartonella* species of zoonotic potential; exotic companion animals, such as reptiles and birds are the main sources of salmonellosis and psittacosis, respectively; in theory any animal species may be considered as a potential reservoir of ESBL-producing E. coli, but among companion animals the main zoonotic risks are likely associated with dogs, cats and horses, as a consequence of the widespread use of antibiotics, especially broad-spectrum antibiotics, in these domestic animals. Dogs and possibly rats are the main reservoir of leptospirosis among companion animals, but their role in transmission of leptospirosis is unclear. Although evidence of dog-to-human transmission has only once been reported in the scientific literature, leptospirosis was included in the list of priority diseases because of the high impact of this disease on human health as well as of the lack of studies analysing

the risk factors for human infections, which makes it difficult to assess the risk of zoonotic transmission from dogs.

With the exception of *B. henselae* and *C. psittaci*, the same pathogens were also ranked as the most relevant in relation to possible economic impact on animal production. The ranking was slightly different since S. enterica was scored as the most important pathogen in this context, followed by *C. jejuni, L. interrogans*, meticillin-resistant *Staphylococcus aureus* (MRSA) and ESBL-producing *E. coli*. Based on the current knowledge, the role played by companion animals in transmission of these pathogens to food animals appears to be limited to Salmonella and Campylobacter.

Bite wound infections were included in the list of priority diseases due to their relatively high incidence and possible serious consequences for human health. However, these infections were not included in the risk assessment since they are not associated with a specific pathogen.

WHAT ARE THE CALLISTO PARADIGMATIC PARASITIC INFECTIONS?

The parasitic pathogens that were ranked as having the overall highest score for human health risks were *Echinococcus granulosus* sensu lato, *Leishmania infantum, Toxoplasma gondii, Echinococcus multilocularis* and *Giardia* genotypes. With the exception of *L. infantum*, humans are infected with these pathogens by the oral route, frequently by exposure to infected faeces, food, soil or water. *Leishmania infantum* is a vector-borne pathogen transmitted by the bite of female sand flies. The five diseases associated with these zoonotic pathogens are endemic in EU Member States, with variable prevalence rates in different regions. Leishmaniosis is endemic in Southern Europe where vector sand flies are abundant, while *E. multilocularis* infection causing alveolar echinococcosis is more prevalent in central, eastern and northern Europe. *Echinococcus granulosus* sensu lato and *L. infantum* are associated with dogs as the main reservoir, while *E. multilocularis* is associated with foxes, but may also be transmitted by domestic dogs. *Toxoplasma gondii* is excreted in cat faeces and can be transmitted by ingestion of felid faecal material, but is also frequently transmitted by eating contaminated meat of intermediate hosts, notably undercooked meat. Dogs and cats are also hosts of *Giardia* species, but transmission of these pathogens may often be anthroponotic (e.g. human to human), which makes it difficult to assess the risk of zoonotic transmission from pet animals.

Four of the five highest-scoring zoonotic pathogens are also in the group of the five highest-scoring pathogens with animal health relevance. These are *E. granulosus* sensu lato, *Giardia* genotypes, *T. gondii* and *L. infantum*. However, *Neospora caninum*, which ranked as the highest-scoring parasitic disease relevant for animal health is not a zoonotic agent. The dog is the definitive host and cattle are the main intermediate hosts, suffering from reproduction losses mostly by vertical transmission.

Based on the current knowledge, companion animals play an important role in the transmission of parasitic diseases to food animals. The fact that four of the five highest scoring parasitic diseases that threaten human health in Europe are also ranked among the highest scoring diseases impacting on animal health in Europe stresses the importance of preventing these diseases in coordinated One Health efforts which include veterinary as well as human health officials and resources.

WHAT ARE THE RISK FACTORS FOR TRANSMISSION OF THE CALLISTO PARADIGMATIC PATHOGENS?

The second cycle of CALLISTO focused on the assessment of risk factors for spread of these diseases within companion animal populations or to human beings. These risk assessments were based on an analysis of relevant published literature identified by interrogation of PubMed and Google. Papers were subdivided into (1) those relating to import risk assessments (IRAs) for regions where a disease was absent, and (2) evaluation of risk factors in endemic areas for a disease. For diseases present throughout Europe, IRAs were considered not to be relevant and only evaluation of risk factors for endemic areas were considered. For diseases exotic to all European countries, evaluation of risk factors for endemic areas was considered not relevant and only IRAs were considered.

Import Risk Assessments

Four of the 12 evaluated diseases (CCHF, rabies, leishmaniosis and alveolar ecchinococcosis) were considered to be emerging in at least some EU countries. Most IRAs were focused on the risk of introduction and not to the risk specifically posed by companion animals. However, all IRAs showed that the set of measures in place, if properly implemented, would be effective in reducing the risk to negligible values. The only relevant route of introduction remaining was the smuggling of infected animals.

In the case of vector-borne diseases, geographical and ecological assessments were crucially important in the assessment of the possible pathways of spread.

Evaluation of Risk Factors

All 12 considered diseases were endemic in at least part of the EU. For 10 of these 12 diseases a study of risk factors was performed. Risk factors for infection of pet animals were evaluated for nine diseases. The main risk factors included pet intrinsic factors such as age (campylobacteriosis, leptospirosis, cat scratch disease, cystic echinococcosis and giardiosis) or gender (leptospirosis); lifestyle related factors such as going outdoors, deworming, having been stray, killing game, being a working dog (camplyobacteriosis, leptospirosis, cat scratch disease and cystic echinococcosis) or being kept for long time in captivity (salmonellosis); health-related factors, such as having fleas (cat scratch disease), having been hospitalized (ESBL) or not having received antihelmintic treatment (cystic or alveolar echinococcosis); or environmental factors such as season and land use (leptospirosis), presence of vectors (leishmaniosis), or density of other key hosts involved in the cycle (leptospirosis, campylobacteriosis).

Risk factors for infection of humans were evaluated for eight diseases. Most studies made an assessment as to whether keeping a pet per se, or keeping a pet with known risk factors, was a risk factor for humans relative to other risks (campylobacteriosis, leptospirosis, salmonellosis, cat scratch disease, campylobacteriosis, toxoplasmosis and alveolar echinococcosis). This allowed some studies to report the population attributable fraction (PAF) of the incidence of human disease due to companion animals (campylobacteriosis, salmonellosis, toxoplasmosis). The PAF is the percentage of total cases that may be attributed to the action of a specific risk factor (e.g. the ownership of a companion animal or the consumption of a specified food item). In some cases (for example cystic and alveolar echinococcosis) risk factors for pets and risk factors for humans were integrated, defining a single risk factor reflecting both components (e.g. owning a dog that is allowed to eat offal or carrion). For the two viral diseases considered, there was no published information on risk factors for either pets to get the infection or for humans to get the infection from pets. In the case of vector-borne diseases, geographical and ecological assessments were important in the assessment of the possible pathways of spread.

The most important conclusions drawn from these analyses were:

1. In the case of studies performed in Europe, the results are directly applicable by decision makers, while in the case of studies performed in third countries only the methodologies are applicable to Europe.
2. For a proper evaluation of the levels of risk posed by companion animals, the estimation of the PAF and the use of source attribution methods are of crucial importance.

3. Ecological assessments are useful, especially for vector-borne diseases, but are not limited to these (e.g. ecological risk factors have been studied for leptospirosis in the USA).
4. All IRAs considered were general and were not specifically aimed at evaluating the risks posed by companion animals.
5. Companion animals may be reservoir or source of infection for humans (i.e. toxoplasmosis or alveolar echinococcosis). These two scenarios must be clearly separated.

WHAT ARE THE CALLISTO RECOMMENDATIONS ON COMPANION ANIMAL ZOONOSES?

The CALLISTO final recommendations are grouped into five strategic areas:

1. Demographics and tracing/movement of companion animals
2. Education and communication
3. Surveillance and infection control
4. Risk assessment
5. New tools for diagnosis, prevention and therapy

The recommendations are categorized as those related primarily to policy, those related primarily to scientific research and those applicable to both areas. Each recommendation is prioritized using a 3-star ranking (*, ** or ***). In the more detailed descriptions of the recommendations given, the target user groups were also defined by a coding system.

