Department of Equine and Small Animal Medicine
Faculty of Veterinary Medicine
University of Helsinki
Finland

Species-specific and Indication-based Use of Antimicrobials in Dogs, Cats, Cattle and Horses in Finland

- *Data collected using three different methods*

Katariina Thomson

ACADEMIC DISSERTATION

To be presented, with the permission of the Faculty of Veterinary Medicine of the University of Helsinki, for public examination in Viikin Kartano, Väentupa, Viikinkaari 8A, Helsinki
on 17th December 2010, at 12 noon.

Helsinki 2010

Supervisors

Professor Outi Vainio, DVM, PhD, DiplECVPT
Department of Equine and Small Animal Medicine
Faculty of Veterinary Medicine
University of Helsinki, Finland

Docent Liisa Kaartinen, DVM, PhD
Finnish Food Safety Authority
Research Department for Veterinary Virology
Helsinki, Finland

Merja Rantala, DVM, PhD
Department of Equine and Small Animal Medicine
Faculty of Veterinary Medicine
University of Helsinki, Finland

Reviewers

Docent Irmeli Happonen, DVM, PhD
Finnish Medicines Agency
Helsinki, Finland

Docent Antti Hakanen, MD, PhD
Antimicrobial Resistance Unit
National Institute for Health and Welfare (THL)
Turku, Finland

Opponent

Vibeke Frøkjær Jensen, Senior Researcher, DVM, PhD
National Food Institute (DTU Food)
Division of Microbiology and Risk Assessment
Technical University of Denmark
Søborg, Denmark

ISBN 978-952-92-8240-1 (paperback)
ISBN 978-952-10-6714-3 (PDF) (http://ethesis.helsinki.fi/)

Helsinki University Printing House
Helsinki 2010

Abstract

Increasing antimicrobial resistance in bacteria has led to the need for better understanding of antimicrobial usage patterns. In 1999, the World Organisation for Animal Health (OIE) recommended that an international *ad hoc* group should be established to address human and animal health risks related to antimicrobial resistance and the contribution of antimicrobial usage in veterinary medicine. In European countries the need for continuous recording of the usage of veterinary antimicrobials as well as for animal species-specific and indication-based data on usage has been acknowledged.

Finland has been among the first countries to develop prudent use guidelines in veterinary medicine, as the Ministry of Agriculture and Forestry issued the first animal species-specific indication-based recommendations for antimicrobial use in animals in 1996. These guidelines have been revised in 2003 and 2009. However, surveillance on the species-specific use of antimicrobials in animals has not been performed in Finland. This thesis provides animal species-specific information on indication-based antimicrobial usage. Different methods for data collection have been utilized.

Information on antimicrobial usage in animals has been gathered in four studies (studies A-D). Material from studies A, B and C have been used in an overlapping manner in the original publications I-IV.

Study A (original publications I & IV) presents a retrospective cross-sectional survey on prescriptions for small animals at the Veterinary Teaching Hospital of the University of Helsinki. Prescriptions for antimicrobial agents (n = 2281) were collected and usage patterns, such as the indication and length of treatment, were reviewed. Most of the prescriptions were for dogs (78%), and primarily for the treatment of skin and ear infections most of which were treated with cephalexin for a median period of 14 days. Prescriptions for cats (18%) were most often for the treatment of urinary tract infections with amoxicillin for a median length of 10 days.

Study B (original publication II) was a retrospective cross-sectional survey where prescriptions for animals were collected from 17 University Pharmacies nationwide. Antimicrobial prescriptions (n = 1038) for mainly dogs (65%) and cats (19%) were investigated. In this study, cephalexin and amoxicillin were also the most frequently used drugs for dogs and cats, respectively.

In study C (original publications III & IV), the indication-based usage of antimicrobials of practicing veterinarians was analyzed by using a prospective questionnaire. Randomly selected practicing veterinarians in Finland (n = 262) recorded all their antimicrobial usage during a 7-day study period. Cattle (46%) with mastitis were the most common patients receiving antimicrobial treatment, generally intramuscular penicillin G or intramammary treatment with ampicillin and cloxacillin. The median length of treatment was four days, regardless of the route of administration.

Antimicrobial use in horses was evaluated in study D, the results of which are previously unpublished. Firstly, data collected with the prospective questionnaire from the practicing veterinarians showed that horses (n = 89) were frequently treated for skin or wound infections by using penicillin G or trimethoprim-sulfadiazine. The mean duration of treatment was five to seven days. Secondly, according to retrospective data collected

from patient records, horses (n = 74) that underwent colic surgery at the Veterinary Teaching Hospital of the University of Helsinki were generally treated according to national and hospital recommendations; penicillin G and gentamicin was administered preoperatively and treatment was continued for a median of three days postoperatively.

In conclusion, Finnish veterinarians followed well the national prudent use guidelines. Narrow-spectrum antimicrobials were preferred and, for instance, fluoroquinolones were used sparingly. Prescription studies seemed to give good information on antimicrobials usage, especially when combined with complementary information from patient records. A prospective questionnaire study provided a fair amount of valuable data on several animal species. Electronic surveys are worthwhile exploiting in the future.

Contents

List of original publications

This thesis is based on the following publications, which will be referred to by their Roman numerals:

I Rantala M, **Hölsö K**, Lillas A, Huovinen P, Kaartinen L. Survey of condition-based prescribing of antimicrobial drugs for dogs at a veterinary teaching hospital. Veterinary Record 2004, 155, 259-262.

II **Hölsö K**, Rantala M, Lillas A, Huovinen P and Kaartinen L. Prescribing antimicrobial agents for dogs and cats via University Pharmacies in Finland – patterns and quality of information. Acta Veterinaria Scandinavica 2005, 46, 87-93.

III **Thomson K**, Rantala M, Hautala M, Pyörälä S, Kaartinen L. Cross-sectional prospective survey to study indication-based usage of antimicrobials in animals: results of use in cattle. BMC Veterinary Research 2008 14;4:15.

IV **Thomson K**, Rantala M, Viita-aho T, Vainio O, Kaartinen L. Condition-based use of antimicrobials in cats: results from two surveys. Journal of Feline Medicine and Surgery 2009, 11, 462-466.

Abbreviations

AFSSA ANMV	French Agency for Veterinary Medicinal Products
AMR-Report UK	Antimicrobial Resistance Report from the United Kingdom
APUA	Alliance for the Prudent Use of Antibiotics in the United States of America
AVMA	American Veterinary Medical Association
BSAVA	British Small Animal Veterinary Association
CCAR	Canadian Committee on Antibiotic Resistance
CVMA	Canadian Veterinary Medical Association
CVMP	Committee for Medicinal Products for Veterinary Use
DANMAP	Danish Integrated Antimicrobial Resistance Monitoring and Research Programme
DDDcow	Defined daily dose per cow
EC	European Community
EEC	European Economic Community
EMA (former EMEA)	European Medicines Agency
EPR	Electronic patient record
FAAIR	The project on Facts about Antibiotics in Animals and the Impact on Resistance by APUA
FAO	Food and Agriculture Organization of the United Nations
Fimea	Finnish Medicines Agency (former NAM)
FINRES-Vet	Finnish Veterinary Antimicrobial Resistance Monitoring and Consumption of Antimicrobial Agents
FVE	Federation of Veterinarians of Europe
MARAN	Monitoring of antimicrobial resistance and antibiotic usage in animals in The Netherlands
MMM	Finnish Ministry of Agriculture and Forestry
MRL	Maximum residue limit
NAM	National Agency for Medicines, Finland
NASS	National Agricultural Statistics Service, USA
NORM NORM-Vet	A Report on Usage of Antimicrobial Agents and Occurrence of Antimicrobial Resistance in Norway in animals and humans
OIE	World Organisation for Animal Health
PRB	Population Reference Bureau
SVARM	Swedish Veterinary Antimicrobial Resistance Monitoring
SVJ	Swedish Board of Agriculture
TIKE	Information Centre of the Finnish Ministry of Agriculture and Forestry
VetStat	The Danish system for surveillance of the veterinary use of drugs for production animals, funded by The Danish Ministry of Food, Agriculture and Fisheries
VMD	Veterinary Medicines Directorate, the United Kingdom
WHO	World Health Organization

1 Introduction

Emerging bacterial resistance to antimicrobials can be considered as one of the biggest current and future threats to the welfare of mankind. Ever since the discovery of the first active substances for killing human pathogenic microbes, resistance has been evolving towards these life-saving drugs. Bacteria always seem to be one step ahead of the development of new antibacterial drugs. After a century of being effective in curing disease, antimicrobials are losing their effect. The importance of bacterial resistance in animals is focused on the zoonotic nature of certain animal pathogens and the possibility of transfer of elements conferring resistance from animal bacteria to human bacteria. This has been shown to happen, for example, in *Salmonella* spp. isolated from food producing animals and humans (Dunne et al. 2000).

The development of bacterial resistance to antimicrobials is a complex issue. It has, however, been shown that the use of antimicrobial agents aggravates the problem, and that suboptimal dosing (Harigaya et al. 2009) and prolonged periods of treatment (Guillemot et al. 1998), in particular, induce and promote resistance. The use of antimicrobials as growth promoters in livestock was prohibited by law in the European Union (Commission Directive 97/6/EC) after it was demonstrated that there was increasing resistance to vancomycin in enterococci isolated from poultry (Bager et al. 1997). Vancomycin is a critically important drug in human medicine and is used in the treatment of life-threatening infections caused by Gram-positive bacteria. The use of avoparcin, a glycopeptide analogue of vancomycin, as a production enhancer was thought to cause cross-resistance to vancomycin (Wegener 1999), and was therefore banned along with virginiamycin and other antimicrobial agents commonly used for growth promoting purposes. The use of cephalosporins and fluoroquinolones has been shown to be a risk factor for acquisition of genes coding for the expression of extended spectrum betalactamases in Gram-negative bacteria (Kaier et al. 2009). Cephalosporins are frequently used antimicrobials in companion animals in several countries (Regula et al. 2009, SVARM 2008, Weese 2006). The use of fluoroquinolones has also increased in companion animals (DANMAP 2008, Prescott et al. 2002), and consequently also the risk of multidrug-resistant infections (Black et al. 2009, Cooke et al. 2002).

In discussions of the impact of antimicrobial use in animals on public health, emphasis is put on food-producing animals and the risk for transmission of bacterial resistance via human consumption of food of animal origin. However, the growing rate of resistant bacteria isolated from infections in companion animals is a major point of concern. Companion animals live in close proximity to humans and the risk of transmission of resistant bacteria or genetic material conferring resistance cannot be overlooked. Therefore, it is utmost important that veterinarians are aware of and recognize the importance of judicious antimicrobial use when treating any animal species.

Prudent use guidelines or detailed indication-based instructions on antimicrobial use in animals have been issued in several countries; however, studies on how well guidelines or instructions are followed are very few (Regula et al. 2009, Weese 2006). The need for guidelines and surveillance is usually argued by attempts to minimize the development of antimicrobial resistance in bacteria, and thus avoid the overuse or misuse of potentially lifesaving drugs (Nunnery et al. 2006, WHO 2003, WHO 2004). In order to assess the effects of guiding antimicrobial use, follow-up studies are needed.

This thesis presents baseline information on the indication-based use of antimicrobials in four different animal species in Finland. Compliance with guidelines has also been evaluated. The literature review includes recently published articles on antimicrobial usage in dogs, cats, cattle and horses, introductions of prudent use guidelines and methods that have been used worldwide for the collection of antimicrobial usage data in animals. Animal species-specific results on usage are previously reviewed and discussed in the original publications I-IV and further in this dissertation summary.

2 Review of the literature

The OIE has given recommendations on how to implement systems for monitoring the quantity of antimicrobials used in animal husbandry in the OIE member countries (OIE 2008). The recommendations include examples of sources for antimicrobial usage data collection and what type of data should be collected. This information is needed to aid in the surveillance of antimicrobial resistance in animal pathogens and also to be able to assess whether prudent use guidelines are followed.

In the following sections, recent literature concerning the clinical use of antimicrobials in animals is reviewed and the principles of prudent use guidelines are presented. Furthermore, the most frequently used methods for gathering data on antimicrobial use are reviewed. An insight into Finnish legislation on the distribution and use of veterinary medicines is also given.

2.1 The clinical use of antimicrobials in dogs, cats, cattle and horses

There have been rather few controlled studies in which antimicrobial use in different infectious conditions in animals has been investigated from an indication point-of-view. Clinical case reports are available on the treatment of infectious diseases in individual animals or animal groups, but the reasoning behind the choice of antimicrobial agent is not usually discussed.

2.1.1 Dogs

In a Danish study by Pedersen et al. (2007), the use of antimicrobials in dogs and antimicrobial resistance in canine pathogens was reviewed. The isolated microbes were from clinical diagnostic samples; however, information on which infection had been treated with which antimicrobial was lacking. The authors state that skin, ear and wound infections as well as gastrointestinal infections and urinary tract infections were the most commonly treated infectious conditions in dogs, although no reference is given. The most commonly used drugs in dogs in Denmark in 2005, measured in kilograms of active substance, were betalactams (75%) and trimethoprim-sulfonamides (13%). Approximately 80% of these were oral antimicrobials. This correlates to the usage in Sweden, where betalactams accounted for 72% and trimethoprim-sulfonamides for 9% of the amount (kg) of peroral antimicrobials sold for dogs and cats in 1998. In Norway the respective usage of betalactams was only 10%, and of trimethoprim-sulfonamides 82% of the cases (Odensvik et al. 2001). The reason for this small proportion of betalactams used in Norway could have been that no peroral betalactam antimicrobials were approved for use in animals in the country before 1994. However, a study by Grave et al. (1992) revealed that human preparations were widely used in Norway. Sixty-three percent of prescriptions for dogs were for a preparation registered for human use. Therefore, it can be assumed that human-registered betalactam antimicrobials were used for dogs in Norway.

A study by Meyers et al. (2008) investigated the bacteriology of bite wounds in dogs in South Africa. Based on the susceptibility pattern of bacteria isolated from dog bite wounds, the authors suggested that antimicrobial treatment with aminopenicillins combined with clavulanic acid to be the best choice for empirical treatment.

2.1.2 Cats

There have been few recent articles on antimicrobial usage in cats. One of them concerned the treatment of lower respiratory tract infections caused by *Bordetella bronchiseptica*, which is the most common causative agent of the disease in cat rescue shelters and multi-cat households (Egberink et al. 2009). *B. bronchiseptica* is considered to be a primary pathogen of domestic cats with signs of respiratory infection. The bacterium can be isolated by broncoalveolar lavage and first-line treatment is with doxycycline (Sherding 2000).

Tetracyclines, especially doxycycline, are considered as drugs of choice for the treatment of *Chlamydophila felis* infections in cats (Gruffyd-Jones et al. 2009). Other microorganisms causing respiratory infections in cats include feline calicivirus and feline herpesvirus. Viral infections are not primarily treated with antimicrobials, but broad spectrum antibiotics are sometimes recommended for the prevention of secondary bacterial infections (Thiry et al. 2009, Radford et al. 2009). Broad-spectrum antimicrobials are also recommended as conjunctive therapy in enteritis associated with feline panleukopenia (Truyen et al. 2009). The term broad-spectrum coverage was not further explained in any of these guidelines.

A comprehensive review on the use of antimicrobials in cats conducted by Albarellos and Landoni (2009) presents several classes of antimicrobial drugs and their usefulness in treating infectious diseases in cats. It is directed to practicing veterinarians treating feline patients and presents an easy-to-understand summary of pharmacokinetic and bacteriological information on common infectious diseases in cats. According to this review, amoxicillin-clavulanate is a useful drug combination for common diseases such as bite wounds, pyoderma, cystitis and upper respiratory tract infections in cats. However, the authors do not comment on the superiority of any drug over another, neither the dose nor the length of the treatment, which would all be useful for the practicing veterinarian when making decisions on antimicrobial treatment.

2.1.3 Cattle

A recent study on antimicrobial treatments in dairy operations in the United States has been published by Hill et al. (2009). Information on diseases and antimicrobial treatments was collected from 21 states, accounting for approximately 70% of all dairy populations in the country. The most common indications for antimicrobial treatment in dairy cows were mastitis and lameness. Of 858 herds, 85% reported having cows suffering from mastitis. Antimicrobials were used for mastitis treatment in 92% of these herds. Cephalosporins or other betalactams were used in 39% and 34% of the mastitis cases, respectively. Lameness was recorded in 60% of the herds and treated with antimicrobials in 65% of the cases. Lameness was most commonly treated with cephalosporins (30%), followed by other betalactams (25%) or tetracyclines (23%). The selection of drugs is restricted by a limited number of approved products for production animals. Another important factor affecting the choice of product is the length of the milk withdrawal time, which for cephalosporins is zero hours and in other betalactams 48-96 hours. The withdrawal period is a major issue when, as in the United States, the farmer makes the choice of which antimicrobial drug to use.

Another study by Gow and Waldner (2009) examined antimicrobial usage in 203 Canadian beef cow-calf herds during the calving season (1 January – 30 June). Injectable antimicrobials were used in 80% of the herds for treating infections in calves and a combination of oral and injectable drugs in 46% of the herds. Diarrhoea, pneumonia and omphalitis were the most common indications for treatment in calves. Adult heifers and cows mainly received antimicrobial treatment for metritis and interdigital necrobasillosis. The percentage of herds that had cows or heifers treated with antimicrobials at least once during the calving season was 61%. The most commonly used drugs for calves were oral sulfonamides and florfenicol, followed by injectable tetracycline. More than half of the herds (52%) used injectable tetracyclines in cows, while 21% of the herds reported the use of parenteral penicillin. Enrofloxacin was reported to be used for the treatment of diarrhoea in calves in 8 herds; otherwise, no clarification on indication-based usage was given in the article.

2.1.4 Horses

Weese and Cruz (2009) reported results from a retrospective Canadian study on antimicrobials used perioperatively in horses undergoing arthroscopic surgery. Preoperative parenteral antimicrobials were routinely used, intravenous penicillin being the most frequently used agent (93%). The remaining 7% of the patients received penicillin and gentamicin. Two horses did not receive any perioperative antimicrobials. The majority of the horses (66%) received intravenous antimicrobials for up to 24 hours postoperatively. However, in human medicine it has been shown that in clean surgeries, continuing antimicrobial treatment beyond the cessation of the surgical procedures does not bring any benefit concerning the risk of wound infections (Bratzler et al. 2005).

According to a questionnaire survey performed on diplomates of the American College of Veterinary Surgeons, most of the veterinarians used perioperative antimicrobials in horses undergoing colic surgery. If the surgery was uncomplicated, the average duration of treatment was 24 hours postoperatively. If the surgery involved enterotomy or resection, most veterinarians stated that antimicrobials were used for approximately 3 days postoperatively. (Traub-Dargatz et al. 2002)

2.2 Prudent use guidelines

The prudent or judicious use of antimicrobials is characterized by optimizing the therapeutic effects while minimizing the risk for the development of antimicrobial resistance and preserving the efficacy of available drugs in the future.

Numerous professional groups have published prudent use guidelines on antimicrobial use in animals (OIE 2009, AVMA 2008, Ungemach et al. 2006, CVMA 2002, Anthony et al.