DEMOGRAPHICS AND TRACING/ MOVEMENT OF COMPANION ANIMALS

*** CALLISTO recommends that more robust data be gathered on the numbers and distribution of owned and free roaming (including stray) companion animals in the EU. Such data are essential in order to be able to quantify the actual risks of zoonotic diseases attributable to companion animals and to develop sustainable interventions to prevent transmission to humans and livestock.

*** CALLISTO recommends development of systems for microchip identification of companion animals and registration of these animals in a cross-border accessible database.

** CALLISTO recommends that consideration be given to controlling companion animal movement between areas of the EU endemic for particular zoonoses and areas that are not currently endemic for that disease.

** CALLISTO recommends a specific scientific study of the reasons underlying the re-emergence of rabies in foxes in Eastern Europe.

** CALLISTO recommends the implementation of schemes to assess mortality during transportation of companion animals imported into the EU.

EDUCATION AND COMMUNICATION

*** CALLISTO recommends that any message delivered about companion animal zoonoses achieves a balance between maintaining, or possibly increasing, the benefits of keeping companion animals and mitigating or eradicating potential infectious disease risks.

*** CALLISTO recommends promotion of, and education in, the concept of responsible pet ownership as defined above.

*** CALLISTO recommends that opportunities be created for the education of physicians, veterinarians, owners and other relevant professional categories in companion animal zoonoses. Specifically, from a One Health perspective, increasing the knowledge of human physicians in this area is crucial.

SURVEILLANCE AND INFECTION CONTROL

*** CALLISTO recommends the creation of a European network, linked to EFSA and ECDC, for monitoring the prevalence of known zoonotic agents in the relevant companion animal species and for early detection of new zoonotic infectious diseases using companion animals as sentinels. Such data should be obtained from veterinary practices and commercial veterinary diagnostic laboratories and captured into a computerized database for analysis.

*** CALLISTO recommends that companion animals (particularly dogs, cats and horses) be included in national surveillance programmes on antibiotic resistance.

*** CALLISTO recommends targeted scientific research to address the significance of specific pathogens for which there is currently little information about whether companion animals are sources of these infections and how transmission of these pathogens might occur between man and companion animals.

** CALLISTO recommends implementation of methods for improved reporting of companion animal zoonotic infectious diseases.

** CALLISTO recommends the introduction of systems for monitoring the movement of arthropod vectors of zoonotic infectious disease throughout the EU as climate change increases the geographical range of such vectors.

* CALLISTO recommends the introduction of systems for monitoring companion animals travelling outside of the EU for the potential introduction of exotic pathogens as these animals return to the EU.

RISK ASSESSMENT

*** CALLISTO recommends the initiation of multicentre case-control studies to evaluate the role of companion animals as a source of infection for people by determining the population attributable fraction of disease due to companion animals. Such studies should incorporate molecular genetic analysis in order to identify strains/clones of pathogens shared between humans, companion animals and food animals.

*** CALLISTO recommends the performance of studies to identify risk factors for companion animal infection or colonization with pathogens known to have a relevant role in human disease.

** CALLISTO recommends specific targeted investigations to assess the potential human pathogenicity of a group of pathogens associated with companion animals for which there are currently few data on zoonotic risk.

** CALLISTO recommends the performance of studies to characterize the transmission dynamics of infections moving between companion animal, human and production animal populations in a farm setting.

NEW TOOLS FOR DIAGNOSIS, PREVENTION AND THERAPY

*** CALLISTO recommends introduction of some form of regulation of the use of critically important antibiotics (CIAs) used in human medicine for companion animals, and the development of new alternative veterinary antimicrobials and alternative treatment strategies to manage multidrug-resistant infections in companion animals.

*** CALLISTO recommends the development of rapid field diagnostic test kits for the veterinary practice.

** CALLISTO recommends the development of new vaccines that protect against zoonotic pathogens.

** CALLISTO recommends introduction of schemes for the regulation and certification of diagnostic laboratories and definition of minimum requirements to ensure quality control of diagnostics and susceptibility testing within veterinary hospitals.

* CALLISTO recommends a series of specific targeted research programmes that address the field efficacy of some currently available companion animal vaccines.

* CALLISTO recommends the development of rapid diagnostic test kits for use in the slaughterhouse setting.

CONCLUSIONS

There are very large numbers of companion animals throughout Europe and these animals, of varied species, play an integral role in human society, providing very real human health and welfare benefits. There is however, some risk that close human contact with companion animals may lead to the transmission of zoonotic infectious diseases of numerous different types. Companion animals may also be a source of some infections transmitted to farmed livestock. This risk must be communicated to the pet owning public in a balanced fashion by veterinary and human healthcare professionals, the pet industry and governments. The risk may be somewhat ameliorated if the owners of companion animals subscribe to the principles of responsible pet ownership.

Nevertheless, there are further policy and research actions that could be implemented by the EU and/or national governments to further reduce the risks associated with the close integration of companion animals into human society. These include the development of systems for identifying and registering the most common companion animal species and establishing surveillance programmes that capture data on zoonoses that occur in these animals. Closer attention should be paid to the health status of animals entering or re-entering the EU from third countries and the welfare surrounding companion animal cross-border movement. Data collection and pathogen assessment in the less studied exotic companion animals being kept is also needed to better understand risks. Disease and disease vector spread within Europe should be monitored and solutions found to limit such spread. The emergence of antimicrobial resistance in companion animals should be monitored. Controls should be placed on the use of human critically important antibiotics in companion animal species, but new approaches to companion animal antimicrobial therapy must be developed in parallel.

CALLISTO 3rd CYCLE FINAL REPORT: INTRODUCTION

The following report details the final recommendations related to companion animal zoonoses made by the CALLISTO Project.

STRUCTURE OF THE REPORT

All recommendations in this report have been written using the following common format (see also Appendix I):

Why? Description of why the recommendation is considered important by the CALLISTO consortium.

How? Explanation on how the recommendation could be implemented, taking into account feasibility and existing infrastructures at the EU and national levels.

Type of recommendation: research (R) or policy (P) recommendation.

Priority: priority taking into account feasibility and impact on human (or animal) health based on expert opinion: * (important priority), ** (very important priority), *** (top priority).

End Users: relevant end users to the recommendation are indicated using the following abbreviations: Animal food Industry (AF), Academic Research community (AR), Companion animal care takers (C), Doctors (D), EU Commission (EU), Farmers (F), Food industry (FO), Human-animal bond organizations (HAB), International animal and human health organizations (IHO), Diagnostic Laboratories (L), Owners (O), Pharmaceutical Industry (P), Police and armed forces (PF), Public health and veterinary/food institutes (PVI), Veterinary staff and other professionals in contact with companion animals (V), Member State Veterinary Offices (VO), Pet/Zoo shops (Z).

1. DEMOGRAPHICS AND TRACING/ MOVEMENT OF COMPANION ANIMALS

1.1 COLLECTING DATA ON THE NUMBERS AND SPECIES OF COMPANION ANIMALS IN THE EU AND THEIR GEOGRAPHICAL DISTRIBUTION INCLUDING MONITORING TRENDS OF COMPANION ANIMALS IMPORTED INTO THE EU

Why?

The numbers of companion animals in the EU are growing continuously. Recent estimates suggest that there are around 66 million cats, 61 million dogs, 39 million ornamental birds, 6 million horses and 9 million aquaria in the EU. However, while figures may be available for some regions, there is an absence of clear and reliable data for the whole EU. Lack of data is even more pronounced for other animal species being kept as pets. Cloven-hoofed animals such as miniature pigs are occasionally kept as pets. In a recent survey, more than 40% of owners fed food waste to miniature swine kept as pets. This, and failure to comply with other biosecurity measures, may pose a risk for introduction and spread of primarily livestock-associated diseases such as African swine fever or foot-and-mouth disease. Fruit bats are also kept as pets. These animals may harbor a variety of pathogens, including rabies-like viruses that are highly pathogenic for people.

Special attention should be given to stray animals, especially cats and dogs. Stray dogs, in particular, may pose serious health and welfare problems for humans and animals, including the transmission of zoonotic diseases such as rabies.

Better information on animal populations is indispensable for risk assessment and in deciding on effective and proportionate measures to prevent or mitigate such risks. Without knowing the numbers of companion animals or the variety of species they comprise, and how they are distributed across Europe, it is very difficult to quantify the actual risks of zoonotic diseases attributable to companion animals, and to develop sustainable interventions to prevent transmission to humans and livestock.

Knowledge of trends of imported companion animals can provide an early warning signal of which specific animal species should be paid more attention for the presence of pathogens of importance for human

and food animal health. For example, increased numbers of cases of salmonellosis in children in the 1980s was reflected by high importation of red-eared slider terrapins that were a reservoir of Salmonella.

How?
This could be done by exploiting existing national databases and by involving relevant partners such as the veterinary services, the companion animal food industry (e.g. FEDIAF), animal welfare organizations, competent authorities and international organizations, border inspection posts, dealers, traders and breeder associations, etc. Identification and registration of dogs would be helpful to get a better understanding of the EU dog population. Companion animal surveillance systems (see recommendation 3.1) could also provide information on numbers and geographical distribution of animals. A 'Eurobarometer' survey to address problems and controversial issues related to pet ownership and stray animals in the EU should be considered.

Trends of companion animals (i.e. numbers of individuals of each species) imported into the EU can be performed via data already registered on importation permits, and at large importation centres (e.g. Amsterdam, London, Hamburg and Paris) in the first instance.

Until now, importation of live reptiles and amphibians for commercial purposes is unregulated at EU level in terms of; facilities, bio-security and competency (excepting CITES and Customs regulations). Establishing an EU licensing regulation controlling commercial importation of live reptiles and amphibians for commercial purposes by setting down minimum standards would:

1. Reduce the number of importers by ensuring minimum standards.
2. Enable regulatory bodies to ensure importers have adequate facilities & knowledge.
3. Address issues of biosecurity, such as invasive species.

Type of recommendation: P
Priority: ***
End users: V, C, F, O, V, Z, EU, AF, IHO

1.2 IDENTIFICATION AND REGISTRATION OF COMPANION ANIMALS IN A DATABASE LINKED ACROSS EU MEMBER STATES

Why?

A specific measure that falls within the scope of responsible pet ownership is the identification and registration (I&R) of animals, preferably with a microchip implant which is registered on an accessible database. In some situations, appropriate identification systems are already in place. General principles on identification and traceability of live animals are laid down in the Terrestrial Animal Health Code of the World Organisation of Animal Health (OIE). For example, cats, dogs and ferrets that are taken across national borders need to be identified. Purebred animals are often identified to be sure about their lineage, and many owners already have their animal identified to allow it to be returned when lost. However, identification without registration in a cross-border accessible database is of limited value for zoonotic disease prevention and control, epidemiological studies and surveys.

Such an initiative would be in line with current policies of the EU Commission. As stated in the EU Commission proposal for an Animal Health Law "Efficient traceability is a key element of disease control policy. Identification and registration requirements...should be in place in order to facilitate the effective application of the disease prevention and control rules".

The registration of companion animals on national databases which are linked to a European database would also have positive consequences on animal welfare. Trafficking of animals could be better controlled if the animals were identified and registered. Missing or displaced animals could be re-united with the owners and equally, the owners of lost or abandoned animals could be traced.

How?

These goals may be achieved through mandatory identification of companion animals and registration of the identified animal in an electronic database, linked across member states, and containing all relevant information related to the animal, such as the microchip number, species, gender, breed, date and place of birth, owner details and address at which the animal is kept.

Experience obtained with the identification and registration of farm animals and horses will be very helpful in setting up a comparable system for companion animals. Due to feasibility, priority should be given initially to the identification and registration of dogs, to be followed by cats. However, owners of other pet animal species should be encouraged to voluntarily identify and register their pets.

Type of recommendation: P
Priority: ***
End users: EU, VO, V, O

1.3 DETERMINING THE ORIGIN OF RABID FOXES INVADING SOUTHERN AND EASTERN EUROPE

Why?
Although rabies is largely under control in Europe through oral vaccination of red foxes, rabies virus has re-emerged in Italy, Greece and Poland. This shows that there is a risk of re-emergence of rabies in Europe, with potential involvement of domestic dogs and cats, and impact on human health. Understanding the origin of these rabid foxes would allow directed measures to be taken (e.g. vaccination barriers) in appropriate geographical areas, and consequently reduce the risk of rabies re-emergence.

How?
Phylogenetic analysis of rabies virus strains, preferably organized in a central database, would allow the origin of rabid foxes to be identified.

Type of recommendation: R
Priority: **
End users: VO, EU, P, L

1.4 MONITORING CAUSES OF TRANSPORT MORTALITY IN COMPANION ANIMALS IMPORTED INTO THE EU

Why?
Monitoring for specific pathogens and the causes of otherwise unexplained deaths in imported companion animals that die during transport can provide the first clue to which pathogens of importance for human and food animal health are present.

How?
Monitoring for specific pathogens and cause of death can be performed for a selection of companion animals found dead during transport by the collection of necropsy tissue specimens for histopathological examination and for molecular biological detection of specified pathogens (e.g. viruses, bacteria and protozoa).

Type of recommendation: P
Priority: **
End users: VO, V, C, D, O, F, Z, EU, L, AR

1.5 LEGISLATIVE INITIATIVES TO LIMIT THE SPREAD OF ZOONOTIC PATHOGENS ACROSS BORDERS

Why?

Considering the zoonotic potential of infections such as echinococcosis, leishmaniosis and dirofilariosis, specific legislative rules should regulate animal movements within the EU. The OIE international standards on animal health are recognized by the World Trade Organisation as reference for ensuring safe transport and trade of live animals and could serve as a good basis. Transmission of echinococcosis from stray and working dogs is particularly important in regions with inadequate educational standards and veterinary control. In addition, the presence of dogs infected with Leishmania and Dirofilaria species in endemic areas (e.g. the Mediterranean region), where their vectors perpetuate, represents a threat for public health. Therefore, a suitable policy to control movement of infected animals across European borders is essential.

How?

Dogs travelling across borders should have health certificates issued by a veterinarian proving absence of infections with Leishmania, Dirofilaria and Echinococcus spp. if one or more of these pathogens are known to be endemic in the country of departure. Preferably, certificates should be electronic and part of the registration system recommended in section 1.2. Furthermore, measures for prevention and control should be enforced in areas where these pathogens are endemic. Recommendations specifically for echinococcosis are: (1) compulsory anthelminthic treatment of infected dogs, (2) control and humane reduction of stray dogs, (3) supervision of livestock slaughter, and (4) education programs. Additionally, for leishmaniosis and dirofilariosis, anti-vectorial prophylaxis of all animals in endemic areas and initiatives to control vectors are recommended.

Type of recommendation: P
Priority: **
End users: VO, V, D, O, F, L

2. EDUCATION AND COMMUNICATION

2.1 BALANCED RISK COMMUNICATION

Why?

When discussing potential health risks associated with keeping companion animals, it is important to keep a wider perspective and balance the risks with the health benefits obtained from keeping these animals. People use companion animals for a large range of purposes, including company, sport and entertainment, and pet ownership is positively correlated with a better health status. Moreover, tax income in the EU on pet animal related expenses are estimated at approximately €12 billion per year.

At the same time, it should be recognized that living together with animals is not completely risk free. For example, companion animals can carry and spread microorganisms that can cause disease in humans and in other animals, e.g. livestock.

How?

In considering any communication or action, its impact on either the likelihood or the consequences of things going wrong should be weighed against other effects that might occur. Unnecessarily scaring people away from keeping suitable companion animals is counterproductive and must be avoided. If only the negative consequences are presented, pet owners tend to disengage from the disease prevention message. Attempting to address the potential risks associated with keeping companion animals by discouraging the keeping of suitable companion animals would be ineffective. The process of exchange of information and opinions on risk between risk analysts and stakeholders should be subject to fair and rigorous assessment of those risks. This should take into account both the potential benefits and harmful impacts. The final goal is to achieve a balance between maintaining, or possibly increasing, the benefits of keeping companion animals and mitigating or eradicating potential risks.