2001, Wilke 1999, FVE 1999). The guidelines are referred to when providing education on judicious antimicrobial use to veterinarians, students, farmers and pet owners. It is considered to be a common responsibility of veterinarians to comply with the guidelines in order to preserve human and animal health. The general reasoning of these guidelines is overall quite similar. In the following, a brief overview of the basic principles is given.

a. Antibiotics shall primarily be used for the treatment of an infectious disease caused by bacteria. The use of antimicrobials for disease prevention should be restricted to cases where an animal is at notable risk of disease and the use of antimicrobials is likely to prevent morbidity. In surgery, the use of prophylactic antimicrobials shall not replace aseptic techniques. The use of antimicrobials to promote growth was prohibited in the European Union in 1997.
b. Antimicrobials should always be used by or under the supervision of a licensed veterinarian. When a veterinarian dispenses or prescribes medicines to be given by the animal owner, the veterinarian is responsible for giving the owner detailed instructions on how to use the medicine correctly.
c. When a veterinarian makes the decision about treatment, he/she needs to base the choice of the antimicrobial drug on the confirmed or suspected causative agent and the susceptibility to antimicrobial medicines. Antibacterials shall be used only in cases of a bacterial infection. Substances with a narrow spectrum should always be chosen when possible, and drugs classified as critically important in human medicine should be avoided. Further, the correct dosage is to be ordered and treatment should continue for as long as needed, but avoiding unnecessarily prolonged periods of treatment. The risk of adverse effects and cost of treatment should also be minimized.
d. Both veterinarians and farmers must keep a record of all medications used for animals, including the dosage and length of the treatment period. Withdrawal periods should also be strictly adhered to.
e. Veterinarians should encourage the producers to improve livestock management and to favour disease preventative measures where applicable. This includes using grouping of animals, methods such as all-in-all-out, vaccination and improving animal nutrition and health care. It is the responsibility of the veterinarians to be updated on new methods for disease prevention and also on issues concerning antimicrobial resistance. This information should then be transferred to the clients.
f. The pharmaceutical industry should pay attention to marketing strategies and, especially with antimicrobials, take into account prudent use guidelines and promote the judicious use of these precious substances.
g. The usage and disposal of antimicrobials should be carried out in a manner that is safe to animals, people and the environment.

In addition to general prudent use guidelines, some countries have published animal-species-specific treatment guidelines that give recommendations on the choice of antimicrobials in different bacterial infections. The AVMA has developed judicious use principles for aquatic animals, companion animals, horses, beef cattle, dairy cattle, poultry and swine (www.avma.org/issues, last accessed 15.11.2010). The Danish Veterinary Laboratory of the Danish Veterinary and Food Administration has given recommendations for the treatment of infectious diseases in poultry, cattle and swine (Fødevarestyrelsen 2009, Fødevarestyrelsen 2007). The CVMA has also issued animal species-specific indication-based guidelines for poultry, beef cattle and dairy cattle (CVMA 2008 a, b, c). Furthermore, Finland has issued the second revision of detailed treatment guidelines for poultry, cattle, swine, horses, dogs and cats, fur animals, fish and bees (Evira 2009).

2.2.1 Finnish guidelines for judicious antimicrobial use in animals

The Finnish Ministry for Agriculture and Forestry set up a working group in 1995 to establish recommendations for the use of antimicrobials in animals and to suggest measures to improve the surveillance of antimicrobial resistance in animal pathogens in Finland. There was growing concern of bacterial resistance in human medicine, and the need for guidelines on prudent antimicrobial use and evidence-based medicine was recognized. The recommendations on the judicious use of antimicrobials in animals were a contribution from the veterinary field. The booklet, which was first published in 1996, contains indication-based suggestions on first-line treatments, secondary choices and additional comments for the treatment of common infectious diseases in cattle, swine, horses, fish, poultry, dogs and cats, bees and fur animals (MMM 1996). When giving the recommendations, several aspects were considered: current evidence-based medical literature, the current national animal disease status, antimicrobial resistance in domestic bacterial isolates, available medicinal products, the pharmacokinetic and -dynamic properties of the available drugs and the subjective experiences of clinical efficacy evaluated by different veterinary specialists. The recommendations have subsequently been revised in 2003 and 2009 (MMM 2003, Evira 2009).

In the latest revision of the recommendations (Evira 2009), most of the updating concerned the guidelines for horses; treatment recommendations for ocular infections were added and changes in recommended medications were made for several conditions. In the renewed recommendations, local perfusion and local infusion techniques are favoured in treatment of septic arthritis, osteomyelitis and endometritis in horses. For dogs and cats, topical treatment of pyoderma and otitis externa is emphasized. Systemic antimicrobials are recommended as second line choices or in conjunction with local medications. The indications for the use of fluoroquinolones or higher generation cephalosporins have been critically evaluated and their use is advised to be restricted to cases of non-susceptibility to other substances. Some examples of changes in recommendations over the years are presented in Table 1.

2.2.2 Surveillance of antimicrobial resistance in animal pathogens in Finland

National surveillance of antimicrobial resistance is performed by the Finnish Food Safety Authority (Evira) (www.evira.fi/portal/en). A systematic surveillance programme called FINRES-Vet was established in 2002. Reports on resistance in zoonotic organisms, animal pathogens and indicator bacteria are regularly published. In addition, resistance is continuously monitored in projects and from clinical samples submitted daily to the Evira laboratory.

Table 1. Examples of changes in the Finnish national antimicrobial prudent use recommendations from 1996 to 2009: first- and second-line choices.

Horses	**Recommendation 1996**	**Recommendation 2009**
Rhodococcus equi– pneumonia in foals	1.Erythromycin 2. Aminoglycoside + penicillin G	1. Erythromycin + rifampicin OR clarithromycin + rifampicin 2. Azithromycin + rifampicin
Wounds penetrating articular compartments	Not applicable	1. Local lavage (joint, tendon sheath) and intra-articular antibiotic, eg. gentamicin/amikacin 2. Penicillin G + gentamicin
Infectious gastrointestinal diseases (*Salmonella*, clostridia)	1. Penicillin G 2. Nitroimidazoles	1. Isolation, supportive therapy, no antimicrobials 2. Metronidazole (not for salmonella) Intensive care, treatment of salmonellosis only in life-threatening cases, based on susceptibility
Dogs and cats		
Pyoderma	1. Clindamycin or trimethoprim-sulfonamides 2. 1st gen. cephalosporin or amoxicillin-clavulanate	1. Local treatment with chlorhexidine wash solution and fucidic acid. 1st gen. cephalosporin 2. Amoxicillin-clavulanate, clindamycin (according to susceptibility testing), fluoroquinolones (if heavy scar formation)

The reports by the FINRES-Vet programme demonstrate that even though the resistance of animal pathogens in Finland has been considered to be low, an increasing number of cases of both clinical infection and asymptomatic carriage of resistant organisms has been reported. Drug resistance in *Salmonella* in cattle, pigs and poultry has increased from no resistance to any of the tested antimicrobial agents in 2005 to resistance towards several groups of antimicrobials in 2008 and 2009 (Table 2). Finland has a very low prevalence of *Salmonella* in food producing animals, and the national objective is to keep the incidence below 1%. It is, however, of concern that resistance has emerged in isolated species of *Salmonella* within a few years. (FINRES-Vet 2004, FINRES-Vet 2005-2006, FINRES-Vet 2007-2009).

Resistance has increased markedly also in strains of canine *Staphylococcus (pseud)intermedius*, isolated from clinical specimens sent in to the Finnish Food Safety Authority from several parts of the country (Table 3) (FINRES-Vet 2004, FINRES-Vet 2005-2006, FINRES-Vet 2007-2009). In 2009 there was a sudden increase in oxacillin/methicillin resistant strains suggestive of an outbreak. The investigation of a possible common source is still pending. If this trend stays permanent, this affects significantly on the prudent use recommendations of treatment of canine pyoderma as the efficacy of betalactams, including cephalosporins, is jeopardized.

Table 2. Occurrence of resistance (%) in Salmonella spp. isolated from samples from cattle, pigs and poultry; meat and eggs in Finland in 2004-2009 (FINRES-Vet 2004, 2005-2006, 2007-2009).

Antimicrobials	**2004 (n = 31)**	**2005 (n = 32)**	**2006 (n = 28)**	**2007 (n = 38)**	**2008 (n = 21)**	**2009 (n = 22*)**
			%			
Ampicillin	3	0	0	5	14	23
Cefotaxime	0§	0	0	0	0	0
Chloramphenicol	3	0	0	3	10	14
Ciprofloxacin	NA	0	11	3	5	14
Gentamicin	0	0	0	0	0	0
Nalidixid acid	0	0	0	0	5	14
Sulfametoxazole	3	0	0	16	14	23
Tetracycline	3	0	0	18	10	14
Trimethoprim	0	0	0	3	10	0

* only cattle and poultry included

§ figure for ceftiofur

NA not applicable

Table 3. Occurrence of resistance (%) in Staphylococcus (pseud)intermedius isolated from canine skin, wounds or otitis externa in Finland in 2004-2009 (FINRES-Vet 2004, 2005-2006, 2007-2009).

Antimicrobials	**2004 (n = 46)**	**2005-2006 (n = 47)**	**2007 (n = 31)**	**2008 (n = 49)**	**2009 (n = 70)**
			%		
Cephalotin	2	9	3	7	26
Clindamycin	17	17	21	12	35
Enrofloxacin	4	6	6	8	21
Erythromycin	17	19	24	14	39
Gentamicin	2	6	0	2	18
Oxacillin	2	13	3	7	26
Tetracycline	46	45	24	31	47
Penicillin	83	72	82	85	85

2.3 Data collection methods

There are several ways of collecting data on the use of antimicrobial drugs in animals. The choice on which method is most suitable is made based on what specific information is sought. Usage data can be collected on different levels, such as manufacturing data, distribution data, prescription data and end-user data (DeVincent and Viola 2006b) or animal species-specific usage data (see for example Chauvin et al. 2008, Chicoine et al. 2008, Grave et al. 2008).

Systematic information on antimicrobial drug consumption in animals can be collected as sales data from the pharmaceutical industry, such as in the Netherlands (MARAN 2007) and the United Kingdom (AMR Report-UK 2004, VMD 2008/09), from pharmacies, as in Sweden (SVARM 2008, 2009), or from pharmacies and feed mills, as in Denmark (DANMAP 2008, DANMAP 2007). Wholesaler statistics may also be used, as in Finland (NAM 2009) and Norway (NORM NORM-Vet 2009). However, in most European countries, no systematic surveillance on antimicrobial usage is available (Kools et al. 2008).

In the United States, the non-profit organization APUA formed a panel in 1999 to investigate issues concerning antimicrobial resistance and the use of antimicrobials in animals. One of the main conclusions of the 2-year project FAAIR was that information on antimicrobial drug use in animals is poorly documented and difficult to collect. As a sequel to this, in the spring of 2002 the Advisory Committee on Animal Antimicrobial Use Data Collection in the United States was established in order to address methodological issues surrounding animal antimicrobial use surveillance (DeVincent and Viola 2006a). The committee consisted of 17 members who represented academics/researchers, government officials, animal health industry representatives, public interest scientists and advocates, food animal producers and veterinary professionals. The committee was assigned to identify and describe different methods for collecting data on antimicrobial usage in animals. Each stakeholder was also asked to inform of relevant issues concerning the surveillance of antimicrobial use from their point of view. These inputs resulted in stakeholder position papers from the perspective of, for instance, an economist, a small animal veterinarian, a dairy producer, the animal health pharmaceutical industry and public health. Concerning the methodological options, the committee did not reach a uniform conclusion on which method or methods would be the best for collecting information on antimicrobial use in the United States. However, there was mutual agreement that a combination of two or more methods would together give sufficient and accurate information. A summary of the different methods and the views of each stakeholder were published in a special issue of Preventive Veterinary Medicine (Prev Vet Med (2006) Vol 73, Issues 2-3).

2.3.1 Wholesaler or pharmacy sales data

Data collection from wholesalers or pharmacies is useful when reviewing annual national trends and for international comparison, as they provide comparable figures on the total amount in kilograms of the distributed antimicrobial substances. Several EU countries compile and publish annual consumption data, for instance Denmark (DANMAP 2007, 2008), Norway (NORM NORM-Vet 2007, 2008, 2009), Sweden (SVARM 2008, 2009), Finland (NAM 2009), the Netherlands (MARAN 2007) and the United Kingdom (AMR Report-UK 2004, VMD 2008/09). The figures of sold antimicrobials are usually shown in tonnes of active substance. Companion animals such as dogs and cats are due to their small body weight using a neglible amount of antimicrobials counted in kilograms active substance than production animals such as cattle, pigs and horses. The statistics database Eurostat maintained by the European Commission shows figures on meat production in tonnes of carcasses slaughtered annually (Eurostat 2009) which gives perspective to the used amount of antimicrobials in different countries.

The CVMP has carried out a qualitative risk assessment on antimicrobial resistance and collected background information on resistance surveillance and antimicrobial usage in the European Union in 1999 (EMEA 1999). Concerning antimicrobial usage data, the CVMP concluded that information on amounts and consumption patterns are, with a few exceptions, not available. The CVMP recommended regular species-specific monitoring of all antimicrobials used in animals.

The Finnish Medicines Agency Fimea (former National Agency for Medicines, NAM) has since 1995 provided annual figures on the sales of different groups of antimicrobial substances registered for animals based on the sales data from wholesalers (NAM 2009). These figures are comparable between years and they can be compared against the annual numbers of registered production animals in order to determine whether overall consumption is rising or declining. Information on veterinary drug sales is collected from wholesaler statistics also in Norway (NORM NORM-Vet 2007, 2008 and 2009).

Swedish data are collected from pharmacies, as all pharmacies in the country belong to the National Corporation of Swedish Pharmacies, Apoteket AB, and all antimicrobials for animals are dispensed via a veterinary prescription. Species-specific sales data are reported on an annual basis (SVARM 2008). Previously, Swedish data were collected from the wholesalers who sell the drugs to pharmacies.

Odensvik and colleagues (2001) used data from Sweden and Norway to report antimicrobial drug use in dogs and cats over a 9-year period. Although only crude data on sold packages were available, it enables the sales trends over the years to be examined. The number of sold packages increased steadily in both countries during the study period. In Sweden the number of sold packages was doubled during the study period when the number of animals stayed the same.

The most detailed surveillance system for animal antimicrobial usage is in Denmark. The Danish VetStat system collects information from pharmacies, which provide 95% of all antimicrobials used in production animals in the country (Stege et al. 2003). In addition to pharmacies, a small proportion is distributed to end-users by feed mills. Pharmacies report monthly information on all dispensed prescriptions. Information on the animal species and dosage can be obtained from this prescription data.

Based on the sources mentioned above, Table 4 shows the annual usage of veterinary antimicrobials in proportion to kilograms of meat produced in Norway, Finland, Sweden and Denmark in 2008.

In France, the monitoring of antimicrobials is performed by the AFSSA ANMV. The data is collected from marketing authorization holders by sending them a questionnaire and requesting the amount of antimicrobials sold between the 1 January and the 31 December each year. The information is converted to tonnes of active substance in order to facilitate comparison. In a study by Moulin et al. (2008) the usage of antimicrobials in veterinary medicine from 1999 to 2005 is reviewed. The consumption of antimicrobials of different classes was steady during the study period without any significant increase or decrease in any class. Tetracyclines were used the most, approximately 650 tonnes a year, followed by trimethoprim-sulfonamides; 250 tonnes a year.

Wholesaler or pharmacy sales of antimicrobials registered for veterinary use give crude information on the scale of antimicrobial usage in different countries. When put into proportion with the information on e.g. head count of production animals or kilograms of meat produced annually you get a comparable figure.

Table 4. Sales of antimicrobial drugs for veterinary use in Norway, Sweden, Finland and Denmark in 2008 expressed in mg of active antibacterial substance sold per kg of slaughtered meat.

Sales of antimicrobials	**Norway**	**Sweden**	**Finland**	**Denmark**
Antimicrobials (AM tonnes)	7,2[1]	16,4[2]	17,0[3]	120,2[4]
Meat production (MP tonnes)	318,000[5]	526,200[6]	401,300[6]	2,014,600[6]
AM/MP mg/kg (milligrams of active substance/kg meat produced)	23	31	42	60

1 NORM NORM-Vet 2008
2 SVARM 2008
3 NAM 2009
4 DANMAP 2008
5 KLF 2009
6 EUROSTAT 2009

2.3.2 Prescription data

A prescription is a veterinarians' order to the pharmacy to dispense a certain medication to whomever the prescription is addressed to. In Finland, the information required in a prescription is enacted in a Decree of the Ministry of Agriculture (MMMa 7/EEO/2008). Therefore, in addition to collecting data on drug use in animals, prescription habits can also be evaluated.

In some countries, such as Sweden and Norway, all veterinary antimicrobials are available by prescription only. Nationwide information is gathered from wholesaler statistics or veterinary drugs dispensed from pharmacies to veterinarians or end-users. In order to be able to definitely say to what animal species and for which condition a certain drug was dispensed, farm-level data has to be added to sales figures from pharmacies. (Grave et al. 1999)

In a Swedish-Norwegian study (Grave et al. 1999), information about antimicrobial drug use in cattle was examined with special reference to mastitis. Veterinary formulations registered for mastitis in cattle were identified and in order to be able to compare different formulations and dosages of the same drug, a tentative defined daily dose per cow (DDDcow) was implemented. WHO's definition on a defined daily dose (DDD) is a statistical measurement on drug consumption in humans where the DDD is the assumed average maintenance dose per day for a drug used for its main indication in adults. A point of comparison was developed by calculating DDDcow/1000 cows at risk per day. Cows at risk were defined as the counted number of dairy cows on 31 July in each year. Assessments of annual variations and trends could then be recorded and results from the two countries could be compared. Briefly, the study showed that the use of injectable antimicrobials for the treatment of mastitis in cows in Sweden was almost double that in Norway. The use of enrofloxacin in cows was 3- to 8-fold greater in Sweden than in Norway. Intramammaries, however, were used three to four times more frequently in Norway than in Sweden during the years 1990-1997. The authors considered this to be mainly due to differences in treatment practises. Although this DDDcow principle was introduced 10 years ago, for some reason it has not gained popularity. One reason could be that there are major differences in dose and dosing intervals between countries.

Chauvin et al. (2002) surveyed French veterinary pig practitioners on their prescribing habits. Using a questionnaire, the authors collected information on the last group-level antimicrobial treatment prescribed by the corresponding veterinarian. Information on the clinical indication or diagnosis was collected together with the product name, dosage and length of treatment. Information from a total of 159 prescriptions was reviewed. Diarrhoea and cough were the most common indications for the use of antimicrobials in pigs. Colistin and tylosin were used in diarrhoea and penicillins and tetracyclines in respiratory diseases. Dosages were within commonly approved limits and the treatment period varied from 3 to 21 days.

Pedersen et al. (2007) reported in kilograms the quantities of different antimicrobial substances sold for companion animals in Denmark in 2005. Information was derived from the centralized database VetStat, which is funded by the Danish Ministry of Food, Agriculture and Fisheries (Stege et al. 2003). Information was also collected from prescriptions on drugs registered for small animals that were dispensed from pharmacies to companion animals or veterinary practises. Betalactams and cephalosporins accounted for 75% of the antimicrobials sold for companion animals in 2005. As the article concentrated on antimicrobial resistance, no further information on drug usage was reported.