Type of recommendation: P
Priority: ***
End users: VO, V, D, Z, AF, HAB

2.2 PROMOTION OF RESPONSIBLE PET OWNERSHIP

Why?
Keeping an animal comes with a commitment to the animal. Assuming ownership of an animal will mean taking responsibility for the health and welfare of the animal itself and its offspring. There is also a responsibility for any consequences that animal may have for other animals, people or the environment. These duties may be termed responsible pet ownership, and can involve both a 'duty of care' and a 'duty to protect'.

CALLISTO definition: Responsible pet ownership (RPO) is a duty of care based on the principle that animals are sentient beings having intrinsic value, which depend on humans for their health and welfare and are part of an ecosystem. Responsible pet ownership aims to maintain a good level of animal health and welfare, to maximize physical and psychological benefits to people and to minimize the potential risk that pets may pose to the public, other animals, or the environment. This duty starts with responsible acquisition and continues with providing appropriate care and protection for pets and their offspring.

Examples of RPO contributing to reduced disease risk as evidenced by low infection rates in people already exist (e.g. rabies control in Bali; control of echinococcosis and possibly also leishmaniosis in Sardinia).

How?
Veterinarians, breeders and pet retailers should explain to potential companion animal owners what RPO means. Furthermore, campaigns explaining RPO to established and potential owners should be initiated to ensure that the term is broadly known and the principles implemented. Education is the key to success.

Type of recommendation: P
Priority: ***
End users: VO, V, O, Z, HAB, IHO

2.3 EDUCATION OF PHYSICIANS, VETERINARIANS, OWNERS AND RELEVANT PROFESSIONAL CATEGORIES ON COMPANION ANIMAL ZOONOSES

Why?

Several zoonotic diseases (e.g. cat scratch disease and psittacosis) are likely to be underdiagnosed by physicians due to lack of knowledge of these diseases and their clinical presentations, often characterized by mild and non-specific symptoms. Furthermore, owners and to some extent veterinarians and animal care takers (e.g. persons working in pet shops) do not perceive companion animals as possible sources of infections, indirectly increasing exposure and infection risks. This is of special concern for YOPIs (people who are very young, old, pregnant or immunocompromised) who are particularly susceptible to infections.

A particular issue in which education of owners is important is the prevention of dog bites. Current and future dog owners should be aware of the importance of proper socialization of puppies in reducing unwanted behaviour and why it is important to teach children to interact safely with dogs. Owners should also be taught proper hygiene when they are in contact with companion animals. This is relevant for prevention of most infections, for example Salmonella is present in most reptiles and can be easily transmitted by the faecal-oral route.

There is a general shortage of national experts able to educate veterinary professionals and the general public on companion animal zoonoses.

How?

Using the experience of previous campaigns in some Nordic countries (e.g. educational brochures for pet owners in veterinary waiting rooms and booklets for children) or at the EU level (e.g. FECAVA posters on antibiotic resistance, the Blue Dog Programme) or the OIE Platform on Animal Welfare for Europe, campaigns targeting pet owners and breeders should be coordinated centrally and implemented nationally by veterinary organizations. Uptake of educational messages would be further supported by using various communication technologies, such as social media. Whenever appropriate, support from the private sector (e.g. pharmaceutical industries, kennel clubs, pet shops, insurance companies) should be enhanced to facilitate implementation of campaigns.

Education of healthcare professionals should be optimized at pre- and postgraduate level, the former by giving companion animal zoonoses and antimicrobial resistance/therapy the necessary space and attention in medical and veterinary curricula and generating opportunities for joint courses and seminars for veterinary and medical students. Availability of experts on companion animal zoonoses should be assessed at the national and the EU level, and shortage of experts should be overcome by developing appropriate training programmes and ongoing educational activities under the umbrella of EU veterinary and medical organizations. Networking and knowledge transfer between institutions, between countries and between sectors should be promoted and coordinated at the EU level. Educational information and sharing of data on zoonoses associated with pets could be published on the ECDC website through the creation of a 'Healthy Pets-Healthy People' initiative similar to that run by the CDC (http://www.cdc.gov/healthypets/).

Type of recommendation: P
Priority: ***
End Users: V, VO, EU, D, Z, HAB

2.4 STRENGTHENING OF THE ONE HEALTH APPROACH

Why?
Companion animals and humans share several common pathogens, albeit ones whose pathogenicity can vary considerably between species. Obviously, many disease prevention and control measures are comparable in animals and people. The main principles, such as infection control and quarantine measures, can be applied to both. Moreover, many medicinal products used to treat disease can be effective both in people and animals. In the case of antimicrobial agents, the other side of the coin is that antimicrobial use in animals may lead to loss of effectiveness in humans by favouring the development of antimicrobial resistance. It is also necessary to consider the psychosocial benefits derived from human-pet interactions (known as the human-animal bond) and to remember that the One Health concept is not just about physical disease.

How?
Continuous promotion of the 'One Health' concept should be facilitated, for example through the Veterinary Week initiative and by encouraging participation by both human physicians and veterinarians in such disease prevention campaigns.

The European Commission could support the OIE-FAO-WHO in the organization of One Health conferences on a regular basis. These events could act as potential mechanism for information exchange between professionals working in the medical, veterinary and environmental sectors. Thus, we recommend efforts to continue the cooperation achieved between OIE-FAO-WHO. We can learn from the experiences gathered over many years at the global level and consider maintaining and developing sustainable mechanisms for better addressing the 'One Health' goals. This should include ways to encourage greater involvement by those working in the environmental sciences.

In fulfilling its main mandate to improve animal health worldwide, the OIE should continue to develop programmes and mechanisms to support member countries in complying with international animal health standards, including those for the control of companion animal zoonoses, through its partnership with other international organizations like WHO and FAO.

ECDC and EFSA should continue their join activities to strengthen collaboration between animal and human health sectors at the EU level.

Type of recommendation: P
Priority: ***
End users: EU, VO, V, D, F, P, L, IHO

3. SURVEILLANCE AND INFECTION CONTROL

3.1
SET UP THE BASIS FOR THE CREATION OF A EUROPEAN NETWORK FOR MONITORING THE PREVALENCE OF KNOWN ZOONOTIC AGENTS IN THE RELEVANT COMPANION ANIMAL SPECIES AND FOR EARLY DETECTION OF NEW ZOONOTIC INFECTIOUS DISEASES USING COMPANION ANIMALS AS SENTINELS

Why?

There are many studies on the prevalence of zoonotic pathogens in companion animals, but the amount of data available varies considerably between pathogens and species and the methods used may differ significantly between studies. Under these conditions, it is difficult to develop an overview of the dispersal of a pathogen over time and space due to differences concerning study populations, sampling methods, sample processing and data interpretation. Furthermore, the available data are often limited to certain species, some countries and geographical regions within the EU.

In addition to a general lack of consistent harmonized prevalence data, there are no coordinated networks enabling early detection of new zoonotic pathogens. Prevention and control of infectious diseases is an area of great importance in the era of globalization. Being able to follow dissemination of new pathogens across borders is key to establishing rapid and effective measures to prevent and control disease spread. Animals can be usefully employed as sentinels of human infectious diseases, as demonstrated by various recent outbreaks of emerging zoonotic diseases that have shown clear linkages between animal health events and human risks (e.g. West Nile virus, Monkeypox and Avian Influenza). Companion animals such as hunting dogs represent ideal animal sentinels for early detection of new emerging zoonoses due to their susceptibility to human pathogens and frequent exposure to the environment and wild fauna.

How?
EU calls/funding are needed for establishing the basis for a novel European network linked to EFSA and ECDC for surveillance of zoonotic pathogens in companion animals. Such a network should be created based on experience from existing smaller networks on companion animal health problems, for example the Small Animal Veterinary Surveillance Network (SAVSNET), the UK VetCompass project and the Worms and Germs blog. These online networks obtain information directly from the field. The OIE World Animal Health Information System (WAHIS) is used for online notification of OIE-listed diseases by 195 countries and territories throughout the world. VetCompass already has a surveillance presence in further EU countries, as proof of concept and pilot projects have been undertaken in Germany, working with EZVet, and in Spain with QVet. Additionally, there is interest in a VetCompass approach in the Netherlands, Denmark and France. Subject to funding, these EU-based VetCompass projects could be expanded rapidly across Europe. Discussions are also taking place with view to extending the SAVSNET model to other European countries.

Lessons could also be learned from the Global Early Warning System (GLEWS). This is a joint system that builds on the added value of combining and coordinating the alert and disease intelligence mechanisms of OIE, FAO and WHO for the international community and stakeholders to assist in prediction, prevention and control of animal disease threats, including zoonoses, through sharing of information, epidemiological analysis and joint risk assessment. At the EU level, lessons could also be learned from the Food- and Water-borne Disease Network (FWD-net), which is a network coordinated by ECDC that aims to ensure surveillance, early detection and response to food and waterborne diseases outbreaks, including zoonoses such as salmonellosis and campylobacteriosis.

The network should work in close collaboration with ECDC and EFSA, and would benefit tremendously from access to passive surveillance data generated by veterinary diagnostic laboratories, including commercial laboratories. Collaboration with these laboratories, which receive the vast majority of clinical specimens from companion animals, and perhaps even making it compulsory for these laboratories to share data on disease prevalence in the companion animal population are therefore highly recommended.

Type of recommendation: R/P
Priority: ***
End Users: VO, L, EU, AR, V, D

3.2 REPORTING OF ZOONOSES IN COMPANION ANIMALS

Why?

Many zoonoses are reportable or notifiable in humans and farmed animals, but not in companion animals. It is therefore impossible to identify possible common geographical distributions or common patterns in temporal trends. Such common patterns could be an indication of a relevant role or a change in the role of companion animals as a source of infection for humans, or at least of the exposure to similar risk factors by both companion animals and humans. Seven of the 15 CALLISTO paradigmatic pathogens are notifiable to the OIE via the WAHIS and information about their occurrence and spread is available through the OIE World Animal Health Information Database (WAHID).

How?

The zoonoses to be reported, either on a voluntary or (preferably) compulsory basis, are those for which their reporting or notification is already compulsory in the human sector or in both human and farm animals sectors. The reporting may be cumulative, and it does not necessarily imply the adoption of specific measures on the affected animals. The persons expected to report are companion animal practitioners and directors of veterinary diagnostic laboratories. The information flows may be the same - or very similar to those - followed for the reporting of zoonotic diseases in farmed animals.

Type of recommendation: P
Priority: **
End Users: EU, VO

3.3 INCLUSION OF COMPANION ANIMALS (DOGS, CATS AND HORSES) IN NATIONAL SURVEILLANCE PROGRAMMES ON ANTIBIOTIC RESISTANCE

Why?

Surveillance programmes for antimicrobial resistance in humans, animals and food of animal origin have been established in several EU countries following EU legislation. However, with few exceptions (e.g. Sweden and Norway) dogs, cats and horses are not part of these programmes despite the recent emergence of important multidrug-resistant bacteria in these animals along with increasing use of antibiotics and a relatively high consumption of broad-spectrum antibiotics compared with food animals. Systematically collected, harmonized data on resistance development in companion animals are needed to follow trends of resistance over time and to evaluate the effect of antibiotic stewardship initiatives regulating antibiotic use. Availability of data on prevalence of resistance would allow comparison with patterns of antimicrobial consumption in companion animals in the various EU Member States, as the latter data are currently collected and analyzed as part of the European Surveillance of Veterinary Antimicrobial Consumption (ESVAC). By showing linkages between antimicrobial usage and antimicrobial resistance, this comparison would form the basis to develop targeted interventions aimed at correcting irrational patterns of antimicrobial usage and to prevent zoonotic risks to humans.

How?

National authorities should be encouraged to include companion animals in existing surveillance programmes for antimicrobial resistance. In order to make surveillance cost-effective, collaboration with veterinary diagnostic laboratories with data on clinical isolates is recommended (see also section 3.1). However, harmonization of susceptibility testing procedures and representative sampling designs are prerequisites for this activity (see also section 5.2.3). It would also be advisable to set up representative monitoring of resistance in indicator bacteria in healthy companion animals (e.g. sampled at vaccination visits). This would better reflect the baseline risk of transmission of resistance determinants to humans through contact with companion animals.

In countries where surveillance programmes for antimicrobial resistance in animals are already established, economic resources could be freed

through reduction of surveillance activities in food animals, for example by stopping monitoring of resistance phenotypes of little relevance to both human and animal health. In this way, this recommendation could be implemented without any additional costs.

Type of recommendation: P
Priority: ***
End Users: EU, VO, V, L

3.4 ASSESSMENT OF ALTERNATIVE COMPANION ANIMAL SOURCES AND ROUTES OF TRANSMISSION OF PATHOGENS ASSOCIATED WITH COMPANION ANIMALS

Why?
The relative shortage of studies for some pathogens and companion animal species could imply that yet undefined hosts and transmission routes exist. Here we provide five examples of pathogens for which companion animal hosts may be more important than previously expected:

- The agent of cat scratch disease (CSD), Bartonella henselae, has been detected sporadically in dogs, but the role played by these animals in human CSD is unknown. Possible transmission by dog bites would have a large impact on diagnosis and treatment of bite wound infections.

- Playing in a sandbox has been recognized as a major risk factor for Salmonella infection in children. Accordingly, cats (and to some extent dogs) may play a bigger role than previously expected for transmission of this pathogen.

- Certain viral pathogens including cowpox virus (CPV), hantavirus (HV) and lymphocytic choriomeningitis virus (LCMV) can all be highly pathogenic in humans and may occur in rodents. Despite the increasing popularity of pet rodents, and centralized large-scale production of pet rodents for international sale that can contribute to rapid and widespread international exposure to pathogens such as LCMV, no studies have investigated systematically the prevalence of such pathogens in pet and laboratory rodents.

- While dogs and cats are at most risk of becoming infected with classical rabies virus, they also may become infected with other lyssaviruses (e.g. European bat lyssavirus), for example as a result of contact with bats. Determining the prevalence of lyssavirus infections – both classical rabies virus and divergent rabies-like viruses – in dogs and cats in Europe would help to determine the level of risk of human infection by such divergent viruses.

- Some Giardia species and assemblages can infect humans as well as companion and farm animals and cause gastrointestinal disorders. It is not clear to what extent animals are responsible for human infection and whether being in contact with animals is a risk factor for humans.

How?

- Large-scale screening of dogs for the presence of B. henselae is needed to estimate the true burden of carriage across populations (e.g. domestic, stray etc.) and geographical regions. In addition, case control studies are needed to clarify whether dog bites are a risk factor for human Bartonella infections.

- The role of dogs and cats in relation to human salmonellosis should be investigated by case control studies and by genetic comparison of isolates from human cases and companion animals in their households.

- For CPV, HV and LCMV, virological examination of a selection of rodents in pet stores and research laboratories would provide a baseline for further evaluation of the human risks associated to pet rodents.

- A prevalence study of lyssavirus infection would require the sampling of a selected number of dogs and cats in Europe, both to determine the presence of lyssavirus (current infection) and the presence of antibody (past infection). This research might require development and validation of an antibody test that distinguishes vaccination from infection.

- A project on the relationships between Giardia genotypes found in humans and in animals in contact with infected humans is needed to identify if animal infection is a risk factor for humans.

Type of recommendation: R
Priority: ***
End Users: AR, D, O, V

3.5 EVALUATE THE INCURSION OF EXOTIC PATHOGENS BY DOGS AND CATS TAKEN ON VACATION OUTSIDE THE EU

Why?

Companion animals may acquire several zoonotic pathogens (including resistant bacteria) when travelling to exotic destinations. Here we highlight two pathogens of particular concern

- Crimean-Congo haemorrhagic fever virus (CCHFV) infection is primarily of concern to people, and results in an approximately 30% fatality rate. Several recent outbreaks of CCHF have occurred in Turkey and clusters of cases have been observed recently in Balkan countries. Importation of CCHFV-infected dogs and cats (together with adult Ixodes spp. ticks) taken on vacation to such endemic areas is one route by which the virus potentially could be introduced into CCHFV-free countries.