Similar to Finland, in Switzerland most of the antimicrobials are sold from distributors directly to veterinarians and not via pharmacies. Therefore, end-user data or veterinary prescription data are the only reliable sources to study the animal species-specific indication-based usage of antimicrobials in animals. Regula et al. (2009) performed a large study in which they collected information from prescriptions made by veterinarians during a 2-year period. Eight practices, mainly working with food-producing animals, were recruited. A total of 61 212 treatments with antimicrobials were recorded. In large animals (cattle, pigs and horses), sulfonamides and tetracyclines were the most frequently used antimicrobials. In small animals, betalactams and cephalosporins accounted for three quarters of all antimicrobials used. Detailed indication-based information was not possible to gather because veterinarians infrequently reported the indication for use and number of treated animals.

Weese (2006) carried out a retrospective study on prescriptions for dogs and cats at a veterinary teaching hospital in Ontario, Canada. During the 10 years of study, 21 152 prescriptions were given. An average of 21% of admitted animals received antimicrobials on prescription. Betalactams and first-generation cephalosporins were used the most, even in this study population. As the study did not investigate for what indication the medications were prescribed, compliance with prudent use guidelines on this aspect could not be evaluated.

As a conclusion, prescription data have a potential to provide very detailed information on antimicrobial use in animals, but this necessitates rigorous discipline from veterinarians, i.e. they have to complete all fields required in a prescription such as the indication, dosage and length of treatment. In addition, prescriptions on different medications dispensed to veterinarians as *ad usum proprium* create some bias, as the target species and indication cannot be ascertained.

2.3.3 Animal data forms

Individual animal data forms can be a very valuable tool for collecting information about species-specific drug use if the forms have been filled out accurately and completely. In Finland, the law requires veterinarians to document all medicines used for animal as well as those handed over to animal owners for home care (MMMa 8/EEO/2008). This documentation has to include the name of the owner, identification of the animal or group of animals, the time and place of delivery and detailed information on the drug, including the price.

2.3.3.1 Electronic patient records

The use of EPRs provides a systematic tool for documenting patient care, including medications. Ideally, national EPR systems would allow patient information to be available wherever the patient is treated. This would reduce the cost of repeated laboratory or diagnostic imaging measures and facilitates a more accurate review of the patient's situation, as all information is available even if the patient is relocated to another health care facility. EPRs should improve the cost-effectiveness of health services, as the need for hand-written patient files and their storage is reduced. Computerized systems should also reduce the chance of clinical errors and make surveillance of diseases or medications easier.

As with all electronic systems, there is a growing concern for security issues (The House of Commons HC-422-I, 2007). Health data are to be kept private and therefore there is a huge demand that EPRs have strict barriers to protect privacy. Only persons truly medically involved in the care of a specific patient are to access the files. This is usually enabled by personal logins and strong access control. In animal care, the issue of privacy is usually not as sensitive as in human patients; however veterinarians have an obligation of confidentiality towards the clients and their animals (AVMA 2008).

In veterinary medicine, few studies have been carried out on the implementation of electronic patient record programs. Zaninelli et al. (2007) described the integration of a new EPR system to the School of Veterinary Medicine in Milan, Italy. The scope of the study was to develop and test the compatibility of the EPR program with programs for viewing digital images in the department for diagnostic imaging and cardiology. User opinions were asked via questionnaires. The vast majority of the users felt that all clinical data was readily available, the quality of information was satisfactory and that the program made work more efficient.

Pollari and Bonnett (1996) assessed the use of electronic medical records at veterinary private practises. They found that mainly basic identification data and pre-coded procedures were documented on the computer. Therefore, the electronic record was mainly used for administrative and billing reasons rather than as a clinical tool.

Estberg and others (1998) examined the usefulness of search functions in free-text electronic patient records at the Veterinary Medical Teaching Hospital in Davis, California. The study group consisted of horses undergoing colic surgery. This is a limited population and the surgical findings are predictable enough to make a list of the most common diagnoses. For each patient, a diagnosis or description of the surgical finding was recorded in a free-text area in the electronic patient record. Surgical reports were compared with the text in this field for each patient and a summary of used terms was made. There was marked variability in naming, even though there were no discrepancies between the diagnosis on the surgery report and the one recorded on the computer. The authors concluded that to facilitate surveillance and research, a uniform naming of diagnoses as a drop-down menu would be more user-friendly than free-text records.

2.3.3.2 Manual data forms

Despite the computerized world, a large portion of animal health care data is still stored as handwritten paper documents. In many veterinary clinics and hospitals, some of the patient records are also stored as paper documents, such as cover letters from the referring veterinarian, electrocardiography-strips and night-time laboratory results.

Research in which information has to be derived from written paper forms is a time-consuming and laborious method for collecting data, but where such data are not available in electronic form, it is very valuable. Chauvin and his co-workers (2005) studied the use of antimicrobials in poultry in France. Farm owners sent a hand-written form to the slaughterhouse before sending a flock for slaughter. This form contained basic information such as the age and size of the flock and also more detailed data about medications used in the animals. Copies of the forms were then sent to a laboratory, where one of the authors entered information from the forms into a computer program for further data analysis. Usually, the information in the forms was easy to understand and unambiguous. The authors considered the data collection to be cheap and easy, as the only cost was for the postage of the forms from the slaughterhouse to the laboratory. However, in a recent study, Chauvin and others (2008) agreed that the collection of farm-level data is time-consuming and laborious.

Ortman and Svensson (2004) conducted a study where information about the use of antimicrobials in Swedish heifers was collected. The farmers recorded all usage for individual animals on separate forms that were checked every second month by a veterinarian, who also transferred the data into individual health records. The data on diseases and treatments were further collected into electronic data sheets. In total, information was collected from records for over 3000 animals, of which 335 received antimicrobials. The authors in this study did not discuss the feasibility of the data collection method.

2.3.4 Questionnaires

Questionnaire studies can be used for compiling antimicrobial drug usage data on all levels. They are especially suitable for surveying distributors (veterinarians) or end-users (farmers or companion animal owners) since they are the ones that make the final decision on how and when antimicrobials are used in animal patients.

2.3.4.1 Surveys of veterinarians

Chauvin and others (2002) sent out questionnaires to French veterinarians surveying their prescription habits for pigs. In France, all antimicrobials are prescription drugs. In order to determine which antimicrobials are used in pork-production, a questionnaire was sent to veterinarians in which they were asked to report information on their most recent group-level prescription for pigs. The researchers used a one-page questionnaire that was mailed to veterinarians specifically working with pigs or with intensive livestock production. The study group was selected using a veterinary yearbook. The questionnaire contained basic questions about the practice and more detailed questions about the most recent prescription they had made for a group of animals. Questions included for example the diagnosis, the prescribed drug, dosage and the duration of treatment. To non-respondents, a second copy of the questionnaire was sent out 3 weeks after the first one. The overall response rate was 54% after the first questionnaire and rose to 70% after the reminder. However, of all the respondents, only 37% were actively involved in pig production and had prescribed group-level treatment to pigs within the enquired time frame. Despite these shortcomings, the researchers found a mailed questionnaire to be cost-effective and easier to perform than personal or telephone interviews.

Canadian veterinarians performing bovine surgery were surveyed by Chicoine and others (2008) about their use of perioperative antimicrobials. A questionnaire was mailed to practitioners who were members of the Western Canadian Association of Bovine Practitioners. The survey contained questions about antimicrobial usage habits during surgeries performed on cattle. The response rate was 41%. As the replies were anonymous, no reminders could be sent out to non-respondents, which could be considered a limitation of the study. Other identified limitations were that only a quarter of veterinarians in Western Canada are members of the Association and therefore the study sample might not have been representative of the entire profession, and that the questions required making estimations of antimicrobial use instead of, for instance, continuous recording of daily use.

A problem encountered in mailed questionnaires is a low response rate. An interesting example of a successful response rate is a human study in which the response rate of 100% was reached (Paradiso-Hardy et al. 2002). The study population comprised of 33 human adult cardiac surgery centres in Canada. The one-page questionnaire concerning antimicrobial prophylaxis in cardiac surgery accompanied by a cover letter was addressed to the Head of Cardiovascular Surgery. Shortly after the first contact, another letter with a copy of the questionnaire was sent out to non-respondents. Furthermore, a reminder by phone was given to those who had not responded after the second contact. By this method, all centres responded to the survey. The high response rate is not discussed in the article, but the low number of targets and two contacts by mail followed by a phone reminder probably had a significant influence on the response rate. Also, the fact that the questionnaire was short and concerned a limited specialist field probably interested the respondents and encouraged them to reply.

2.3.4.2 Surveys of end-users

As a part of a larger Western Canadian study on cow-calf herds, Gow and Waldner (2009) studied antimicrobial use in these herds. As animal records did not give enough detailed information on antimicrobial use, a questionnaire directed to herd owners was used at the end of the study to complete the missing information. As the quality of animal treatment records was in 20% of the cases assessed as less than satisfactory and the questionnaire was given at the end of the study, the overall quality of the usage information was less than optimal. The authors suggested that to obtain the best possible information, prospective recording of individual animal treatments would be required.

Similar studies have also been conducted on antimicrobial usage for pigs in Western Canada by Rajić and others (2006). Herd owners were asked to complete a questionnaire on antimicrobial use indicating whether antimicrobials had been used in feed or water or for therapeutic purposes during the previous 12 months. A significant finding was that over 60% of the farms used antimicrobials added to the feed during the entire growth phase of a pig. Therefore, even if the study was conducted retrospectively, reliance on the farm owner's memory should not present a significant bias since the usage was continuous and persistent. The questionnaire itself lacked questions about the type of use, dosage and duration of treatment, issues that the authors noted as limitations of their study.

Stevens and others (2007) carried out an analogous study on pigs in the UK, also using a mailed questionnaire to farmers. The response rate was rather low (26%), even though a reminder was sent and a prize was raffled amongst the respondents. The authors discussed the reasons for the low response rate and presumed that non-respondents might not have wanted to reveal their unrigorous usage patterns. The questionnaire was nine pages long and took up to 45 minutes to complete. This could have affected the response rate, while a shorter questionnaire could have resulted in a higher response rate.

2.3.4.3 Owner compliance

Owner compliance is an elementary aspect when interpreting usage data. The fact that a veterinarian has prescribed a course of antibiotics to an animal does not automatically tell that the drug is given to the animal or how accurately it is given. Several studies on owner compliance have been carried out and have indicated considerable variability in how accurately antimicrobials are administered to animals. Owner compliance is often investigated using questionnaires either completed at the time of the control visit (Adams et al. 2005) or by giving the questionnaire to the owner at the same time as the prescription is handed over. Owner compliance surveys by telephone can also be performed (Grave and Tanem 1999).

In a study performed by Adams and others (2005), both the veterinarian treating the animal and the animal owner filled out separate questionnaires concerning how accurately the owner had followed the instructions given by the veterinarian. Client self-report turned out to be an inaccurate way of assessing client compliance, because the clients often over-estimated themselves as being more compliant than a pill count revealed them to be. Furthermore, the authors reported the major problem with questionnaires being unanswered questions or complete non-response.

Grave and Tanem (1999) also used pill counts as a tool for investigating client compliance. However, instead of having independent reviewers perform the pill count, as in the study of Adams et al. (2005), they enrolled the owners to do the pill count and the information was gathered by using a telephone interview. The owners were unaware of the study until they were contacted by phone. The authors discussed the problems with having the owner do the pill count instead of the investigator and concluded that this might have falsely given a higher rate of compliance, as animal owners often overestimate their compliance. Exactly which types of questions were asked, how many questions there were and possible limitations of the study caused by the inquiry form were not discussed.

2.4 Regulations on the distribution, prescription and use of antimicrobials in animals in Finland

In Finland, as in Sweden and Norway (Odensvik *et al*. 2001), all systemically administered antimicrobial drugs for animals are available on prescription only (NAM 2003). In Finland, veterinarians are allowed to buy medicinal products directly from wholesalers or from pharmacies. Veterinarians are also allowed to dispense drugs for the treatment of animals or groups of animals that they have examined and treated or have an ongoing healthcare surveillance agreement with. This is different compared, for example, to Denmark, where veterinarians do not have the right to dispense, but all veterinary medications are available via pharmacies. Furthermore, Danish wholesalers can only distribute medicines to pharmacies or other wholesalers (www.dvfa.dk last accessed 15.11.2010).

According to the Decree of the Ministry of Agriculture and Forestry on the use and distribution of veterinary medicinal products in Finland (MMMa 6/EEO/2008), a veterinarian has to choose the treatment that is best for the animal both medically and from an animal welfare point of view. The choice is made in mutual understanding between the veterinarian and the animal owner. The veterinarian has to comply with instructions and restrictions of use, which have been set when the marketing authorization has been granted for the veterinary medicinal product. If national recommendations for use are given for certain treatments, these also need to be taken into account. Concerning antimicrobials in specific, the Decree stipulates that if a veterinarian dispenses antimicrobials to treat a group of food-producing animals of a certain age and for the same indication more than twice a year, bacteriological culture and susceptibility testing of the causative agent has to be performed before the next treatment. Further, a veterinarian can dispense antimicrobials only for the treatment of a current disease. However, if the veterinarian and herd owner have signed a healthcare surveillance agreement and the veterinarian visits the farm 4-6 times a year, injectable antimicrobials can be dispensed for the later treatment of septic arthritis or tail biting in fattening pigs and piglets.

According to the Finnish Medicines Act (395/1987), a veterinarian who dispenses medicines to animal owners is not allowed to gain any financial benefit or to obtain income from profitable sale of the medicines.

The use of drugs in animals is further regulated by the cascade provisions of the Ministry of Agriculture and Forestry and the European Parliament and of the Council (MMMa 6/EEO/2008, Article 10 of Directive 2001/82/EC amended by Directive 2004/28/EC), which declare that animals have to primarily be treated with medicines that have been approved for use in that animal species and for the specific indication of concern. Secondary options are that an animal is treated with a drug approved for that species but for another indication or for another species. If no suitable treatment fulfilling these criteria is available, the veterinarian can choose a product approved for humans or a preparation available on special license from the NAM. As a last resort, an *ex tempore* preparation can be prescribed. The cascade is restricted to food-producing animals, as only active substances for which a MRL has been established can be used (EU 37/2010 (Table 1), EC 470/2009).

Horses are classified as food-producing animals, although in Finland the annual number of horses slaughtered for human consumption is very low, being 770 horses in 2008 and 833 in January-October 2010 compared to 266 815 cows that were slaughtered in 2008 and 190 927 in January-October 2010 (www.matilda.fi → Teurastamotilasto. Last accessed 15.11.2010). In addition to medicines approved for use in food-producing animals, horses that have a valid equine passport can be treated with substances approved by the European Commission (EC No 1950/2006). This regulation provides a list of substances essential for the treatment of equidae. The antimicrobials listed are ticarcillin for *Klebsiella* spp. infections, azithromycin and rifampin for the treatment of *Rhodococcus equi* infections and amikacin for septic arthritis as an alternative to gentamicin or other aminoglycosides. These antibiotics can be used in horses with a withdrawal period of 6 months. Horses that have been treated with, for example, metronidazole or other antimicrobials listed in Commission Regulation EU 37/2010, Table 2 cannot be slaughtered for human consumption, because no MRL has been established for these substances.

A Finnish national Regulation of the Ministry of Agriculture and Forestry on restriction of the usage of certain drugs for the treatment of animals first entered into force in 1996 (MMMp 515/1996). The Regulation was established to ensure that no such drugs are used in animals that can harm human health, animals or the environment or jeopardize the treatment of diseases in humans. In 1998, section 3a was added prohibiting the use of certain antimicrobials in animals (MMMp 935/1998). The Regulation was replaced in 2008 by a Decree of the Ministry of Agriculture and Forestry (MMMa 847/2008) and presently the 11th section of the Decree comprises a list of antimicrobial agents that are prohibited for use in all animal species in Finland:

1) avoparcin, vancomycin and teicoplanin
2) virginiamycin
3) third and fourth generation cephalosporins
4) rifampicin and rifabutin (*rifabutin added in 2008*)
5) moxifloxacin, ofloxacin, levofloxacin and gatifloxacin, with the exception of local treatment of ocular infections in horses and companion animals *(added in 2008)*
6) tigecycline (*added in 2008)*
7) mupirocin (*added in 2008)*
8) telitromycin (*added in 2008)*
9) daptomycin (*added in 2008)*
10) linezolid (*added in 2008)*
11) quinupristine-dalfopristine (*added in 2008)*
12) carbapenems (*added in 2008)*
13) monobactams (*added in 2008)*

The abovementioned drugs can, however, be used in animals if the drug has marketing approval in Finland or it is available as a veterinary product on a special license issued by Fimea. In order to obtain such a special license, the veterinarian has to provide sufficient scientific evidence that no approved product is useful for the animal or animals. As an exception to the Decree, rifampicin can be used in combination with azithromycin, erythromycin or clarithromycin for the treatment of infections caused by *Rhodococcus equi* in foals. To date, two products containing a third-generation cephalosporin have been approved in Finland by the centralized authorisation procedure of the European Union, i.e. cefovecin registered for dogs and cats and ceftiofur for cattle and pigs, and thus they can be legally used for these animal species.

In addition to the abovementioned list, the use of antimicrobials such as nitrofurans, nitroimidazoles (for example metronidazole) and chloramphenicol is forbidden in food-producing animals due to their potential hazard to human health (section 9 of MMMa 847/2008). These drugs can, however, be used in horses that have been removed from the food chain by making a note in the individual equine passport (EC 1950/2006).

Overall, the use of antimicrobials in animals in Finland is widely restricted by law. So far, the relatively low grade of resistance in animal pathogens has enabled the use of narrow-spectrum drugs and a rather limited arsenal of antimicrobials.

3 Aims of the study

1. To explore the clinical use of antimicrobials in dogs, cats, cattle and horses in Finland;
2. To analyze the antimicrobial usage with respect to prevailing national animal species-specific and indication-based prudent use guidelines on antimicrobial use;
3. To gain experience of the different methods used for collecting antimicrobial usage data in Finland.

4 Materials and methods

Four separate sets of data on antimicrobial use in dogs, cats, cattle and horses (studies A-D) were collected and analysed using different methods of data collection. The methods used included retrospective cross-sectional surveys of prescriptions, surgery log books and patient records from the electronic database of the Veterinary Teaching Hospital of the University of Helsinki (later Veterinary Teaching Hospital), a retrospective cross-sectional survey of prescriptions from the University Pharmacies and a prospective survey to practitioners on antimicrobial usage. Information gathered from studies A, B and C has been published in an overlapping manner in the original publications I-IV.

4.1. Study A: survey of prescriptions from the Veterinary Teaching Hospital patient record database (I and IV)

In study A, data were collected by a retrospective computer search of the patient record database of the Veterinary Teaching Hospital. Antimicrobial prescriptions for companion animals were included from a 6-month period, November 2000 to April 2001. During the study period, 2281 prescriptions were dispensed. Of these, 1780 were for dogs (78%) and 421 for cats (18%). The additional 91 (4%) prescriptions were for other animals.

Information such as the patient ID number, animal species, trade name of the drug, pharmaceutical form and dosage of the prescribed drug, length of the treatment period and the indication was gathered. The data were then sorted by animal species, antimicrobial group and indication.