- Bluetongue virus (BTV) infection is primarily of concern to livestock and wildlife: severe disease from BTV infection may occur in certain breeds of sheep and some species of deer. Similarly, dogs and cats taken on vacation to BTV-endemic countries in Africa and Asia could potentially become infected with BTV and transport the virus to non-endemic countries in the EU. If the climatic conditions were favourable upon arrival it is possible that Culicoides midges in the country of destination could feed off these viraemic imported dogs or cats and in turn pass on the virus to the domestic ruminant population.

How?

A comprehensive research project is needed to evaluate the risks associated with travel of dogs and cats to countries where CCHFV and BTV are endemic. The first step in this evaluation is to determine, by interviews, the destinations of vacations involving dogs and cats. Subsequently, by comparing antibody levels to CCHFV, BTV and other pathogens in sera from dogs and cats resident in virus-free areas to those from dogs and cats taken on vacation to virus-endemic areas (e.g. Anatolia-Turkey and Kosovo for CCHFV, Sardinia and Greece for BTV), it will be possible to evaluate the risk of virus incursion via this route. To estimate this risk in more detail, it is also important to determine experimentally the duration and level of viraemia of CCHFV and BTV in dogs (and cats) and the duration of tick attachment to dogs (and cats).

Type of recommendation: R
Priority: *
End Users: VO, V, C, D, O, F, EU

3.6 MONITORING THE GEOGRAPHICAL DISTRIBUTION AND TRENDS OF VECTORS FOR RELEVANT ZOONOSES

Why?
In the case of vector-borne diseases the transmission of the infection from an infected host to a susceptible animal or human is mediated primarily or solely by the action of invertebrate vectors. The ongoing climate changes may be responsible for the geographical expansion of vectors and, therefore, for the expansion of areas affected by vector-borne diseases. Climatic changes may also modify the vector capacity (a quantitative measure of the ability of the vector to spread the infection) by changing its life expectancy, the speed of enzymatic and biochemical processes and the speed of virus replication.

How?
EFSA and ECDC have recently launched 'VectorNet', a 4-year project aimed at developing a common database on vectors of diseases affecting humans and/or animals. The project relies on data provided by a network of institutions and research bodies across the EU. In relation to this project, we recommend investigations on the geographical distribution and medium and long term trends of zoonoses vectors. Such studies should be performed through entomological investigations and by the monitoring the climatic and environmental changes in areas close to where vectors are known to be distributed currently.

The zoonoses transmitted by vectors identified during the 2nd cycle or listed in the alternative list of the virology group were:
Crimean-Congo haemorrhagic fever virus (transmitted by ticks of several genera, predominantly Hyalomma spp.)
West-Nile virus (transmitted by mosquitos of the subfamily Culicinae)
Leishmania infantum (transmitted by sand flies of the subfamily Phlebotominae)
Therefore, the vectors to be monitored with priority are those of the subfamilies Hyalomminae, Culicinae and Phlebotominae.

Type of recommendation: R
Priority: **
End Users: V, AR

3.7 DETERMINE THE ROLE OF COMPANION ANIMALS AS VECTORS OF EXOTIC ZOONOSES

Why?

Transmission of avian and human influenza viruses to domestic dogs and cats are increasingly reported. Domestic dogs, cats and ferrets may therefore represent new 'bridge species' for transfer of zoonotic influenza viruses from animals to humans. In particular, the continued presence of highly pathogenic avian H5N1 influenza virus in poultry of several Asian and African countries poses an ongoing risk of transfer to humans and food animals in Europe, including through companion animals. It is therefore important to determine the level of risk of dogs, cats and ferrets as bridge species of avian influenza virus (AIV) between poultry and humans.

How?

Experimental infection studies in dogs and cats, using different strains and subtypes of AIV, would provide the necessary information to assess the risk of dogs and cats as a bridge species for AIV.

Type of recommendation: R
Priority: **
End Users: VO, C, D, O, F, EU, F

4.
RISK ASSESSMENT

4.1 IDENTIFICATION AND CHARACTERIZATION OF ZOONOTIC RISKS ASSOCIATED WITH COMPANION ANIMALS

4.1.1. ASSESSMENT OF THE ROLE OF COMPANION ANIMALS AS SOURCE OF INFECTION FOR HUMANS - PART 1: MULTI-CENTRE CASE-CONTROL STUDIES

Why?

Most knowledge on zoonotic infections associated with companion animals rely on case reports, and the true attribution of companion animals to human disease remains speculative. Quantitative knowledge is essential to estimate the risks associated with animal contact and ultimately to justify and weigh recommendations to omit such risks.

How?

This area deserves a specific call for research. Research institutions, ECDC, EFSA and public- and animal health agencies studying sources and risk factors of human infections are encouraged to join forces (i.e. multicenter strategy) and structure case-control studies in such a way to include also the relevant types of contacts with companion animals (e.g. contacts with young animals with diarrhoea) and to estimate the population attributable fraction due to all relevant sources, including companion animals. Researchers and professionals in the human sector should, whenever possible, interact with veterinary professionals in the design and implementation of this research. Human-animal bond organizations, which are strongly interested in the results of this research, and pet traders, who have a direct contact to owners, would be valuable partners in projects addressing this problem and contribute to encouraging pet owners to participate in these studies.

Type of recommendation: R
Priority: ***
End Users: D, V, AR, HAB, O

4.1.2. ASSESSMENT OF THE ROLE OF COMPANION ANIMALS AS SOURCE OF INFECTION FOR HUMANS - PART 2: GENETIC AND MOLECULAR EPIDEMIOLOGICAL STUDIES

Why?

Molecular epidemiology may complement classical epidemiology in investigating the sources of infection and the population attributable fraction of each source. This approach has the advantage of less interaction with the patients than the classical case-control studies approach and excludes the need to perform a double investigation on patients (cases) and on matched unaffected people (controls).

How?

Research projects in this area should build on the existing EU surveillance framework. ECDC and EFSA are collecting molecular typing data and are currently establishing a common surveillance database with typing data on microorganisms originating primarily from humans, food and food animals. Data collection should be expanded to cover more isolates from companion animals. This research should be done in collaboration with human and animal research organizations working with zoonotic pathogens.

When sufficient data are available, genetic analysis should be done to identify strains/clones of organisms shared between humans, companion animals and food animals. Data might be linked with epidemiological data to trace dissemination of strains/clones between countries. This approach could be extended to mobile genetic elements mediating resistance to clinically important antimicrobial agents, such as plasmids encoding extended-spectrum beta-lactamase (ESBL) and gene cassettes encoding methicillin resistance in Staphylococcus aureus.

Type of recommendation: R
Priority: ***
End Users: D, V, AR, L

4.1.3. MULTI-CENTRE CASE-CONTROL STUDIES IN COMPANION ANIMAL OWNERS FOR THE IDENTIFICATION OF RISK FACTORS RELATED TO COMPANION ANIMALS

Why?

Companion animal owners have been identified as a category at risk for infection with several pathogenic organisms such as Campylobacter. Knowledge of the risk factors that promote transmission of infections from companion animals to in-contact humans is essential for effective prevention of the human infections. Such knowledge may be acquired through case-control studies, i.e. investigations of the types of exposure observed in pet-owning patients (cases) and in matched, unaffected pet owners (controls).

How?

The pathogens to investigate are those for which a relevant role of companion animals has already been documented in human disease. This research should be performed using a multicentre approach through structured interviews with pet owners affected by the disease under study and a corresponding set of matched, unaffected pet owners. A statistical analysis of the data collected should be performed to identify any significant associations between the presence of the disease and the exposure to specific risk factors. The weight of each risk factor may be calculated (population attributable fraction), to assess the number of cases due to each significant risk factor and to estimate the possible benefits following the removal of risk factors.

Type of recommendation: R
Priority: ***
End Users: D, V, AR

4.1.4. ASSESSMENT OF HUMAN PATHOGENICITY OF LESS STUDIED PATHOGENS ASSOCIATED WITH COMPANION ANIMALS

Why?