The Veterinary Teaching Hospital serves as a both a primary care clinic for the larger capital city area of Helsinki as well as a referral hospital for patients nationwide. No geographical investigation of the patients was performed, but the majority of the patient load is from southern parts of the country and areas surrounding the capital city.

4.2. Study B: survey of prescriptions from the University Pharmacies (II)

A cross-sectional retrospective study on prescriptions for animals dispensed by all University Pharmacies (n = 17) in Finland (Table 5) was performed during a one month period in April 2001. A total of 2719 prescriptions were dispensed, 1898 for dogs (70%), 384 for cats (14%) and the rest for other species. Of all prescriptions 53% were for antimicrobials.

Two persons went manually through the printouts on dispensed prescriptions and information was collected into Excel spreadsheets. Pharmacies were asked to provide the total numbers of dispensed prescriptions during the investigation period (Table 5).

The following information was collected from each prescription: animal species, trade name of the prescribed drug, formulation, dosage, package size, indication and duration of the treatment. It was also recorded whether the prescribed drug was registered for humans or animals. Antimicrobial agents were further divided into subgroups according to the active substance.

The data were grouped according to animal species, antimicrobial group and indication. The length of treatment was recorded as a mean and range for all animals of the same species receiving a certain drug for a specific condition.

Table 5. Prescriptions dispensed for dogs and cats during April 2001 from University Pharmacies (n = 17) in Finland (II, IV).

University Pharmacy (n = 17)	Prescriptions for animals	% of total	Total number of prescriptions
Helsinki I	3	0.06	4 624
Helsinki II	547	16.5	3 309
Helsinki III	226	0.8	27 561
Helsinki IV	68	0.4	18 270
Helsinki V	139	0.5	27 405
Joensuu	304	2	15 578
Jyväskylä I	163	1	16 258
Jyväskylä II	7	0.1	5 284
Kemi	41	0.4	9 682
Lahti	72	0.4	18 695
Lappeenranta	154	1.2	13 178
Oulu	247	1	24 635
Pori	155	0.9	17 314
Salo	62	0.5	12 391
Savonlinna	104	1.1	9 164
Tampere	245	0.8	30 518
Turku	182	0.7	24 561
Total	**2 719**	**1.0**	**278 427**

4.3. Study C: prospective survey of practitioners (III and IV)

A prospective cross-sectional survey was carried out via a questionnaire (Appendix 1) sent out to randomly selected practitioners nationwide. Ninety-six percent of the Finnish veterinarians were members of the Finnish Veterinary Association in 2002. Only practicing veterinarians were chosen as the source population (n = 681). Since veterinarians represented different type of practices and the size of these groups varied, weighted random computer-assisted sampling was carried out to ensure a representative sample of each group and to ensure that the final respondents would represent the source population (III).

Practitioners were asked to complete one questionnaire form for each animal they treated with antimicrobials during a 7-day period in May 2002. A similar questionnaire survey had previously been carried out in human medicine (Rautakorpi et al. 2001), and for veterinary purposes this questionnaire was modified in order to take into account veterinary-specific aspects (Table 6). Information from all individual animals was separately analysed, even if mass treatment had been carried out. During the study period, 2850 animals received antimicrobial treatment, most commonly cattle (n = 1308), dogs (n = 989) and cats (n = 311). The duration of clinical signs was estimated by the veterinarian according to the history provided by the owner of the animal. The prescribed length of the treatment was counted as the treatment duration.

Table 6. Information collected in the prospective survey of practitioners (III, IV) and variables entered into the database.

Data recoded	Type of variable	Description
1. Animal species	Coded	Dog, cat, horse, cattle, pig, fur animal, fish, other
2. Type of visit	Coded	Normal daytime visit, on-call visit or prescription by phone
3. Main diagnosis	Coded	18 pre-coded alternatives or a possibility to give own diagnosis
4. Duration of clinical signs	Coded	0-3, 4-7, 8-14 days or longer
5. Clinical examination or diagnostic tests	Coded	8 pre-coded alternatives[1] and possibility to describe other tests or procedures
6. Antimicrobial drug administered by the veterinarian	Text	Product name and strength; amount given
7. Antimicrobial drug given to the owner to continue the treatment (peroral or injectable)	Text	Product name and strength; duration of treatment
8. Antimicrobial drug given to the owner to continue the treatment (local treatment, including intramammaries)	Text	Product name and strength; duration of treatment
9. Was the choice of product affected by allergy, other disease, owner's wishes, recurrent or chronic infection or something else?	Coded	
10. Was this the first visit or a follow-up visit?	Coded	

[1)] Clinical examination, urinary dipstick, secretion microscopy, leucocytes, clavulanic acid test, bacterial culture and resistance, X-ray or ultrasound examination, California Mastitis Test

In addition to the questionnaire, each participant received a cover letter explaining the aims of the study and instructions on how to fill out the questionnaire. Background information was also collected from each respondent. Anonymous responses were accepted, although the questionnaire had a number indicating the group to which the responding veterinarian belonged. The following background information was collected from each participating veterinarian: the geographical area (province), the gender, the year of graduation, the degree and the field of specialization.

4.3.1. Statistical analysis

In the prospective survey for practitioners (publications III and IV), a χ^2 test was performed in order to determine whether the sample population was representative of the source population, analysing characteristics such as the type of practice, geographical area, gender, year of graduation, degree and field of specialization. These characteristics were pre-coded in the questionnaire so it could be transferred into a database in ASCII format. Both SAS (version 9.1, SAS Institute Inc, NC, USA) and Microsoft Excel (version 10, Microsoft Corporation, Redmond. WA, USA) programs were used for the data analysis.

4.4 Study D: survey on equine patient records from the Veterinary Teaching Hospital (unpublished data)

The use of antimicrobials for equine patients was studied using two different data collection methods. As the equine results have not been previously published, they are presented in this thesis in order to share the information.

The first set of data was collected using a questionnaire survey to practitioners (see 4.3), and included information on 89 horses.

A second study concerning antimicrobial use in horses was performed by utilizing the electronic patient records at the Veterinary Teaching Hospital. Antimicrobial usage was recorded from a targeted population of horses undergoing colic surgery during 2005-2007. The surgery log book and patient-specific anaesthesia forms were examined to collect the patients and to record information on administered perioperative antimicrobials. Thereafter, the electronic patient records were reviewed and all antimicrobial agents administered to each patient were collected in a spreadsheet, along with information on the duration of treatment. Only horses that survived until discharge (n = 74) were included in further studies on antimicrobial use.

According to a survey to diplomates of the American College of Veterinary Surgeons in the United States of America, antimicrobials should be administered perioperatively and for 1-10 days postoperatively (Traub-Dargatz et al 2002). The aim of this study was to determine the usage patterns at our facility and to unify the practice of antimicrobial use in equine patients undergoing colic surgery.

5 Results

The conclusions concerning usage of antimicrobials in dogs and cats, respectively, were uniform in studies A and B (dogs) and studies A, B and C (cats), respectively, as can be seen from the original publications. To widen the horizon on animal species-specific use, the results here are shown per species.

5.1. Antimicrobial usage in dogs (I and II)

Antimicrobial usage in dogs was investigated by using two different sets of data: prescriptions on antimicrobials for patients at the Veterinary Teaching Hospital (study A) and prescriptions dispensed from University Pharmacies (study B). The animal species distribution in study A is illustrated in Figure 1 and for study B in Figure 2. From these sets of data, further analyses were performed for dogs as well as cats.

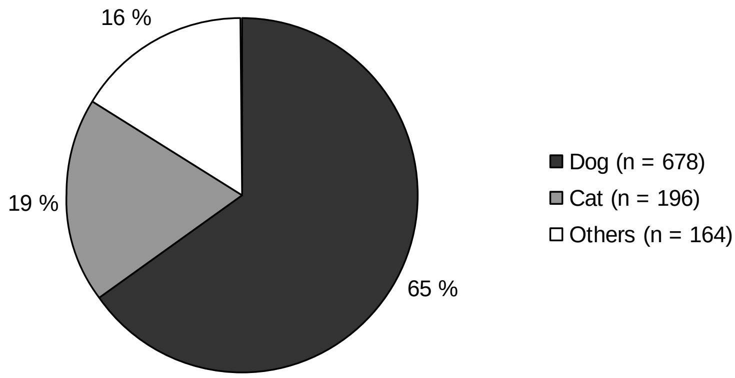

Figure 1. Distribution of animal species for which peroral antimicrobial drugs were prescribed at the Veterinary Teaching Hospital (I, IV) (N_{tot} = 1732). Others include rodents, rabbits, birds, pigs and reptiles.

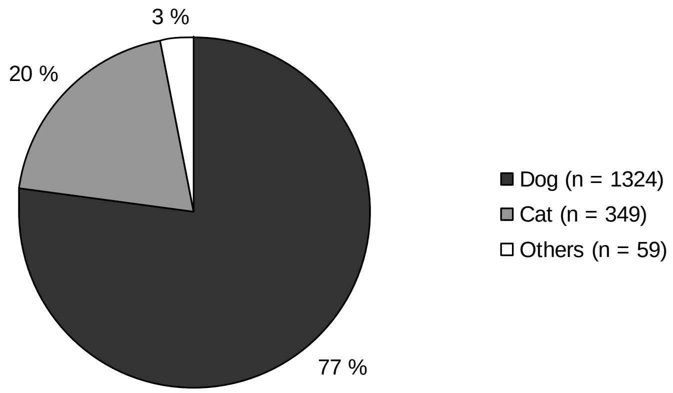

Figure 2. Distribution of animal species for which peroral antimicrobial drugs were dispensed from the University Pharmacies (II, IV) (N_{tot} = 1038). Others include cattle, rodents, birds, pigs and fish.

A total of 2739 prescriptions on antimicrobials for dogs were reviewed. Of these, 73% (n = 2002) were orally administered antimicrobials. Betalactams were the most frequently prescribed peroral antimicrobials, in 66% of the cases in both studies. Table 7 summarises the distribution of different groups of antimicrobials prescribed for dogs.

Table 7. Characteristics of the antimicrobial drugs prescribed for dogs at the Veterinary Teaching Hospital (I) and dispensed from the University Pharmacies (II).

	Study A (Veterinary Teaching Hospital)	**Study B (University Pharmacies)**
Prescriptions (n_{tot} = 2739)	**1780**	**959**
Oral formulations (n_{tot} = 2002)	*74% (n = 1324)*	*71% (n = 678)*
Topical formulations (n_{tot} = 737)	*26% (n = 456)*	*29% (n = 281)*
Distribution of oral drugs		
Betalactams	**66% (n = 880)**	**66% (n = 448)**
Penicillins and aminopenicillins	*19%*	*16%*
Amoxicillin-clavulanate	*32%*	*38%*
Cephalexin	*49%*	*45%*
Trimethoprim-sulfonamides	**18%**	**18%**
Lincosamides and macrolides	**8%**	**8%**
Fluoroquinolones	*	*
Others [1]	*	**5%**

[1] Aminoglycosides, fungal drugs, metronidazole, nitrofurantoin and tetracyclines

* Minor number of treated animals, total percentage of less than 5%

In study A, information was gathered from patient files, in which the diagnosis and reason for treatment could be found in 95% (n = 1694) of the cases. In the remaining 5% (n = 86), no reason for prescribing an antimicrobial agent could be identified. In study B, the indication for which the medication had been prescribed was clearly stated in only 28% (n = 273) of the prescriptions. The distribution of different antimicrobials for a variety of conditions in dogs is presented in Table 8.

Table 8. Distribution of oral formulations of antimicrobials prescribed for dogs for different indications in prescriptions from the Veterinary Teaching Hospital (I) and the University Pharmacies (II).

Distribution of oral antimicrobials prescribed for dogs	**Skin and ear infections (n = 568)**	**Genito-urinary infections (n = 248)**	**Gastro-intestinal infections (n = 225)**	**Respiratory infections (n = 112)**
Betalactams	**82% (n =464)**	**39% (n = 97)**	**48% (n = 107)**	**81% (n = 91)**
Penicillins and aminopenicillins	*21%*	*21%*	*21%*	*23%*
Amoxicillin-clavulanate	*19%*	*64%*	*67%*	*47%*
Cephalexin	*60%*	*15%*	*12%*	*30%*
Trimethoprim-sulfonamides	**6%**	**50%**	**18%**	**10%**
Lincosamides and macrolides	**6%**	*	**26%**	*
Fluoroquinolones	*	**9%**	*	*
Metronidazole	*	*	**6%**	*
Others [1]	*	*	*	*

[1] Fungal drugs, nitrofurantoin and tetracyclines

* Minor number of treated animals, total percentage of less than 5%

Infections of the skin and external ear canal were the most common reasons for prescribing antimicrobial treatment for dogs in both studies, accounting for 45% and 54% of the prescriptions, respectively. Both peroral and topical drugs were used for the treatment of these diseases. Urinary tract infections were also frequently diagnosed and treated (12% and 16% of the prescriptions in studies A and B, respectively).

In systemic treatment of skin and ear infections, betalactams were used the most. Cephalexin was the most popular, comprising 49% of all prescriptions. Furthermore, amoxicillin+clavulanate was prescribed in 15% of the cases. According to the prevailing national antimicrobial guidelines (MMM 1996), they were both second line drugs, as clindamycin and trimethoprim-sulfonamides were the recommended first line antimicrobials at the time. In study A, the mean period of treatment for skin infections was 14 days with cephalexin (range three to 33 days), and 13 days with amoxicillin+clavulanate (range three to 20 days).

Trimethoprim-sulfonamides were used most frequently for the treatment of urinary tract infections, as 50% of the dogs received trimethoprim-sulfonamides (Table 8). The mean treatment period was 9 days (range seven-21 days). In addition, amoxicillin+clavulanate was used in 25% of the cases. This usage pattern was consistent with the recommendations.

Of the peroral drugs, fluoroquinolones comprised 4% of the prescriptions (Table 7). In study B, the majority (40%) of the fluoroquinolones were used for the treatment of genitourinary infections.

5.2. Antimicrobial usage in cats (II and IV)

The indication-based use of antimicrobials to feline patients was investigated using three methods. In study A, prescriptions of antimicrobials for cats treated at the Veterinary Teaching Hospital were reviewed. In study B, prescriptions for cats were collected from the University Pharmacies in Finland. Finally, in study C, the condition-based use of antimicrobials for cats was investigated in a nationwide survey of practitioners.

A total of 958 cats were treated using antimicrobials in the three studies. Oral drugs were the most frequently used, as 77% (n = 738) of the cats received per oral antimicrobials (Table 9).

Table 9. Characteristics of the antimicrobial drugs prescribed for cats at the Veterinary Teaching Hospital (IV), dispensed from the University Pharmacies (II) and used by practitioners participating in the nationwide survey (IV)

	Study A Veterinary Teaching Hospital	**Study B University Pharmacies**	**Study C Practitioners**
Prescriptions or treatments (n_{tot} = 958)	**421**	**226**	**311**
Oral formulations (n_{tot} = 738)	*83% (n = 349)*	*87% (n = 196)*	*62% (n = 193)*
Topical formulations (n_{tot} = 220)	*17% (n = 72)*	*13% (n = 30)*	*38 % (n = 118)*
Distribution of oral drugs			
Betalactams	**89% (n = 311)**	**78% (n = 153)**	**91% (n = 175)**
Penicillins and aminopenicillins	*62%*	*52%*	*50%*
Amoxicillin-clavulanate	*26%*	*39%*	*42%*
Cephalexin	*12%*	*10%*	*7%*
Lincosamides and macrolides	*	**9%**	*
Fluoroquinolones	*	**5%**	*
Tetracyclines	**5%**	*	*
Others [1]	*	**6%**	*

[1] Fungal drugs, metronidazole and trimethoprim-sulfonamides

[*] Minor number of treated animals, total percentage of less than 5%

In study A the diagnosis and reason for antimicrobial treatment were available in 94% (n = 397) of the cases. In the remaining 6% (n = 24), no valid reason for prescribing an antimicrobial agent could be identified. In study B, the indication for which the medication had been prescribed was clearly stated in 38% (n = 85) of the prescriptions.

The distribution of oral antimicrobials for the four most common conditions is presented in Table 10. Skin and ear infections (including bite wounds and scratches) were the most common diagnoses in studies A and C. The recommendations were complied with, since the most frequently used antimicrobials were betalactams, primarily penicillins and aminopenicillins, followed by amoxicillin-clavulanate. Urinary tract infections were the most common (study B) or second most common (studies A and C) indication for antimicrobial treatment. Aminopenicillins and amoxicillin-clavulanate were the first and second line drugs of choice in the guidelines. Compliance with the recommendations was good, as 84% of the treatments consisted of these two medications (Table 10).

Table 10. Distribution of oral formulations of antimicrobials used for different indications in cats in prescriptions from the Veterinary Teaching Hospital (IV), University Pharmacies (II) and in the prospective survey of practitioners (IV).

Distribution of oral antimicrobials distributed for cats	**Skin and ear infections (n = 191)**	**Genito-urinary infections (n = 190)**	**Gastro-intestinal infections (n = 74)**	**Respiratory infections (n = 69)**
Betalactams	**94% (n = 179)**	**88%(n = 167)**	**82% (n = 61)**	**71% (n = 49)**
Penicillins and aminopenicillins	*54%*	*59%*	*49%*	*57%*
Amoxicillin-clavulanate	*30%*	*36%*	*48%*	*35%*
Cephalexin	*16%*	*5%*	*3%*	*8%*
Trimethoprim-sulfonamides	*	**5%**	*	*
Lincosamides and macrolides	*	*	**16%**	**6%**
Fluoroquinolones	*	**7%**	*	*
Tetracyclines	*	*	*	**20%**
Metronidazole or fungal drug	*	*	*	*

[*] Minor number of treated animals, total percentage of less than 5%

5.3. Antimicrobial usage in cattle (III)

Of the 2850 animals that were treated with antimicrobials during the seven-day questionnaire survey of practitioners, cattle were the animal species treated most frequently as 46% (n = 1308) of the animals were cows.

Of a total of 262 practitioners who responded to the survey (response rate 38%), 42% (n = 109) treated cows during the study week. The number of treated animals varied between 1 and 42, the median and mode being 4 animals. Mastitis and dry-cow therapy were the most common indications for antimicrobial therapy in cattle (Figure 3).

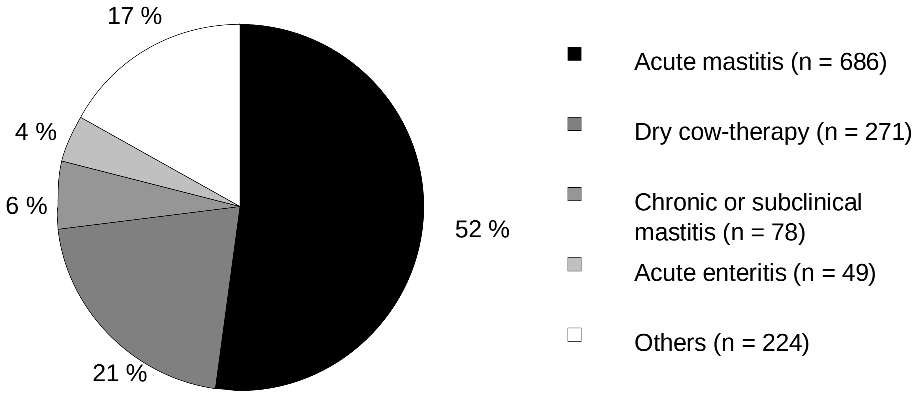

Figure 3. The four most common reasons for antimicrobial treatment in cattle during the seven-day study on practitioners' antimicrobial usage patterns (III).

In acute mastitis, treatment was initiated within 0-3 days in 70% of the (n = 482). In 18% (n = 122) and 4% (n = 30) of the cases, treatment was begun in 4-7 and over 8 days, respectively, from the point at which the first signs of mastitis were noticed.

Acute mastitis was most commonly treated with penicillin G (83%) or enrofloxacin (11%). This was in line with the prevailing national recommendations (MMM 1996) which suggested that acute mastitis caused by Gram-positive cocci should be treated with penicillin G, and if the clinical signs refer to mastitis caused by *Escherichia coli*, the second line choice was enrofloxacin or trimethoprim-sulfonamides. Before initiating systemic antimicrobials, supportive therapy should be given and the effect monitored. The median length of treatment of acute mastitis was 4 days (range 1-8 days).

Group treatments (3-20 animals at the same visit) were carried out in 31% (n = 34) cases, and during these visits a total of 177 (14%) animals were treated. Of these, 108 (61%) animals received dry-cow therapy: 58 cows were administered intramammaries only, 24 cows were treated with parenteral drugs, 23 animals were treated with a combination therapy of a parenteral drug and intramammaries and three received an oral drug. Of the parenteral drugs, benzyl- and procaine penicillin was used most frequently (n = 38; 81%), followed by enrofloxacin (n = 5) and oxytetracycline (n = 4). The oral drug used was dihydrostreptomycin tablets.

5.4. Antimicrobial usage in horses (unpublished data)

5.4.1. Questionnaire survey

Antimicrobial use in horses was investigated in a survey of practitioners (study C). During the seven-day study period, a total of 89 horses received antimicrobial treatment. Thirteen of the horses received only a single dose of an antimicrobial during the primary visit. The rest of the horses (n = 76) received antimicrobials as a course. Sixty-eight horses (89%) received either benzylpenicillin (n = 36; 47%) or trimethoprim-sulphadiazine (n = 32; 42%). Seven horses (9%) were treated with topical preparations only. One horse (1%) received a five-day course of gentamicin.

The diagnosis was mentioned for 60 horses (67%), of which 29 (48%) horses were treated with trimethoprim-sulphadiazine and 31 (52%) horses with benzylpenicillin. The most common indication was skin infections (n = 21) and infection of the urogenitals, mainly retention secundarium and endometritis (n = 18). According to the prevailing Finnish guidelines on antimicrobial use, penicillin G and trimethoprim-sulfonamides were the first and second line choices in skin infections in horses (MMM 1996). Compliance with the guidelines was therefore considered satisfactory. For puerperal endometritis, the recommendation was penicillin G combined with either gentamicin or trimethoprim-sulfonamides.

The length of the course of treatment was similar, regardless of the indication, trimethoprim-sulfadiazine was used for a mean of seven days whereas the mean length of treatment with benzylpenicillin was five days (Table 11).

Table 11. The length of antimicrobial treatment of 60 horses which were treated for various infectious conditions by veterinarians participating in the prospective survey of practitioners (unpublished data).

Antimicrobial drug	**Length of treatment (days)**			
	Mean	**Mode**	**Min**	**Max**
Trimethoprim-sulfonamides (n = 29)	6,9	7	2	14
Benzyl penicillin (n = 31)	5,4	5	2	10

5.4.2. Equine Teaching Hospital patient record data

A total of 125 horses had colic surgery throughout 2005-2007 at the Veterinary Teaching Hospital (study D). Of these, 27 (22%) horses were euthanized or died in surgery and were excluded from further studies.

Of the remaining 98 horses that recovered from surgery, a total of 74 (59%) horses survived to discharge from the hospital. The survival-to-discharge rate in horses that needed bowel resection was five horses out of 13 (38%), while the rate in the non-resection group was 69 horses out of 85 (81%).

The most frequently used therapy both pre- and postoperatively was the combination of penicillin G and gentamicin. This choice was correct according to the prevailing Finnish guidelines on antimicrobial use (MMM 2003). Preoperatively, out of a total of 74 horses, 65 horses (88%) received antimicrobials, 55 (85%) of them penicillin G and gentamicin. Penicillin alone was given to nine horses (12%) and another nine horses were not recorded to have received any preoperative antimicrobials. One horse was administered penicillin G and trimethoprim-sulfadiazine.

In the immediate postoperative period <24 hours after surgery, out of a total of 74 horses, 57 patients were administered antimicrobials; 38 (67%) were given penicillin G and 19 (33%) penicillin G combined with gentamicin. Amongst these 57 horses, nine horses did not receive any antimicrobials preoperatively. Fourteen horses (78%) that received gentamicin postoperatively had not received it preoperatively.

Antimicrobial treatment was discontinued within the first 24 hours in two horses. The remaining 72 horses were medicated for a median of three days (average length of treatment 10 days; range 0-34 days). The most commonly used medication consisted of penicillin G and gentamicin, as 92% (n = 68) were treated with that combination. Horses which were treated with penicillin alone or in combination with gentamicin were all treated for a maximum of nine days (n = 45; 61%). The longer the course of treatment was the more number of drugs were involved. Nineteen horses (26%) received trimethoprim-sulfadiazine, 11 horses (15%) enrofloxacin, six horses (8%) metronidazole and one horse (1%) erythromycin usually in combination with other antimicrobials.

The length of stay in hospital varied between four to 31 days; 53% of the patients (n = 39) stayed in the hospital for 10-14 days. The average length of antimicrobial treatment was 10 days. No obvious relation between the length of antimicrobial treatment and length of stay in hospital was observed.

6 Discussion

Due to growing concern over the further development of antimicrobial resistance in both human and veterinary medicine, it is important that detailed information is obtained about antimicrobial usage patterns. To achieve this purpose, indication-based and animal species-specific usage data are needed. On the basis of these data it is possible to assess for which indications antimicrobials are being prescribed and whether prudent use guidelines are being followed. Information about the usage patterns may also provide a basis for the updating of prudent use guidelines and continuing education of veterinarians on the proper use of antimicrobials, as well as providing information to animal owners about the risks of antimicrobial resistance.

6.1 Indication-based use of veterinary antimicrobials in Finland and compliance with prudent use guidelines and legislation

In our research, emphasis was put on obtaining a detailed overview of the animal species-specific use of veterinary antimicrobials in Finland, as this information was not previously available. Data were collected from prescriptions issued by veterinarians at the Veterinary Teaching Hospital, from prescriptions dispensed from the University Pharmacies to end-users and by using a questionnaire directed to practicing veterinarians enquiring about their antimicrobial usage habits. In addition, direct use in hospitalized patients was investigated.

Prudent use guidelines were complied with well in all studies, and the use of second line drugs, such as fluoroquinolones, was moderate. No illegal use of prohibited antimicrobial substances was noted in any of the studies (A-C). Mupirocin had been used in a few dogs and cats for topical treatment of skin infections, however, mupirocin was prohibited for use in animals only in 2008 (MMMa 847/2008).

6.1.1 Antimicrobial use in dogs and cats (I, II, IV)

Antimicrobial agents were the most commonly used group of medicines in small animals in Australia (Watson and Maddison 2001) and Norway (Grave et al. 1992). In our research aminopenicillins and cephalexin were the most commonly used antimicrobials in dogs and cats. Betalactams are also widely used in other Nordic countries (Odensvik et al. 2001). In Norway, trimethoprim-sulfonamides were the most commonly used drug in dogs and cats in 1990-1998. However, betalactams were introduced to the veterinary market as late as 1994. Since then, the percentage use of betalactams has increased. (Odensvik et al. 2001). In our research material, infections of the skin and wounds were the most common reason for antimicrobial treatment in both dogs and cats. According to the national guidelines at the time of the collection of our research data, macrolides and lincosamides or trimethoprim-sulfonamides were the first choices for systemic treatment of skin infections (MMM 1996). However, according to our research, amoxicillin-clavulanic acid and cephalexin were the drugs used most frequently. Bacteria causing skin infections are commonly staphylococci, which in Finland showed increased resistance to clindamycin at the end of the 20th century and was over 20% in 2002-2003 (FINRES-Vet 2001-2005). However, since then the resistance to clindamycin has decreased annually and was down to 12% in 2008 (FINRES-Vet 2007-2009, FINRES-Vet 2005-2006, FINRES-Vet 2001-2005). The resistance of canine staphylococci to first generation cephalosporins has been less than 10% until 2009, when it suddenly rose to 22% (FINRES-Vet 2007-2009, FINRES-Vet 2005-2006, FINRES-Vet 2001-2005). This drastic rise is due to an increase in the number of oxacillin resistant strains in clinical samples. The investigation of the affair is still pending.

The national guidelines have been updated subsequently and the most recent recommendation for treatment of deep skin infections in dogs and cats is first generation cephalosporins and amoxicillin-clavulanate. Clindamycin is recommended for use only after susceptibility testing (Evira 2009). This point of the recommendations needs to be closely monitored, though, as the percentage of oxacillin/methicillin-resistant strains in canine staphylococci is imminently rising and thus makes the bacteria resistant also to cephalosporins and other betalactams most commonly used for treatment of skin infections in dogs (FINRES-Vet 2007-2009).

The length of treatment of skin infections in dogs in our studies was approximately 14 days, which can be considered a rather short course. According to guidelines on effective treatment of pyoderma in dogs the recommended length of treatment should extend seven days after the clinical signs have withdrawn and typically a course of 3-6 weeks is needed for clinical cure (Dowling 1996). There are, however, to my knowledge no controlled studies on optimal length of treatment with antimicrobials in infections in animals. It is known that suboptimal dosing with low doses and long courses promote the development of antimicrobial resistance (Guillemot et al. 1998). Therefore, it would be important to pay attention to dosage and length of treatment when giving recommendations on indication-based antimicrobial use in animals.

Urinary tract infections in dogs were most commonly treated with trimethoprim-sulfonamides, which is in line with the national recommendations. In cats, amoxicillin and amoxicillin-clavulanic acid were frequently used for urinary tract infections. These are mostly effective drugs in treating urinary tract infections caused by bacteria in cats, as the most commonly isolated pathogens include susceptible *E.coli*, *Staphylococcus* spp. and *Streptococcus* spp. (Kruth 2006).

6.1.2 Antimicrobial use in cattle

In our study penicillin G was the most commonly used antimicrobial in cattle. Penicillin was also the most frequently used antimicrobial in cattle in Sweden and Norway (Grave et al. 1999).

Mastitis is the most common reason for antimicrobial treatment in dairy cattle (Pol and Ruegg 2007, Grave et al. 1999). In our study material, acute or subclinical mastitis was the indication for treatment in 58% of the cattle. Penicillin G is widely used in mastitis in cattle in Finland, as staphylococci frequently cause clinical mastitis in dairy cows (Taponen and Pyörälä 2009). The use of penicillin G in mastitis is appropriate, as in Finland 75% of the bovine staphylococci are susceptible to penicillin (FINRES-Vet 2005-2006). According to the guidelines, penicillin G is the drug of choice when treating mastitis caused by streptococci or penicillin-sensitive staphylococci (Evira 2009). In acute mastitis the treatment is usually initiated before the microbiological culture and susceptibility results are ready. Therefore, the clinical signs, history of mastitis in the cow in question and history of mastitis on a herd level direct the choice of antimicrobial in cases of acute mastitis. Usually preliminary results show already after one day whether the causative agent is a gram-positive cocci or *E.coli* and treatment can be corrected thereafter.

Acute mastitis was in 11% of the cases treated with enrofloxacin, a fluoroquinolone recommended as a second-line choice in coliform mastitis. In Finland approximately 12% of the acute clinical mastitis cases are caused by coliforms, thus it can be concluded that Finnish veterinarians followed the guidelines well (Nevala et al. 2004).

6.1.3 Antimicrobial use in horses (unpublished data)

In the study on the antimicrobial usage patterns among practitioners (study C), most horses were treated with penicillin G or trimethoprim-sulfonamide, regardless of the condition. This is probably due to the minimal arsenal of available approved antimicrobial drugs for horses. Antimicrobials registered for use in horses in Finland include trimethoprim-sulfonamide and penicillin G (Pharmaca Fennica® Veterinaria 2009). In addition, antimicrobials registered for use in other production animals can be used and, if a note has been made in the horse's passport that the horse cannot be slaughtered for human consumption, drugs listed in Commission Regulation EU 37/2010 Table 2 can also be used. The majority of the patients in the study were treated for skin infections or endometritis. According to the national guidelines that were in force when the study was performed, penicillin G and trimethoprim-sulfonamide were the first- and second-line choices for systemic treatment of superficial skin disorders. For endometritis, the recommendation included combining penicillin G with either trimethoprim-sulfonamides or gentamicin (MMM 1996). Therefore, it can be concluded that the guidelines were fairly well complied with, even though the number of animals was very limited. The study was performed during a 7-day period in May, which might have affected the proportion of different conditions, as endometritis would probably not be a common indication during the winter. The treatment recommendations have been updated in 2009 (Evira 2009), and concerning skin infections, systemic treatment is listed as a second-line choice. Skin infections should primarily be treated locally with antiseptic preparations to avoid systemic exposure to antimicrobials. For the same reason, endometritis is now recommended to be primarily treated with local uterine lavage, and systemic antimicrobials are only used in the case of generalized disease.

In study D, antimicrobial use in horses undergoing colic surgery was investigated. Preoperative administration of antimicrobials was common, as 88% of the horses received either penicillin G alone (14%) or combined with gentamicin (85%). Broad spectrum antimicrobials are recommended in surgeries where the risk of infection exceeds 5% (Southwood 2006). In surgeries where the post-operative risk of infection is high, such as in colic surgeries, a perioperative antimicrobial treatment consisting of penicillin G and gentamicin is recommended (Santschi 2006). This is in line with results from our study and with the national recommendations (MMM 2003). According to an American study by Traub-Dargatz et al. (2002) veterinarians who are diplomates of the American College of Veterinary Surgeons performing equine surgery at veterinary teaching hospitals also use a preoperative antimicrobial protocol of penicillin G and gentamicin in horses undergoing colic surgery. The duration of treatment depends on the clinical findings (Traub-Dargatz et al. 2002). In horses not requiring bowel resection, the recommended duration of treatment is 72 hours (three days) postoperatively (Traub-Dargatz et al. 2002, Santschi 2006). The median period of treatment in our study was three days.

In conclusion, Finnish equine practitioners seemed to comply fairly well with national prudent use guidelines on antimicrobial usage.

6.2 Problems and benefits of different data collection methods

Different methods for data collection on antimicrobial usage in food-producing animals have been thoroughly reviewed by The Advisory Committee on Animal Antimicrobial Use Data Collection in the United States (DeVincent and Viola 2006a, b). However, considering the population and the geographical dimensions of the United States and other large countries compared to small countries such as Finland and Scandinavian countries, the methods, aims and means for studying antimicrobial usage are different (Table 12). In Finland the production structure is similar nationwide and also similar to other Scandinavian countries. In Finland for example the dairy units are small, usually family owned and with no paid manpower. Herd size on dairy farms varies from tens to one- to two-hundred heads. In contrast, 30% of dairy cattle in the United States is farmed in herds of over 2,000 animals (USDA 2010).

Table 12. Dimensional differences between Finland, Scandinavia and the United States of America (USA).

Countries	Population[1]	Land area (km^2)[2]	Cattle head count[3]
Finland	5 400 000	338 145	918 280
Scandinavia[4]	25 500 000	878 213	3 956 179
USA	309 600 000	9 629 091	94 500 000

[1] PRB 2010

[2] PRB 2009

[3] TIKE 2009 (Finland), SVJ 2008 (Sweden), Statistics Norway 2009 (Norway), Statistics Denmark 2009 (Denmark) and NASS 2009 (USA)

[4] Includes Sweden, Norway and Denmark

6.2.1 Wholesaler and pharmacy sales data

The OIE recommends all member countries to keep annual records of antimicrobials used in animal husbandry (OIE 2008). The easiest way to do this is by using the Veterinary Anatomic Therapeutic Chemical classification and requesting wholesalers or pharmacies to provide annual sales figures of drugs belonging to each class. Thereby, information on how many kilograms of antimicrobials have been sold can be tabulated and compared to previous years. Valuable facts on, for example, the use of fluoroquinolones or other substances listed as critically important antimicrobials for human medicine (WHO 2007) can be derived. However, because many substances are registered for use in several animal species, conclusions on which animals have been treated cannot be drawn. This has been a point of discussion for several years among both international expert groups (EMEA/CVMP/353297/2005) and in Finland, where the Fimea provides wholesaler statistics on annual antimicrobial consumption (NAM 2009). There has been a 25% rise in the use of injectable penicillin during the last five years, but no definitive explanation for the rise can be given, since it is unclear whether the consumption is increasing in cattle or swine. The use of injectable tetracyclines has also increased by a tremendous 300%. The total amount of distributed antimicrobials increased from 13 000 kg to almost 17 000 kg during 2001-2008 (NAM 2009). This rise cannot be explained by an increase in the number of animals, since the number of cattle has steadily decreased by 10-20 000 heads per year and the number of swine has remained steady since 2000 (www.mmmtike.fi, last accessed 15.11.2010). An educated guess is, however, that an increased amount of antimicrobials is being used in pig production. In order to be able to focus the actions for reducing antimicrobial use, more detailed knowledge on where the increasing amounts of drugs are being used is needed.

The Danish Veterinary and Food Administration is funding a statistical program (VetStat) that provides information on the animal species for which a particular drug has been dispensed (Jensen et al. 2004). This material is available with a reasonable delay, and if imprudent use is noticed, actions can be taken rather quickly. When the data on animal species-specific use is available it can be evaluated together with national resistance data.

In every case, the sales figures from wholesalers or pharmacies show the amounts of antimicrobials sold or dispensed for use in animals and that are also assumed to have ended up in the animals. Therefore, it must be noted that a certain amount is left in storage by the end-user and might be left unused or used later. However, no distinct information is available on how big a proportion of drugs sold or dispensed is wasted.

In conclusion, wholesaler or pharmacy data seem to be useful in nationwide surveillance of trends in antibiotic consumption in animals. The data is also useful for international comparison when calculated in proportion to the annual meat production or number of animals of concern. This approach, however, does not take into account the differences in potency and hence in dosage of individual antimicrobials.

6.2.2 Prescription studies

Information from prescriptions can be gathered either from patient records or when the prescription is dispensed at a pharmacy. Collecting information from prescriptions is one way of gathering data from end-users or evaluating veterinarians' prescribing patterns at distinct clinics. At best, circumstantial information can be derived from prescriptions, including the dosage, indication and length of treatment.

When comparing the two prescription surveys that were performed, it was noted that there were no major differences in prescription practices for dogs and cats at the Veterinary Teaching Hospital (study A) and the prescriptions dispensed from the University Pharmacies (study B).

In both of our studies, compliance to the Decree of Ministry and Agriculture and Forestry on the information that has to be included in a prescription (MMMa 7/EEO/2008) as well as the prescribing patterns were also evaluated. One major problem with collecting data from prescriptions is the extent of missing information in them. Compared to the study performed by Weese (2006), in which no information on indications was collected, in our study performed at the Veterinary Teaching Hospital (study A) all missing data could be complemented from electronic patient records, and the indication and length of treatment could therefore in the majority of cases be confirmed. This allowed thorough evaluation of compliance with national prudent use guidelines (MMM 2003). Missing data were manually collected separately from each patient record. This was very time-consuming and burdensome. However, once all the data are entered in spreadsheets, analyses are easy to perform.