Pathogenicity and burden to human disease must be assessed for various less studied companion animal pathogens of uncertain zoonotic potential. Examples of these include less studied species within the genera Bartonella, Campylobacter, Chlamydophila, Giardia and Cryptosporidium. These neglected bacterial and parasitic species of uncertain zoonotic potential are associated with a variety of common and less common companion animal species.

How?

Human pathogenicity of less studied pathogens should be further investigated and assessed. A first step would be to enhance awareness of these pathogens in human medicine and to improve diagnostic methods to optimize their detection. If a clear role in human disease is established, risk assessments and genetic comparison of pathogens should be performed to assess the role of companion animals in human disease.

Type of recommendation: R
Priority: **
End Users: AR, D, O, V, C, L

4.2 IDENTIFICATION AND CHARACTERIZATION OF RISK FACTORS FOR INFECTION OR HEALTHY CARRIAGE OF ZOONOTIC AGENTS IN COMPANION ANIMALS

Why?

A better understanding of risk factors for disease and pathogen shedding in companion animals is important to ensure proper and targeted infection control practices. For example, animals at increased risk of infection may be vaccinated when possible. Furthermore, risk factors for pathogen shedding (e.g. use of certain antibiotics promoting multiresistant pathogens) may be limited.

How?

Large-scale multicentre studies are needed to identify the relevant risk factors for companion animal infection or colonization with pathogens known to have a relevant role in human disease. Such studies should be performed through structured interviews with pet owners whose animals are affected by the disease under study or colonized by the pathogen, and a corresponding set of owners of matched, unaffected/non-colonized animals. The population attributable fraction may be calculated to assess the number of cases due to each significant risk factor and to estimate the possible benefits following removal of risk factors.

Type of recommendation: R
Priority: ***
End Users: V, AR

4.3 IDENTIFICATION AND CHARACTERIZATION OF RISKS TO LIVESTOCK FARMING ASSOCIATED WITH COMPANION ANIMALS

Why?

Food and companion animals share several pathogens of zoonotic relevance. Currently, it is suspected that pet dogs and cats living on farms may play a role in animal-to-man transmission and contribute as vectors for the spread of important zoonotic pathogens such as MRSA between animals and humans. Furthermore, dogs and cats are definitive hosts of important farm animal pathogens, for example Toxoplasma gondii and Neospora caninum, which are among the most important causes of abortion in sheep (T. gondii) and cattle (N. caninum). A better understanding of transmission dynamics may enforce new guidelines to optimize infection barriers within and between farms.

How?

EU support is warranted to enforce this type of research and facilitate formation of academia-industry partnerships in this area. Source attribution studies in farms involving genetic typing of pathogens isolated from companion animals, humans and food animals are needed, as well as case control studies investigating risk factors for infection and carriage in farmers and farm animals. Also recommended are studies on the roaming behaviours of companion animals and their level of contact with humans and food animals.

Type of recommendation: R
Priority: **
End Users: F, O, AR, V

5.
NEW TOOLS FOR DIAGNOSIS, PREVENTION AND THERAPY

CALLISTO

5.1 VACCINATION

5.1.1. VALIDATING THE EFFICACY OF EXISTING VACCINES IN COMPANION ANIMALS

Why?

Vaccination is a powerful measure to prevent infection and reduce the need for antimicrobial therapy, but the efficacy of some existing vaccines is suboptimal. For example, different vaccines available for leptospirosis in dogs have been suggested to have limited efficacy and be associated with adverse events. Another example concerns raccoons, which are occasionally kept as pets and are susceptible to rabies. It is not known how well the rabies vaccine for dogs and cats works for raccoons. This uncertainty can only be removed by targeted research.

How?

Increased knowledge on the geographical distribution of Leptospira serotypes is needed to assess the vaccine requirements in different regions and cohort studies on development of disease in vaccinated and unvaccinated dogs could be undertaken to address the efficacy of existing vaccines in the field. An efficacy study of rabies vaccination in raccoons could also be performed, even though the study population would be relatively small compared with dogs.

Type of recommendation: R
Priority: *
End Users: P, AR, V

5.1.2. DEVELOPMENT OF NOVEL, EFFECTIVE VACCINES AND VACCINATION PROGRAMMES AGAINST SPECIFIC ZOONOTIC BACTERIAL DISEASES IN THE RELEVANT COMPANION ANIMAL SPECIES

Why?

Vaccination is an attractive option to prevent infections that are difficult or expensive to control and treat in other ways. Three pathogens are listed for which either new vaccines or optimized versions of existing vaccines would be attractive.

- *Toxoplasma gondii* is a major cause of infection in humans and every human infection ultimately traces back to a cat shedding oocysts into the environment or from tissue cysts in livestock that have been infected with oocysts. Developing a vaccine preventing oocyst shedding in cats would attack the problem at its source.

- *Leishmania infantum* is transmitted from dogs (primary host) to other dogs and humans by the sand fly. Inhibiting development of Leishmania in the sand fly following vaccination in dogs (transmission blocking vaccine) would be optimal, since dogs may remain as carriers of viable parasites even after treatment.

- Rabies vaccines have existed for many years, however none of them cover divergent rabies-like lyssaviruses, which dogs and cats may acquire following contact with bats (see section 3.4.). Broadening the spectrum of existing vaccines towards these divergent lyssaviruses would be attractive.

It should be noted that vaccine development is an area of great interest to the pharmaceutical industry. As such, this research area is a perfect ground for establishment of industry–academia partnerships.

How?

There are several strategies for development of vaccines and new possibilities have emerged in recent years with the implementation of next-generation sequencing. The ability to sequence bacterial genomes at relatively low cost should promote researchers and the medical industry to search for new vaccine targets.

Specifically for *T. gondii*, a recently completed genome-wide transcriptome analysis yielded a detailed and completely novel description of *T. gondii* gene expression during development in the cat intestine. All intestinal stages of *T. gondii* differ significantly from those developing in the intermediate host. These data close a huge knowledge gap and now make a rational strategy to develop a transmission-blocking vaccine for cats feasible.

Category: R
Priority: **
End Users: P, AR, V

5.2 DIAGNOSTICS

5.2.1. DEVELOPMENT OF RAPID AND POINT-OF-CARE DIAGNOSTIC TESTS FOR CLINICAL VETERINARY USE

Why?

Rapid diagnostic tools with high sensitivity and specificity are important, since they facilitate implementation of proper infection control practices and early treatment. Following are examples of important zoonotic pathogens for which current diagnostic tests are far from optimal.

- Certain bacterial infections (e.g. leptospirosis, psittacosis, cat scratch disease) can be difficult to diagnose because the bacteria cannot be cultured on conventional agar media. Specifically for leptospirosis, serological testing is widely used, but is suboptimal clinically because of the time required (weeks to get convalescent titres) and because of cross-reaction between different serotypes.

- Infection with certain parasites such as *Echinococcus* and *Toxocara* species will go unnoticed to companion animal owners and veterinarians unless coproscopic evaluation (followed by PCR for *Echinococcus*) is performed. These tests have limited sensitivity and are time-consuming.

Apart from assisting treatment and prevention locally, improved diagnostic tests will also help in prevalence studies that aim to understand the ecology and epidemiology of pathogens in the relevant companion animal population. This is another ideal area to promote industry–academia partnerships in the animal health sector.

How?

Implementation of this recommendation requires economic resources for national institutions, diagnostic laboratories and researchers to map and evaluate existing or potential diagnostic methods. As such, EU support and coordination are warranted to enforce this type of research and facilitate formation of academia–industry partnerships in this area.

This research would require dedicated pathogen-specific approaches to develop suitable diagnostic tests. For leptospirosis, a rapid test that can provide a sensitive diagnosis of infection, based on detection of *Leptospira* in urine or blood, is required. For *Echinococcus* and

Toxocara, coproassays for antigen or preferably for DNA with a high sensitivity and specificity need to be developed for pet-side test using lateral flow devices or microfluidic lab-on-chip (LOC) for the specific real-time diagnosis in practices and in the field.