Retrospective prescription studies carry the bias of missing information (Regula et al. 2009). In our data collected from pharmacies (study B), only 30% of the prescriptions contained all the required information. This figure is similar to that in a study performed by Grave et al. (1991), where approximately 20% of the veterinary prescriptions in Norway contained all legally required information. The indication for use was given in 26% of the prescriptions (Grave et al. 1991).

Another problem with prescription studies is the lack of knowledge about owner compliance. Compliance studies would be important to carry out, since it has been shown that treatment with sub-optimal dosing particularly provokes the development of resistance (Harigaya et al. 2009). One method for investigating owner compliance would be to carry out a prospective follow-up study on animals receiving a prescription for antimicrobials. After the course is due to have finished, the investigator could interview the owner by phone to assess the compliance and to gather information on possible adverse effects or lack of efficacy.

6.2.3 Animal data forms

Electronic patient records proved to be a very useful tool in collecting data. In the study on dogs and cats at the Veterinary Teaching Hospital, a search of prescriptions was carried out by the software administrator and delivered in a spreadsheet. The electronic patient record was utilized to complement missing data. In the equine study, all information was manually retrieved from the records by using a list of horses that underwent surgery. This list was gathered from the surgery log book.

If the amount of data is limited, a manual search is not very burdensome. Moreover, if a single investigator collects the necessary information, the bias in calculating, for example, the number of days of treatment or in the interpretation of treatment plans is overcome. Coding is recommended when transferring the information to a spreadsheet, as this facilitates subsequent statistical analysis without having to carry out the coding separately.

Data gathered from electronic or manual animal forms always carry the bias of unmarked medications. However, speculations on incomplete compliance cannot be made without knowing whether the dose was not actually given or whether it was given but not marked in the form. Therefore, when counting the lengths of treatment courses, the default value is days from the first dose to the last dose, unless there is a significant gap of more than one day. Occasional missed doses are noted as a lack of compliance.

Farm animal data are usually recorded in individual animal forms on which the farmer records every medication administered to each animal. The information is used for national surveillance, but also when milk is sent to the dairy or the animal is sent to slaughter. Larger farms use computer-based herd records, but smaller dairy farms in particular still use individual cow cards from which the artificial inseminator collects the information and transfers it to a national database. Once a larger proportion of the dairy farms register with the Finnish national healthcare system and database, Naseva, the collection of medication data from cattle will become more feasible.

Limited search functions caused problems when compiling information from electronic patient records and herd records. Therefore, when implementing new EPR software in a clinic or animal hospital, especially in research facilities such as teaching hospitals, emphasis should be placed on adequate search functions. An optimal EPR in a teaching hospital would also include force functions that should, for example, not accept discharging of the patient without a diagnosis or a prescription without the dosage, length of treatment and indication.

6.2.4 Questionnaire studies

As in any other study, questionnaire studies require very thorough planning, statistical consultation and preferably testing of the questionnaire before sending it out to the target group or performing a phone interview.

The study population that will be included has to be carefully selected, as it should form a representative sample of the source population. In our study C, weighted stratified sampling was used, which ensured that the respondents represented the source population well. Poor representativeness was pointed out as one of the limitations in the study by Chicoine et al. (2008) as their questionnaire was sent out only to members of the Western Canadian Association of Bovine Practitioners. Of all veterinary practitioners in Western Canada, 27% were members of the association. Therefore, it could not be excluded that the patterns of usage were different in non-members or non-respondents.

In order to motivate, for example, busy practitioners to complete a questionnaire it needs to be concise and unambiguous. A prospective study where, for instance, the veterinarian fills out the questionnaire instantly for each patient is considered to be more reliable than a retrospective study. Collecting information retrospectively using a questionnaire carries the risk of false information, as people are asked to rely on their memory, unless the respondent has kept a record of the issues in question.

According to the study plan in our study C, each veterinarian was requested to fill out one form for every patient receiving antimicrobial treatment during the one-week study period. The questionnaire consisted of a cover page with questions about background information and 12 patient-specific questions. The questions were precoded and included lists of alternatives between which the respondent could choose. A space for “other” was also reserved. In our study the questionnaire was quite long and detailed, which might have influenced the response rate. In addition, the questionnaire was mailed to the sample population but no reminder was sent, which also might have somewhat lowered the response rate. By sending a reminder Chauvin et al. (2002) increased the response rate from 54% to 70%, which can be considered satisfactory. In the Canadian study (Chicoine et al. 2008) the response rate was 41%, which is similar to the 38% response rate in our study. As in our study, no reminder was sent out. The response rate might also be influenced by the topic of the study, people who are interested in the study subject are probably more likely to answer than those that are not interested or have limited knowledge about the subject. Paradiso-Hardy and co-workers (2002) demonstrated that with a short and compact questionnaire, using reminders and choosing a limited study population with a special interest in the subject, it is possible to achieve a 100% response rate.

As the percentage of people using the computer is rising, interest towards electronic questionnaire surveys is increasing. Electronic surveys are becoming more widely used and are stated as being cheaper, more practical and more reliable than paper questionnaires (Seebregts et al. 2009, Mukoma et al. 2004). Sending out cover letters and questionnaires by e-mail is fast, easy and cheap, and reminders to non-respondents are easy to send. The availability of e-mail addresses is one limiting factor, as well as the ability to reach those in the population who do not use a computer. One way of overcoming this problem is to send the questionnaire by mail to those not reachable by e-mail.

Questionnaire studies provide a useful tool for collecting detailed information. However, it is challenging to formulate a questionnaire that gives the desired amount of reliable information without being too extensive and time-consuming. The response rate, representativeness and unambiguous and comprehensive answers are the most important measures of the validity of a questionnaire study. In our study, the response rate was moderate and the representativeness good. By sending out a reminder the response rate could have been increased significantly.

6.3 Suitable methods for data collection in different animal groups

6.3.1 Companion animals

Companion animals are usually treated as single individuals and no withdrawal periods need to be considered. The variety of available products is wide, as human products can also be used. The development of resistance is more a concern of the individual patient than a herd problem or a problem for food safety. The impact of the development of resistant pathogens in companion animals cannot, however, be overlooked from a public health point of view. While the number of production animals in Finland continues to decline, the figures for companion animals are increasing. For example, in Denmark, the use of fluoroquinolones was banned for food-producing animals, but at the same time it was noted that this critically important class of antimicrobials is widely used in companion animals without any restrictions (Heuer et al. 2005). In Finland, the use of certain antimicrobials is forbidden in all animals. These include substances highly important in human medicine, such as glycopeptides, mupirocin and newer macrolides and fluoroquinolones (e.g. telithromycin and moxifloxacin) (MMMa 847/2008).

Baseline information on the indication-based use of antimicrobials in companion animals, i.e. dogs and cats, in our study B was collected using a retrospective cross-sectional survey on prescriptions from pharmacies located in various parts of Finland. Prescriptions were also retrospectively reviewed utilizing electronic patient records at the Veterinary Teaching

Hospital (study A). Antimicrobial treatment patters were investigated prospectively by using a questionnaire sent to randomly-selected practitioners in Finland.

The issue on missing information in retrospective prescription studies can be overcome if individual patient records can be utilized to complement the information. When information on prescription patterns is evaluated, the pharmacy databases are convenient for the collection of data.

A prospective study performed on a random selection of small animal clinics would be an effective way of gathering information on antimicrobial use in companion animals. Using a computer-based questionnaire with obligatory fields minimizes the risk of missing information. Considering prescription studies, all electronic patient record programmes should contain obligatory fields in places where there is a legal demand for information to be given to the animal owner. In practice, an electronically written prescription should not be accepted by the computer unless all the required fields are completed. Especially in veterinary teaching hospitals, the programmes could be even more rigorous forcing the entering of information such as the diagnosis and dosage of medications. The more thoroughly the patient records are filled out, the more valuable data can be derived for research and teaching.

On a national level, programmes such as VetStat in Denmark give crude animal species-specific data on antimicrobial use and are valuable for comparing trends over years (DANMAP 2008). This information is useful for the national and international education of veterinarians and animal owners on the emerging threats of antimicrobial resistance or non-compliance with prudent use guidelines.

The results of the studies on dogs and cats showed no significant differences or discrepancies in the quality of information. For cats, three methods of data collection were used and the results were rather similar in all studies. The largest amount of information was derived from the electronic patient records of the Veterinary Teaching Hospital and the prospective questionnaire study of practitioners. The data collected retrospectively from the University Pharmacies was widely incomplete, as a large proportion of the prescriptions lacked at least one of the required parameters such as the indication, animal species or length of treatment.

Animal owner compliance is a very interesting topic when assessing the utility of information derived, for example, from prescription studies. After all, the therapeutic effect is significantly dependent on how accurately the medication is given to the animal. Prescription studies measure the amount of antimicrobials dispensed from pharmacies or the prescription habits of veterinarians, but in order to evaluate actual usage, a study on owner compliance should be combined with the prescription study.

6.3.2 Production animals (horses excluded)

Farmers who keep production animals for human consumption are restricted by several legal requirements that have been established to ensure animal welfare and food safety. Medications administered to food producing animals have to be safe and therapeutically effective for the animal, but in addition, only medications that have proved to be safe for humans can be used in production animals. Regulatory authorities have established MRL values for the maximal amount of foreign substances allowed in edible tissues, milk and eggs

(Miller and Flynn 2000). Only substances that have a defined MRL can be used in production animals, and the determined withdrawal time has to be complied with. Farmers are also obliged to keep records of all medications given to individual animals or animal groups (MMMa 13/EEO/2000). The authorities are allowed to collect all necessary information from animal records kept by the farmers. At present, it is not compulsory for farmers to send any medical information to the authorities. However, the farms that have joined a herd health program have the opportunity to electronically report all disease information and medications to a national animal register. When the animal is sent to slaughter, the information is easily available for the slaughter house.

In Finland, national animal registers do not systematically collect medical information from the entire life span of an individual animal. The electronic pig register (Sikava) does have a field where the farmer or the veterinarian can fill out administered or prescribed medications, but this specific service serves on a voluntary basis. A law on so-called chain information that was enacted in 2004 (EC 852/2004) requires farmers, who send live animals to be slaughtered, to keep records of all medications that have a withdrawal period (EC 852/2004). A list of such medications also has to precede each animal when sent to the slaughterhouse (EC 853/2004). This law has been in force for poultry since 2006, pigs since 2008, horses since 1 January 2009, and for other production animals this information is required from 1 January 2010. Information on medications has to be given for the three months prior to slaughter for all production animals except horses, for which the information has to be available for the previous 6 months (MMMa 134/2006). Data on medications combined with information on animal species and age will be valuable for research in the future.

Information on antimicrobial usage in production animals can be collected by using questionnaires addressed to veterinarians, as in our study, or to farmers, as in the study of Rajić et al. (2006). A relatively short and concise questionnaire including background information can be mailed or sent by e-mail. A prospective questionnaire study on practitioners could ideally be complemented by a questionnaire directed to the farmers, enquiring the response to treatment and compliance with the given instructions. This could be performed by a telephone interview, which could reduce the fallacy of dishonest replies.

In our study, the prospective questionnaire for veterinarians worked well, although a reminder could have given a higher response rate.

To date, Finnish national data on the animal species-specific distribution of antimicrobials among animals has not been available. Therefore, only speculations on target species can be made from wholesaler statistics based on the animal species that a particular substance is registered for. In other countries such as Sweden or Denmark, where all medications are distributed through pharmacies, information can be collected on a species level (Grave et al. 1999, Stege et al. 2003).

6.3.3 Horses

Horses are, in terms of law, somewhat complicated, as the animal owner is allowed in some cases to decide whether a horse is a companion animal or a production animal. According to Commission Regulation 504/2008, all equidae have to be identified and have an official identification document. Previously, only registered horses have had such a document. When a horse is treated with a drug that prevents the animal from being slaughtered for human consumption, the veterinarian has to make a note in the identification document. The owner of a horse can also withdraw the horse from the food chain by requesting a note in the identification document. Due to this option, the assortment of antimicrobials is different for different categories of horses.

As for other production animals, the animal owner has to keep a record of all medications carrying a withdrawal period that have been given to a horse (EC 852/2004). When the horse is sent to be slaughtered, information on medications administered to the animal during the previous six months has to precede the animal. The documentation has to include the names of drugs, dates of administration and withdrawal periods (EC 853/2004). From the registers of the slaughterhouses, information on antimicrobials administered to horses can then be collected.

Data on antimicrobial use in horses can also be collected by using questionnaires sent to veterinary practitioners, equine clinics or horse owners. A prospective study on antimicrobials used in equine patients at one or several distinct clinics would provide valuable information on usage in hospitalized patients or outpatients, depending on the target group. Prospective studies performed, for example, on horses undergoing surgery in an equine hospital can be complemented by a questionnaire survey of the animal owners to evaluate the outcome, complications or compliance with the instructions.

Retrospective data on antimicrobial use in horses can be collected by exploiting patient records or prescriptions; however, this entails the same issues as discussed previously. In our study on horses, the information on antimicrobial use was collected retrospectively and thus missing information could not be complemented. The heterogeneity of the population and types of surgical lesions also affected the choice of antimicrobial and duration of treatment, and only descriptive analyses were therefore applicable.

7 Conclusions

1. When the clinical use of antimicrobials was explored, it was shown that the most common reason for antimicrobial treatment in dogs was pyoderma, which in the majority of the cases was treated with cephalexin. In cats, urinary tract infection was the most frequently diagnosed disease and treated with amoxicillin-clavulanate.

Mastitis was the most common indication for antimicrobial treatment in cattle. For all indications in cattle, penicillin G was used in 81% of the cases.

Horses treated as outpatients most commonly received penicillin G or trimethoprim-sulfonamides for skin or wound infections. Hospitalized horses recovering from colic surgery were usually medicated with penicillin G in combination with gentamicin.

2. Veterinarians complied well with the prevailing prudent use guidelines. Penicillin, aminopenicillins and first generation cephalosporins were widely used. Of the antimicrobials considered as reserve drugs, fluoroquinolones were used sparingly and in the majority of cases for an accepted indication such as urinary tract infections in dogs and mastitis caused by *E. coli* in dairy cattle.

3. The method of data collection which is used has an important impact on the availability of information and the validity of the results. Therefore, several approaches were used to enable an extensive review of the data.

- Data collected from EPRs gives a good overview of the usage patterns at the Veterinary Teaching Hospital. When the national databases for pig and dairy production are up and running and more farms join the national healthcare system, electronic herd records will provide valuable data on antimicrobial use in these animal species.
- Data collection from prescriptions works well in situations where the pharmacy network is uniform and the data can be electronically collected in a national database. Unless the aim is to evaluate the prescribing habits of veterinarians at a limited number of sites, manual retrieval of information from prescriptions cannot be recommended. An end-user prescription study is at its best if followed up by a compliance study performed on the owners of the animals receiving the prescribed medication.
- Questionnaire studies on practitioners provide a good overview of the antimicrobial usage patterns amongst a selected population of veterinarians. A well planned questionnaire with a reasonable number of questions can be sent out by mail and/or electronically. If followed by a reminder to non-respondents, it will most likely result in a reasonable response rate and truthful answers to questions about compliance with guidelines.

8 Future aspects

The present studies provide a basis for the education of veterinarians and the revision of national guidelines on the prudent use of antimicrobials. It is important that veterinary practitioners are familiar with prudent use guidelines and comply with them. To combat the emergence of bacterial resistance, it is important that drugs known to promote resistance are used sparingly. This especially applies to cephalosporins and fluoroquinolones. Cephalosporins were widely used by Finnish veterinarians, and education on optional drugs should be provided. Concerning fluoroquinolones, the focus should be on judicious use and maintaining the efficacy of these important drugs.

In the future monitoring of antimicrobial usage, following aspects should be considered:

- The development of a continuous system for detailed surveillance should be emphasized.
- The utilization of electronic systems would be worthwhile when, for example, planning questionnaire studies. Electronic questionnaires are easy to render and distribute. Remainders are also easy to send out by e-mail and will most likely positively influence the response rate. Analyses on electronic data are quicker, as the stage of entering the data from paper sheets into a database is left out. The risk of typing errors is also reduced.

  Electronic systems can also be used for the distribution of current information on antimicrobial use, prudent use guidelines and treatment recommendations. Educational material can be downloaded from a common website, for instance to a personal digital assistant, and used in daily clinical work.

  EPRs should be brought into use in a wider scale and developed further to include for example force functions in order to gather all relevant data. EPRs should also include electronic prescriptions with obligatory fields to ensure that all legally required information is inserted.
- Owner compliance in veterinary medicine is a multifaceted issue. Veterinarians prescribe medication for an animal on the presumption that the owner will follow the instructions. For the individual animal, therapy failure is the worst consequence of non-compliance. Sub-optimal administration of antimicrobials can also lead to the development of bacterial resistance, which is a potential public health issue. Therefore, studies that collect information on the distribution of antimicrobials require complementary studies on compliance with the given instructions. Only then can valid conclusions on usage be made.
- Indication-based usage of antimicrobials in pigs, poultry and fish should be investigated. Antimicrobials are used in large quantities in pig and poultry industry and it would therefore be important to know whether prudent use guidelines are being followed and if significant overuse of antimicrobials can be noted.

Acknowledgements

This thesis was produced at the Unit of Veterinary Pharmacology and Toxicology, Department of Equine and Small Animal Medicine, at the Faculty of Veterinary Medicine of the University of Helsinki. Financial support from Suomen eläinlääketieteen säätiö, Eläinlääketieteen tutkimuksen tukisäätiö, Helsingin Yliopisto, Orionin ja Farmoksen tutkimussäätiöt, Anna och Karl Eklunds stiftelse and Svenska Studiestödskommitten is gratefully acknowledged.

I want to express my sincere gratitude to my supervising professor Outi Vainio and to my supervisors Liisa Kaartinen and Merja Rantala. You have all been extremely patient with me and supported me during the ups and downs of my PhD studies. I especially want to thank you for supporting me in applying for the graduate school, the two years made all the difference both in the advancement of this work and financially.

Outi, thank you for your friendly and yet precise and professional comments on the work I have done. I also thank you for defending my case in different committees along the way and for providing me a very nice office to work in.

Liisa, you have despite your busy schedule always made the time to meet me when I have needed your help and advice. Thanks to your invaluable comments all texts have improved tremendously.

Merja, you are the reason why I'm writing this today. Almost ten years ago I sat and listened to your lecture when you introduced us to the fascinating world of antimicrobials and resistance. It has always been a huge pleasure to work with you, because despite the fact that we have sometimes walked on different sides of the road, it is still the same road and we are heading in the same direction. You are one of my best friends and my soul mate in academia!

I would like to thank Riitta-Mari Tulamo for continuously supporting me and offering me opportunities to work in the clinics yet allowing a whole lot of latitude to keep writing on my thesis. I also want to thank Jussi Anttila for allowing time for research while working in the hospital.

I'm obliged to Anna-Liisa Myllyniemi for her objective reviewing of my manuscript and for giving valuable comments at a time of contradiction. Thank you also for the encouraging words, things turned out for the best in the end.

Irmeli Happonen and Antti Hakanen are gratefully acknowledged for the official reviewing of this thesis and Vibeke Frøkjær Jensen for agreeing to stand as my honourable opponent.

Words of thanks also to my co-authors Pentti Huovinen, Sari Eerikäinen, Satu Pyörälä, Maria Hautala and Teija Viita-aho.

Iiris Kasanen and Laura Siponmaa, my dear friends, without you this thesis would probably not have seen the light of the day in a long time. You offered me a "fat camp" for doctoral students and gently forced me to write, write and write. At the end of each day there was a reward, exceptionally good quality company, good food, loads of candy and a terrific movie. I cannot thank you enough!

My beloved parents, Irmeli and Jorma, you have shown me over and over again that there is no limit for how much parents can support and encourage their daughter. I'm most indebted to you for always unselfishly offering me and my family a helping hand. I'm very grateful that you have believed in me and been proud of me each passing day. Thank you for everything!

Lastly, I want to express my deepest appreciation to Nika, you are the love of my life and words fail me to tell how grateful I am every day for being with you. ♥ Our beautiful children Viivi and Roy, you show me the true meaning of life! Each moment with you is joyous and fills me with happiness and gratitude. Our beloved dog Snoopy, who was taken away way too soon, I owe you a big hug for keeping me mentally and physically fit during the laborious writing process. You patiently and ever so cheerfully travelled with me to Kuopio numerous times and took my mind off work on our long walks to the lakes. I will always miss you. Slim, Niki and esteemed Doctor Shere Khan, please accept my compliments on your invaluable impact on human mental health just by being there, begging for attention and offering a fur to stroke.

Sipoo 15.11.2010

Katariina Thomson

References

395/1987. Finnish Medicines Act. Lääkelaki. Läkemedelslag. (only in Finnish and Swedish) http://www.finlex.fi/fi/laki/ajantasa/1987/19870395 [15.11.2010]

Adams VJ, Campbell JR, Waldner CL, Dowling PM, Shmon CL, 2005. Evaluation of client compliance with short-term administration of antimicrobials to dogs. J Am Vet Med Assoc. 15:567-74.

Anthony F, Acar J, Franklin A, Gupta R, Nicholls T, Tamura Y, Thompson S, Threlfall EJ, Vose D, van Vuuren M, White DG; Office International des Epizooties Ad hoc Group. 2001. Antimicrobial resistance: responsible and prudent use of antimicrobial agents in veterinary medicine. Rev Sci Tech 20:829-39.

Albarellos GA, Landoni MF. 2009. Current concepts on the use of antimicrobials in cats. The Vet J 180: 304–316.

AMR Report-UK 2004. Overview of Antimicrobial Usage and Bacterial Resistance in Selected Human and Animal Pathogens in the UK: 2004 http://www.dardni.gov.uk/vet-meds.pdf [15.11.2010]

AVMA 2000. American Association of Bovine Practitioners Prudent Drug Usage Guidelines for Cattle. http://www.avma.org/issues/policy/jtua_cattle.asp [15.11.2010]

AVMA 2001. American Association of Equine Practitioners Prudent Drug Usage Guidelines. http://www.avma.org/issues/policy/jtua_horses.asp [15.11.2010]

AVMA 2008. Policy Principles of Veterinary Medical Ethics of the AVMA, April 2008. http://www.avma.org/issues/policy/ethics.asp [15.11.2010]

AVMA 2009. American Association of Feline Practitioners/American Animal Hospital Association Basic Guidelines of Judicious Therapeutic Use of Antimicrobials. April 2009. http://www.avma.org/issuespolicy/jtua_aafp_aaha.asp [15.11.2010]

Bager F, Madsen M, Christensen J, Aarestrup F.M. 1997. Avoparcin used as a growth promoter is associated with the occurrence of vancomycin-resistant *Enterococcus faecium* on Danish poultry and pig farms. Prev Vet Med 31: 95-112.

Ball KR, Rubin JE, Chirino-Trejo M, Dowling PM. 2008. Antimicrobial resistance and prevalence of canine uropathogens at the Western College of Veterinary Medicine Veterinary Teaching Hospital, 2002-2007. Can Vet J 49**:**985-90**.**

BEK nr 482 af 29/05/2007. Fødevarestyrelsen. 2007. Bekendtgørelse om dyrlægers anvendelse, udlevering og ordinering af lægemidler til dyr. https://www.retsinformation.dk/Forms/R0710.aspx?id=32021 [15.11.2010]

Black DM, Rankin SC, King LG. 2009. Antimicrobial therapy and aerobic bacteriologic culture patterns in canine intensive care unit patients: 74 dogs (January-June 2006) J Vet Emerg Crit Care (San Antonio) 19: 489–495.

Bratzler, DW, Houck PM; for the Surgical Infection Prevention Guideline Writers Workgroup. 2005. Antimicrobial prophylaxis for surgery: an advisory statement from the National Surgical Infection Prevention Project. Am J Surg 189: 395–404.

BSAVA 2009. The British Small Animal Veterinary Association (BSAVA) Guide to the Use of Veterinary Medicines, BSAVA April 2009. http://www.bsava.com/Advice/BSAVAGuidetotheUseofVeterinaryMedicines/tabid/294/Default.aspx [15.11.2010]

CCAR 2008. Canadian Committee on Antibiotic Resistance. Infection Prevention and Control Best Practices for Small Animal Veterinary Clinics First Printing, November 2008. http://www.wormsandgermsblog.com/uploads/file/CCAR%20Guidelines%20Final(2).pdf [15.11.2010]

Chauvin C, Beloeil PA, Orand JP, Sanders P, Madec F, 2002. A survey of group-level antibiotic prescriptions in pig production in France. Prev Vet Med 30:109-20.

Chauvin C, Le Bouquin-Leneveu S, Hardy A, Haguet D, Orand JP, Sanders P. 2005. An original system for the continuous monitoring of antimicrobial use in poultry production in France. J Vet Pharmacol Ther 28:515-23.

Chauvin C, Querrec M, Perot A, Guillemot D, Sanders P. 2008. Impact of antimicrobial drug usage measures on the identification of heavy users, patterns of usage of the different antimicrobial classes and time-trends evolution. J Vet Pharmacol Ther 31:301-11.

Chicoine AL, Dowling PM, Boison JO, Parker S. 2008. A survey of antimicrobial use during bovine abdominal surgery by western Canadian veterinarians. Can Vet J 49:1105-9.

Commission Directive 97/6/EC. Commission Directive 97/6/EC of 30 January 1997 amending Council Directive 70/524/EEC concerning additives in feedingstuffs. http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=CELEX:31997L0006:EN:HTML [15.11.2010]

Cooke CL, Singer RS, Jang SS, Hirsh DC. 2002. Enrofloxacin resistance in *Escherichia coli* isolated from dogs with urinary tract infections. J Am Vet Med Assoc 220: 185-189.

CVMA 2002. Canadian Veterinary Medical Association. 2002. CVMA guidelines on the prudent use of antimicrobial drugs in swine. http://canadianveterinarians.net/ShowText.aspx?ResourceID=84 [15.11.2010]

CVMA 2008 a. Canadian Veterinary Medical Association. 2008. Species-specific prudent use guidelines for the administration of antimicrobials in food animals – Phase 2 Poultry. Draft 2, March 26 2008. http://www.cvbc.ca/cfm/index.cfm?It=106&Id=67 [15.11.2010]

CVMA 2008 b. Canadian Veterinary Medical Association. 2008. Species-specific prudent use guidelines for the administration of antimicrobials in food animals – Phase 2 Beef. Draft 2, March 4 2008. http://www.cvbc.ca/cfm/index.cfm?It=106&Id=67 [15.11.2010]

CVMA 2008 c. Canadian Veterinary Medical Association. 2008. Species-specific prudent use guidelines for the administration of antimicrobials in food animals – Phase 2 Dairy. Draft 2, March 26 2008. http://www.cvbc.ca/cfm/index.cfm?It=106&Id=67 [15.11.2010]

Danish Veterinary and Food Administration 2009. Danish Veterinary and Food Administration. Ministry of Food, Agriculture and Fisheries. Distribution and use of veterinary drugs in Denmark. Updated 8. June 2009. http://www.uk.foedevarestyrelsen.dk/AnimalHealth/Veterinary_drugs/forside.htm [15.11.2010]

DANMAP 2007. Danish Integrated Antimicrobial resistance Monitoring and Research Programme. The Danish Ministry of Food, Agriculture and Fisheries and the Danish Ministry of Health. 2007. ISSN 1600-2032. Available at: http://www.danmap.org/pdfFiles/Danmap_2007.pdf [15.11.2010]

DANMAP 2008. The Danish Integrated Antimicrobial Resistance Monitoring and Research Programme. The Danish Ministry of Food, Agriculture and Fisheries and the Danish Ministry of Health. 2008. ISSN 1600-2032. Available at: http://www.danmap.org/pdfFiles/Danmap_2008.pdf [15.11.2010]

DeVincent SJ, Reid-Smith R. 2006. Stakeholder position paper: Companion Animal Veterinarian. Prev Vet Med 73: 183-9.

DeVincent SJ, Viola C. 2006a. Introduction to animal antimicrobial use data collection in the United States: methodological options. Prev Vet Med 73:105-9.

DeVincent SJ, Viola C; Advisory Committee on Animal Antimicrobial Use Data Collection in the United States of the Alliance for the Prudent Use of Antibiotics. 2006b. Deliberations of an Advisory Committee regarding priorities, sources, and methods for collecting animal antimicrobial use data in the United States. Prev Vet Med 73:133-51.

Dowling PM. Antimicrobial therapy of skin and ear infections. Can Vet J. 1996 Nov;37(11):695-9.

Drazenovich N, Ling GV, Foley J. 2004. Molecular Investigation of *Escherichia coli* Strains Associated with Apparently Persistent Urinary Tract Infection in Dogs. J Vet Intern Med 18:301–306.

Dunne EF, Fey PD, Kludt P, Reporter R, Mostashari F, Shillam P, Wicklund J, Miller C, Holland B, Stamey K, Barrett TJ, Rasheed JK, Tenover FC, Ribot EM, Angulo FJ. 2000. Emergence of Domestically Acquired Ceftriaxone-Resistant *Salmonella* Infections Associated with AmpC β-Lactamase. J Am Med Assoc 284: 3151-3156.

EC 504/2008. Commission Regulation (EC) No 504/2008 of 6 June 2008 implementing Council Directives 90/426/EEC and 90/427/EEC as regards methods for the identification of equidae. http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:L:2008:149:0003:0032:EN:PDF [15.11.2010]

EC 852/2004. Regulation (EC) No 852/2004 of the European Parliament and of the Council of 29 April 2004 on the hygiene of foodstuffs. http://www.fsai.ie/uploadedFiles/Reg852_2004(6).pdf [15.11.2010]

EC 853/2004. Regulation (EC) No 853/2004 of the European parliament and of the Council of 29 April 2004 laying down specific hygiene rules for food of animal origin. http://www.fsai.ie/uploadedFiles/Reg853_2004(1).pdf [15.11.2010]

EC 1950/2006. Commission Regulation (EC) No 1950/2006 of 13 December 2006 establishing, in accordance with Directive 2001/82/EC of the European Parliament and of the Council on the Community code relating to veterinary medicinal products, a list of substances essential for the treatment of equidae. http://www.fve.org/veterinary/pdf/medicines/regulation_1950_2006_ec.pdf [15.11.2010]

Egberink H, Addie D, Belák S, Boucraut-Baralon C, Frymus T, Gruffydd-Jones T, Hartmann K, Hosie MJ, Lloret A, Lutz H, Marsilio F, Pennisi MG, Radford AD, Thiry E, Truyen U, Horzinek MC. 2009. Bordetella bronchiseptica infection in cats. ABCD guidelines on prevention and management. J Feline Med Surg. 11:610-4.

EU 37/2010. Commission Regulation (EU) No 37/2010 of 22 December 2009 on pharmacologically active substances and their classification regarding maximum residue limits in foodstuffs of animal origin.
http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=CELEX:32010R0037:EN:NOT [23.12.2010]

EMEA 1999. Antibiotic resistance in the European Union associated with therapeutic use of veterinary medicines. Report and qualitative risk assessment by the Committee for Veterinary Medicinal Products. http://www.emea.europa.eu/pdfs/vet/regaffair/034299ENC.pdf [15.11.2010]

EMEA/CVMP/353297/2005. CVMP Strategy on antimicrobials 2006-2010 and status report on activities on antimicrobials. http://www.emea.europa.eu/pdfs/vet/swp/35329705.pdf [15.11.2010]

Estberg L, Case JT, Walters RF, Cardiff RD, Galuppo LD. 1998. Word search performance for diagnoses of equine surgical colics in free-text electronic patient records. Prev Vet Med 34:161–174.

Evira 2009. Permanent work group on antimicrobials of the Ministry of Agriculture and Forestry. Recommendations for the Use of Antimicrobials against the Most Common Infectious Diseases of Animals. 2009. Evira publications 3/2009. ISBN 978-952-225-032-2 (pdf) (only in Finnish).

FINRES-Vet 2004. Finnish Veterinary Antimicrobial Resistance Monitoring and Consumption of Antimicrobial Agents, Finnish Food Safety Authority Evira, Helsinki, Finland. http://www.evira.fi/attachments/elaintauti_ja_elintarviketutkimus/mbi_ohjeet/eela_082005_finresvet_1_.pdf [15.11.2010]

FINRES-Vet 2005-2006. Finnish Veterinary Antimicrobial Resistance Monitoring and Consumption of Antimicrobial Agents, Finnish Food Safety Authority Evira, Helsinki, Finland, ISSN 1796-4369. http://www.evira.fi/uploads/WebShopFiles/1198141211941.pdf [15.11.2010]

FINRES-Vet 2007-2009. Finnish Veterinary Antimicrobial Resistance Monitoring and Consumption of Antimicrobial Agents, Finnish Food Safety Authority Evira, Helsinki, Finland. Available at http://www.evira.fi [15.11.2010]

Fødevarestyrelsen 2007. The Danish Veterinary and Food Administration of the Ministry of Food, Agriculture and Fisheries. 2007. Behandlingsvejledning til dyrlæger ved behandling af visse svinesygdomme http://www.foedevarestyrelsen.dk/NR/rdonlyres/C2FDF204-0819-438A-86CF-8A4B90325015/0/Behandlingsvejledningantibiotikasvinskema.pdf [15.11.2010]

Fødevarestyrelsen 2009. The Danish Veterinary and Food Administration of the Ministry of Food, Agriculture and Fisheries. 2009. Behandlingsvejledningen for kvæg. http://www.foedevarestyrelsen.dk/NR/rdonlyres/6A0036EF-FAF0-4BE2-A5E1-6B279C23E91D/0/Behandlingsvejledning_kvæg171109.pdf [15.11.2010]

FVE 1999. Federation of Veterinarians of Europe. 1999. Antibiotic Resistance & Prudent use of Antibiotics in Veterinary Medicine. http://www.fve.org/news/publications/pdf/antibioen.pdf [15.11.2010]

Gow SP, Waldner CL. 2009. Antimicrobial drug use and reason for treatment in 203 western Canadian cow-calf herds during calving season. Prev Vet Med 90:55-65.

Grave K, Bangen M, Engelstad M, Søli NE. 1991. An evaluation of the information given on veterinary prescriptions in Norway. Compliance with the legal regulations. J Vet Pharmacol Ther 14:150-5.

Grave K, Bangen M, Engelstad M, Søli NE. 1992. Prescribing of veterinary and human preparations for animals in Norway. Was the preparation approved for the animal species for which it was prescribed? J Vet Pharmacol Ther 15:45-52.

Grave K, Greko C, Nilsson L, Odensvik K, Mørk T, Rønning M. 1999. The usage of veterinary antibacterial drugs for mastitis in cattle in Norway and Sweden during 1990–1997. Prev Vet Med 42:45-55. Erratum in: Prev Vet Med 2000 43:137.

Grave K, Hansen MK, Kruse H, Bangen M, Kristoffersen AB. 2008. Prescription of antimicrobial drugs in Norwegian aquaculture with an emphasis on "new" fish species. Prev Vet Med 83:156-69.

Grave K, Tanem H, 1999. Compliance with short-term oral antibacterial drug treatment in dogs. J Small Anim Pract 40:158-62.

Gruffydd-Jones T, Addie D, Belák S, Boucraut-Baralon C, Egberink H, Frymus T, Hartmann K, Hosie MJ, Lloret A, Lutz H, Marsilio F, Pennisi MG, Radford AD, Thiry E, Truyen U, Horzinek MC. 2009. Chlamydophila felis infection. ABCD guidelines on prevention and management. J Feline Med Surg 11:605-9.

Guillemot D, Carbon C, Balkau B, Geslin P, Lecoeur H, Vauzelle-Kervroëdan F, Bouvenot G, Eschwége E. 1998. Low Dosage and Long Treatment Duration of β-Lactam Risk Factors for Carriage of Penicillin-Resistant Streptococcus pneumonia. J Am Med Assoc 279:365-370.

Harigaya Y, Bulitta JB, Forrest A, Sakoulas G, Lesse AJ, Mylotte JM, Tsuji BT. 2009. Pharmacodynamics of Vancomycin at Simulated Epithelial Lining Fluid Concentrations against Methicillin-Resistant *Staphylococcus aureus* (MRSA): Implications for Dosing in MRSA Pneumonia. Antimicrob Agents Chemother 53: 3894–3901.

HC-422-1. The House of Commons Health Committee, 2007. The Electronic Patient Record. Sixth Report of Session 2006-07, volume 1. By authority of the House of Commons London: The Stationery Office Limited, 13 September 2007. http://www.publications.parliament.uk/pa/cm200607/cmselect/cmhealth/422/422.pdf [15.11.2010]

Heuer OE, Jensen VF, Hammerum AM. 2005. Antimicrobial Drug Consumption in Companion Animals. Emerg Inf Dis 11: 344-345.

Hill AE, Green AL, Wagner BA, Dargatz DA. 2009. Relationship between herd size and annual prevalence of and primary antimicrobial treatments for common diseases on dairy operations in the United States. Prev Vet Med 88: 264–277

Hsiao C-J, Burt CW, Rechtsteiner E, Hing E, Woodwell D, Sisk JE. 2008. Preliminary Estimates of Electronic Medical Record Use by Office-based Physicians: United States, 2008. NCHS Health E-Stat, Dec 2008. http://www.cdc.gov/nchs/data/hestat/physicians08/physicians08.htm [15.11.2010]

Jensen VF, Jacobsen E, Bager F. 2004. Veterinary antimicrobial-usage statistics based on standardized measures of dosage. Prev Vet Med 64: 201–215.

Kaier K, Frank U, Hagist C, Conrad A, Meyer E. 2009. The impact of antimicrobial drug consumption and alcohol-based hand rub use on the emergence and spread of extended-spectrum β-lactamase-producing strains: a time-series analysis. J Antimicr Chemother 63: 609–614.

KLF 2009. Kjøtt- og fjørfebransjens Landsforbund, Oslo, Norway. http://www.kjottbransjen.no/arch/_img/9141597.pdf [15.11.2010]

Kools SA, Moltmann JF, Knacker T, 2008. Estimating the use of veterinary medicines in the European union. Regul Toxicol Pharmacol 50:59-65.