Type of recommendation: R
Priority: ***
End Users: O, L, AR, V

5.2.2. DEVELOPMENT OF RAPID LABORATORY DIAGNOSTIC TESTS FOR SLAUGHTERHOUSE USE

Why?
In the abattoir setting, quick and accurate decisions are important when an animal suspected of having a transmissible infectious disease is brought to be slaughtered and may contaminate meat products or endanger personnel. Toxoplasma gondii is an example of an infectious agent that is found encysted in raw meat and can infect consumers or workers processing the meat. A rapid, sensitive and specific test that can be performed easily at the slaughterhouse could indicate which animal is infected before slaughter, or if tissues post-slaughter are indeed contaminated with a certain dangerous pathogen.

How?
Rapid commercial kits for the detection of specific serum antibodies and antigens in tissue, blood, urine or other body fluids, or for the amplification of specific pathogen DNA sequences from the same sources, can be developed. These kits should not require special conditions for operations, such as those found in research laboratories, but should rather be simple and easy to perform and have results that can be interpreted unequivocally.

Type of recommendation: R
Priority: *
End users: F, AF, L

5.2.3. REGULATION AND CERTIFICATION OF DIAGNOSTIC LABORATORIES AND DEFINITION OF MINIMUM REQUIREMENTS TO ENSURE QUALITY CONTROL OF DIAGNOSTICS AND SUSCEPTIBILITY TESTING WITHIN VETERINARY HOSPITALS

Why?

There are two overall reasons for this recommendation: (i) the quality of diagnostics and consequently treatment of animals should be optimized to ensure best animal health practice and to facilitate infection control locally; (ii) common standards are necessary to enable comparison of prevalence of pathogens and antibiotic resistance from different laboratories and countries. For example, data on antimicrobial susceptibility are almost impossible to compare across laboratories/ countries due to the use of different sampling design, testing methods and criteria for interpretation.

How?

Criteria for certification of diagnostic laboratories should be harmonized across EU member states. Elements from these criteria could form the basis for new minimum requirements directed at smaller laboratories in veterinary clinics. Along with legislation on minimum requirements, veterinarians should be educated about potential pitfalls associated with in-house diagnostics and encouraged to continuously update themselves on performance and interpretation of new technologies and standards for diagnostic tests. Appropriate on-going educational activities should be developed to feed this demand of education.

In the framework of EU legislation on monitoring of resistance in food-producing animals, EFSA and the EURL on AMR have extensive experience on harmonizing activities of representative sampling designs and susceptibility testing procedures in close liaison with the competent authorities and laboratories at national level (see section 3.3).

Type of recommendation: P
Priority: **
End Users: L, V, VO, EU

5.3 THERAPY

5.3.1. REGULATION OF USE OF CRITICALLY IMPORTANT ANTIBIOTICS (CIAS) FOR COMPANION ANIMALS

Why?

Multidrug-resistant (MDR) pathogens such as MRSA, MRSP and ESBL-producers have emerged in companion animals in the past decade, especially in dogs, cats and horses. These organisms are a threat to animal health and potentially also to human health due to the risk of zoonotic transfer of both resistant clones and resistance determinants. Antimicrobial usage, in particular of broad-spectrum veterinary agents such as fluoroquinolones and cephalosporins, is one well-established risk factor for these organisms in companion animals. Prudent antimicrobial use is therefore a key measure to minimize further spread of MDR bacteria in companion animals. Moreover, the increasing usage in companion animals of critically important antimicrobials (CIAs) in human hospitals poses serious concerns regarding the possible risk that veterinary usage may create a reservoir of resistance to CIAs in companion animals and contribute to loss of efficacy of CIAs for treatment of life-threatening human infections.

How?

Veterinary use of antimicrobials that are last-choice in human medicine (e.g. carbapenems, oxazolidones and glycopeptides) should be restricted to an absolute minimum by EU legislation. Use of broad-spectrum antimicrobials licensed for veterinary use (i.e. fluoroquinolones and cephalosporins) should also be limited by national initiatives promoting prudent antimicrobial use, e.g. education of specialists, ongoing education of veterinarians, development and implementation of national guidelines for antimicrobial use. More generally, it is also advisable that permanent monitoring programmes of use of antimicrobials in animals are implemented. The European Medicines Agency (EMA) has experience in coordinating implementation of such representative monitoring programmes of quantities of antimicrobials used in animals.

Type of recommendation: P
Priority: ***
End Users: EU, VO, V, L

5.3.2. DEVELOPMENT OF NEW ALTERNATIVE VETERINARY ANTIMICROBIALS AND ALTERNATIVE TREATMENT STRATEGIES TO MANAGE MULTIDRUG-RESISTANT INFECTIONS IN COMPANION ANIMALS

Why?

The emergence of important multidrug-resistant bacteria in companion animals often leaves veterinarians with the choice of either euthanizing animals or using human last resort CIAs not authorized for veterinary use, with the consequent risk of developing even more resistant pathogens of high zoonotic potential. This has created an urgent need for new solutions in veterinary antibacterial treatment. Moreover, there are zoonotic risks associated with the presence of MDR bacteria in companion animals. Thus, the problem is two-faced with implications to both animal welfare and public health.

This research is in line with the current EU strategies to combat antimicrobial resistance in animals. In April 2013, the European Commission (EC) requested advice from the EMA on the impact of the use of antibiotics in animals on public and animal health and measures to manage the possible risk to humans. The need for new veterinary-specific antimicrobials was indicated in the final document released by EMA. Multidrug-resistant infections in companion animals were listed among the indications for which new antimicrobials are needed.

How?

EU support is warranted to enforce this type of research and facilitate formation of academia-industry partnerships in this area. Focus should be on development of narrow-spectrum, veterinary-specific drugs that cannot be used in humans (for example due to toxicity or pharmacokinetic properties), revitalization of old antibiotics that are no longer of importance in humans due to side effects or better alternatives, and alternative non-antibiotic therapeutic approaches (e.g. phage therapy, bacteriocins, etc).

Type of recommendation: R
Priority: ***
End Users: P, AR, V

APPENDICES

CALLISTO

APPENDIX I
TEMPLATE FOR CALLISTO CROSS EAG REPORT, CYCLE 3

In order to harmonize the recommendations in the final CALLISTO report, all EAGs were asked to follow a common format. The recommendations were prioritized taking into account feasibility and impact on human (or animal) health based on expert opinion. The selected recommendations were ranked as top priority (***), very important priority (**) and important priority (*) to facilitate their presentation and organization in this report and in other dissemination documents. For the same reason, the relevant end-users were indicated for each recommendation according to the following scheme:

- Public health and veterinary/food institutes (PVI)
- Member State Veterinary Offices (VO)
- Veterinary staff and other professionals in contact with companion animals (V)
- Companion animal care takers (C)
- Doctors (D)
- Owners (O)
- Farmers (F)
- International animal and human health organisations (IHO)
- Pet shops (known as Zoo shops in some European countries)(Z)
- EU Commission (EU)
- Pharmaceutical Industry (P)
- Food industry (FO)
- Animal food Industry (AF)
- Diagnostic Laboratories (L)
- Academic Research community (AR)
- Police and armed forces (PF)
- Human-animal bond organizations (HAB)

NB1. More end-user categories can be included if this list is not sufficiently comprehensive.

References were not included in the report - expert opinion was deemed as sufficient.

Description of individual recommendations (maximum 250 words per recommendation)

Category: Indicate whether it is a Research (R) or Policy (P) recommendation
End Users: Use the list of abbreviations (see above)

What?
Describe the recommendation in a way that is comprehensible to non-experts.

Why?
Describe why the recommendation is important by providing the necessary background information and by pointing out the expected outcome and its impact.

How?
Explain how the recommendation could be implemented taking into account feasibility and existing infrastructures at the EU and national levels.

Priority?
*, ** or *** (see explanation above)

Summary (maximum 500 words)

Provide an overview of the EAG's conclusions with focus on top priority (***) recommendations and their implementation. The summary will be used for writing the final cross EAG report.
reate a reservoir of resistance to CIAs in companion animals and contribute to loss of efficacy of CIAs for treatment of life-threatening human infections.

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CALLISTO