Kruth S. 2006. Antimicrobial Therapy of Selected Organ Systems, Urinary Tract Infections. In Antimicrobial Therapy in Veterinary Medicine / editors S. Giguère, J.F. Prescott, J.D. Baggott, R.D. Walker, P.M. Dowling. Blackwell Publishing Professional, Iowa, USA. ISBN: 978-0-8138-0656-3.

Ling GV, Norris CR, Franti CE, Eisele PH, Johnson DL, Ruby AL, Jang SS 2001. Interrelations of Organism Prevalence, Specimen Collection Method, and Host Age, Sex, and Breed among 8,354 Canine Urinary Tract Infections (1969–1995). J Vet Intern Med 15:341–347.

MARAN 2007. Monitoring of antimicrobial resistance and antibiotic usage in animals in the Netherlands in 2006/2007. http://www.cvi.wur.nl/NR/rdonlyres/B6AB3678-EC78-4D80-9190-D8D52587B969/83791/MARAN_2007_def2.pdf [15.11.2010]

Meyers B, Schoeman JP, Goddard A, Picard J. 2008. The bacteriology and antimicrobial susceptibility of infected and non-infected dog bite wounds: Fifty cases. Vet Microbiol 127: 360–368.

Miller GY, McNamara PE, Singer RS. 2006. Stakeholder position paper: economist's perspectives on antibiotic use in animals. Prev Vet Med 73:163-8.

Miller MA, Flynn WT. 2000. Regulations of Antibiotic Use in Animals. In Antimicrobial Therapy in Veterinary Medicine / edited by JF Prescott, JD Baggott, RD Walker . 3rd edition. Iowa State University Press, USA. ISBN: 0-8138-0779-4.

MMM 1996. Work group on antimicrobials of the Finnish Ministry of Agriculture and Forestry. Recommendations for the use of antimicrobials against the most common infectious diseases in animals. Maa- ja metsätalousministeriön mikrobilääketyöryhmä. Käyttöesimerkit mikrobilääkityksistä eläinten tärkeimpiin tulehdus- ja tartuntatauteihin, ss. 1-29. MMM, Helsinki, 1996. (only in Finnish).

MMM 2003. The Ministry Agriculture and Forestry, Finland. Memorandum 2003:9a. Recommendations for the use of antimicrobial agents in the treatment of the most significant infectious diseases in animals. http://wwwb.mmm.fi/julkaisut/tyoryhmamuistiot/2003/tr2003_9a.pdf [15.11.2010]

MMMa 6/EEO/2008. Maa- ja metsätalousministeriön asetus lääkkeiden käytöstä ja luovutuksesta eläinlääkinnässä. Liite 1, luku 1. (only in Finnish) http://wwwb.mmm.fi/el/laki/b/6_EEO_2008_FI.pdf [15.11.2010]

MMMa 7/EEO/2008. Maa- ja metsätalousministeriön asetus lääkkeiden ja lääkerehujen määräämisestä eläinlääkinnässä. Liite 6. Luku 1. (only in Finnish) http://wwwb.mmm.fi/el/laki/b/7_EEO_2008_FI.pdf [15.11.2010]

MMMa 8/EEO/2008. Maa- ja metsätalousministeriön asetus eläinlääkärien lääkekirjanpidosta. Luku 2. (only in Finnish) http://wwwb.mmm.fi/el/laki/b/8_EEO_2008_FI.pdf [15.11.2010]

MMMa 13/EEO/2000. Maa- ja metsätalousministeriön asetus tuotantoeläinten lääkityksestä pidettävästä kirjanpidosta. http://wwwb.mmm.fi/el/laki/b/b7.html [15.11.2010] (only in Finnish)

MMMa 134/2006. Maa- ja metsätalousministeriön asetus alkutuotannolle elintarviketurvallisuuden varmistamiseksi asetettavista vaatimuksista http://www.finlex.fi/fi/laki/alkup/2006/20060134 [15.11.2010] (only in Finnish)

MMMa 847/2008. Maa- ja metsätalousministeriön asetus eräiden lääkeaineiden käytön kieltämisestä tai rajoittamisesta eläimille. http://www.finlex.fi/fi/laki/alkup/2008/20080847 [15.11.2010] (only in Finnish)

MMMa 935/1998. Maa- ja metsätalousministeriön päätös eräiden lääkeaineiden käytön kieltämisestä eläimille annetun maa- ja metsätalousministeriön päätöksen muuttamisesta http://www.finlex.fi/fi/laki/alkup/1998/19980935 [15.11.2010] (only in Finnish)

MMMp 515/1996. Maa- ja metsätalousministeriön päätös eräiden lääkeaineiden käytön kieltämisestä eläimille. http://www.finlex.fi/fi/laki/alkup/1996/19960515 [15.11.2010] (only in Finnish)

Moulin G, Cavalié P, Pellanne I, Chevance A, Laval A, Millemann Y, Colin P, Chauvin C; Antimicrobial Resistance ad hoc Group of the French Food Safety Agency. 2008. A comparison of antimicrobial usage in human and veterinary medicine in France from 1999 to 2005. J Antimicrob Chemother 62:617-25.

Mukoma W, Mathews C, Flisher AJ, Seebregts C, Jansen S, Ahmed N, Klepp KI, Mtshizana Y, Hani A. 2004. Use of electronic questionnaires on handheld devices to evaluate the effects of a school-based HIV prevention programme on adolescent sexual behaviour. ; International Conference on AIDS (15th : 2004 : Bangkok, Thailand). *Int Conf AIDS.* 2004 Jul 11-16; 15: abstract no. TuPeC4886.

NAM 2003. Luettelo lääkeaineista ja valmisteista joita saa toimittaa ainoastaan lääkemääräyksellä. LL DNro 15/01/2003. http://wwwb.mmm.fi/el/laki/b/b19m1.pdf [15.11.2010] (only in Finnish)

NAM 2009. National Agency for Medicines, Finland. Veterinary drug consumption in Finland in 2001-2008. http://www.laakelaitos.fi/instancedata/prime_product_julkaisu/laakelaitos/embeds/PDF_tarkat_tiedot_FI_2009-11-03.pdf [15.11.2010]

NASS 2009. National Agricultural Statistics Service, Agricultural Statistics Board, U.S. Department of Agriculture. U.S. Canadian Cattle Inventory. http://www.gov.mb.ca/agriculture/statistics/pdf/uscancattlejan09.pdf [15.11.2010]

Nevala M, Taponen S, Pyörälä S: Bacterial etiology of bovine clinical mastitis – data from Saari Ambulatory Clinic in 2002–2003. Finnish Veterinary Journal 110:363-369.

NORM NORM-Vet 2006. Usage of Antimicrobial Agents and Occurence of Antimicrobial Resistance in Norway. The National Veterinary Institute of Norway. http://www.vetinst.no/nor/Forskning/Publikasjoner/Norm-Norm-Vet-rapporten [15.11.2010]

NORM NORM-Vet 2007. Usage of Antimicrobial Agents and Occurence of Antimicrobial Resistance in Norway. The National Veterinary Institute of Norway. http://www.vetinst.no/nor/Forskning/Publikasjoner/Norm-Norm-Vet-rapporten [15.11.2010]

NORM NORM-Vet 2008. Usage of Antimicrobial Agents and Occurence of Antimicrobial Resistance in Norway. The National Veterinary Institute of Norway. http://www.vetinst.no/nor/Forskning/Publikasjoner/Norm-Norm-Vet-rapporten [15.11.2010]

NORM/NORM-Vet 2009. Usage of Antimicrobial Agents and Occurrence of Antimicrobial Resistance in Norway. Tromsø / Oslo 2010. ISSN:1502-2307 (print) / 1890-9965 (electronic).

Norris CR, Williams BJ, Ling GV, Franti CE, Johnson DL, Runy AL. 2000. Recurrent and Persistent Urinary Tract Infections in Dogs: 383 Cases (1969–1995). J Am Anim Hosp Assoc 36: 484-492.

Nunnery J, Angulo FJ, Tollefson L. 2006. Public health and policy. Prev Vet Med 73:191-5.

Odensvik K, Grave K, Greko C. 2001. Antibacterial drugs prescribed for dogs and cats in Sweden and Norway 1990-1998. Acta Vet Scand 42:189-98.

OIE 2008. OIE Terrestrial Animal Health Code 17th edition, August 2008. http://www.oie.int/eng/normes/mcode/code2008/a_summry.htm [15.11.2010]

OIE 2009. Terrestrial Animal Health Code (2009) http://www.oie.int/eng/normes/Mcode/en_sommaire.htm [15.11.2010]

Ortman K, Svensson C. 2004. Use of antimicrobial drugs in Swedish dairy calves and replacement heifers. Vet Rec 31:136-40.

Paradiso-Hardy FL, Cornish P, Pharand C, Fremes SE. 2002. A national survey of antimicrobial prophylaxis in adult cardiac surgery across Canada. Can J Infect Dis.13:21-7.

Pedersen K, Pedersen K, Jensen H, Finster K, Jensen VF, Heuer OE. 2007. Occurrence of antimicrobial resistance in bacteria from diagnostic samples from dogs. J Antimicrob Chemother 60: 775–781

Pharmaca Fennica® Veterinaria 2009. Lääketietokeskus Oy. Helsinki 2009. Painoyhtymä Oy, Porvoo. ISSN: 0356-3731. (only in Finnish)

Pol M, Ruegg PL. 2007. Treatment Practices and Quantification of Antimicrobial Drug Usage in Conventional and Organic Dairy Farms in Wisconsin. J Dairy Sci 90:249–261.

Pollari FL, Bonnett BN. 1996. Evaluation of postoperative complications following elective surgeries of dogs and cats at private practices using computer records. Can Vet J 37: 672-678.

PRB 2009. Population Reference Bureau. 2009. World Population Data Sheet. http://www.prb.org/Datafinder/Topic/Bar.aspx?sort=v&order=d&variable=81 [15.11.2010]

PRB 2010. Population Reference Bureau. 2010 World Population Data Sheet. http://www.prb.org/pdf10/10wpds_eng.pdf [15.11.2010]

Radford AD, Addie D, Belák S, Boucraut-Baralon C, Egberink H, Frymus T, Gruffydd-Jones T, Hartmann K, Hosie MJ, Lloret A, Lutz H, Marsilio F, Pennisi MG, Thiry E, Truyen U, Horzinek MC. 2009. Feline calicivirus infection. ABCD guidelines on prevention and management. J Feline Med Surg 11:556-64

Rajić A, Reid-Smith R, Deckert AE, Dewey CE, McEwen SA. 2006. Reported antibiotic use in 90 swine farms in Alberta. Can Vet J 47:446-52.

Rautakorpi UM, Klaukka T, Honkanen P, Mäkelä M, Nikkarinen T, Palva E, Roine R, Sarkkinen H, Huovinen P; MIKSTRA Collaborative Study Group. 2001. Antibiotic use by indication: a basis for active antibiotic policy in the community. Scand J Infect Dis 33:920-6

Regula G, Torriani K, Gassner B, Stucki F, Müntener CR. 2009. Prescription patterns of antimicrobials in veterinary practices in Switzerland. J Antimicrob Chemother 63:805-11.

Santschi EM. 2006. Prevention of postoperative infections in horses. Vet Clin North Am Equine Pract 22: 323-34, viii.

Seebregts CJ, Zwarenstein M, Mathews C, Fairall L, Flisher AJ, Seebregts C, Mukoma W, Klepp KI 2009. Handheld computers for survey and trial data collection in resource-poor settings: Development and evaluation of PDACT, a Palmtrade mark Pilot interviewing system. Int J Med Inform Jan 19. [Epub ahead of print]. Article in press.

Seguin MA, Vaden SL, Altier C, Stone E, Levine JF. 2003. Persistent urinary tract infections and reinfections in 100 dogs (1989-1999). J Vet Intern Med 17:622-31.

Sherding RG. 2000. Chapter 9 Feline Infectious Respiratory Disease; in Saunders manual of small animal medicine / [edited by] Stephen J. Birchard, Robert G. Sherding. – 2nd edition. W.B. Saunders Company. ISBN: 0-7216-7078-4.

Sischo WM. 2006. Stakeholder position paper: dairy producer. Prev Vet Med 73:203-8.

Southwood LL. 2006. Principles of antimicrobial therapy: what should we be using? Vet Clin North Am Equine Pract 22: 279-96, vii.

Statistics Denmark 2009. Danmarks Statistik, Copenhagen, Denmark. http://www.dst.dk/HomeUK/Statistics/focus_on/focus_on_show.aspx?sci=496 [15.11.2010]

Statistics Norway 2009. Statistisk sentralbyrå, Hamar, Norway. Available from: http://www.ssb.no/en/ [15.11.2010]

Stege H, Bager F, Jacobsen E, Thougaard A. 2003. VETSTAT-the Danish system for surveillance of the veterinary use of drugs for production animals. Prev Vet Med 57:105-15.

Stevens KB, Gilbert J, Strachan WD, Robertson J, Johnston AM, Pfeiffer DU. 2007. Characteristics of commercial pig farms in Great Britain and their use of antimicrobials. Vet Rec 161:45-52.

SVJ 2008. Svenska Jordbruksverket. The Swedish Board of Agriculture. Statistics on livestock in Swedish agriculture. http://www.jordbruksverket.se/webdav/files/SJV/Amnesomraden/Statistik%2C%20fakta/Husdjur/JO23/JO23SM0901/JO23SM0901_inEnglish.htm [15.11.2010]

SVARM 2008. Swedish Veterinary Antimicrobial Resistance Monitoring. The National Veterinary Institute (SVA), Uppsala, Sweden 2009. ISSN 1650–6332. Available at http://www.sva.se/ [15.11.2010]

SVARM 2009. Swedish Veterinary Antimicrobial Resistance Monitoring. The National Veterinary Institute (SVA), Uppsala, Sweden 2010. ISSN 1650–6332. Available at http://www.sva.se/ [15.11.2010]

Taponen S, Pyörälä S. 2009. Coagulase-negative staphylococci as cause of bovine mastitis- not so different from Staphylococcus aureus? Vet Microbiol 134: 29-36.

Thiry E, Addie D, Belák S, Boucraut-Baralon C, Egberink H, Frymus T, Gruffydd-Jones T, Hartmann K, Hosie MJ, Lloret A, Lutz H, Marsilio F, Pennisi MG, Radford AD, Truyen U, Horzinek MC. 2009. Feline herpesvirus infection. ABCD guidelines on prevention and management. J Feline Med Surg 11:547-55.

TIKE 2009. Matilda-tietopalvelu, Tike, Maa- ja metsätalousministeriön tietopalvelukeskus. http://www.matilda.fi/ [15.11.2010] (only in Finnish)

Traub-Dargatz JL, George JL, Dargatz DA, Morley PS, Southwood LL, Tillotson K. 2002. Survey of complications and antimicrobial use in equine patients at veterinary teaching hospitals that underwent surgery because of colic. J Am Vet Med Assoc. 220:1359-65.

Truyen U, Addie D, Belák S, Boucraut-Baralon C, Egberink H, Frymus T, Gruffydd-Jones T, Hartmann K, Hosie MJ, Lloret A, Lutz H, Marsilio F, Pennisi MG, Radford AD, Thiry E, Horzinek MC. 2009. Feline panleukopenia. ABCD guidelines on prevention and management. J Feline Med Surg 11:538-46.

Ungemach FR, Müller-Bahrdt D, Abraham G. 2006. Guidelines for prudent use of antimicrobials and their implications on antibiotic usage in veterinary medicine. Int J Med Microb 296, Suppl 2: 33-38.

USDA 2010. United States Department of Agriculture, National Agricultural Statistics Service. Farms, Land in Farms, and Livestock Operations 2009 Summary February 2010. ISSN: 1930-7128. http://usda.mannlib.cornell.edu/usda/current/FarmLandIn/FarmLandIn-02-12-2010_new_format.pdf [29.9.2010]

VMD 2008/09. Veterinary Medicines Directorate Annual Report&Accounts 2008/09. The Department for Environment, Food & Rural Affairs, the United Kingdom. ISBN: 978-0-10-295955-0. http://www.official-documents.gov.uk/document/hc0809/hc05/0552/0552.pdf [15.11.2010]

Watson ADJ, Maddison JE. 2001. Systemic antibacterial drug use in dogs in Australia. Austr Vet J 79: 740-746.

Weese JS. 2006. Investigation of antimicrobial use and the impact of antimicrobial use guidelines in a small animal veterinary teaching hospital: 1995-2004. J Am Vet Med Assoc 15:553-8.

Weese JS, Cruz A. 2009. Retrospective study of perioperative antimicrobial use practices in horses undergoing elective arthroscopic surgery at a veterinary teaching hospital. Can Vet J 50:185-8.

Wegener Henrik C, Aarestrup Frank M, Jensen Lars Bogø, Hammerum Anette M, Bager Flemming. 1999. Use of Antimicrobial Growth Promoters in Food Animals and Enterococcus faecium Resistance to Therapeutic Antimicrobial Drugs in Europe. Emerg Inf Dis 5:329-335.

WHO 2003. 1st Joint FAO/OIE/WHO Expert Workshop on Non-human Antimicrobial Usage and Antimicrobial Resistance: Scientific assessment, Geneva, Switzerland 2003. http://www.who.int/foodsafety/publications/micro/nov2003/en/ [15.11.2010]

WHO 2004. 2nd Joint FAO/OIE/WHO Workshop on Non-human Antimicrobial Usage and Antimicrobial Resistance: Management Options, Oslo, Norway, 2004. http://www.who.int/foodsafety/publications/micro/mar04/en/ [15.11.2010]

WHO 2007. Critically important antimicrobials for human medicine. Categorization for the development of risk management strategies to contain antimicrobial resistance to non-human antimicrobial use. Report of the second WHO expert meeting, Copenhagen, 29-31 May 2007.World Health Organization, Department of Food Safety, Zoonoses and Foodborne Diseases. ISBN 978 92 4 159574 2. www.who.int/entity/foodborne_disease/resistance/antimicrobials_human.pdf [15.11.2010]

Wilke. 1999. Leitlinien für den sorgfältigen Umgang mit antimikrobiell wirksamen Tierarzneimitteln Stand: 1999. Bundesgesundheitsblatt - Gesundheitsforschung - Gesundheitsschutz 43: 235-236.

www.dvfa.dk. Danish Veterinary and Food Administration. Ministry of Food, Agriculture and Fisheries, Denmark. Distribution and use of veterinary drugs in Denmark. http://www.uk.foedevarestyrelsen.dk/AnimalHealth/Veterinary_drugs/forside.htm [15.11.2010]

www.matilda.fi. Statistical Group of the Information Centre of the Ministry of Agriculture and Forestry (Tike). Information Service of Agricultural Statistics in Finland. [15.11.2010]

http://www.mmmtike.fi/www/en/index.php. Information Centre of the Ministry of Agriculture and Forestry in Finland. [15.11.2010]

Zaninelli M, Tangorra FM, Castano S, Ferrara A, Ferro E, Brambilla PG, Faverzani S, Chinosi S, Scarpa P, Di Giancamillo M, Zani D, Zepponi A, Saccavini C. 2007. The O3-Vet project: a veterinary electronic patient record based on the web technology and the ADT-IHE actor for veterinary hospitals. Comput Methods Programs Biomed 87:68-77.

Appendix 1

The use of antimicrobial drugs in animals – a survey questionnaire, 20–26 May 2002

Background information about the veterinary surgeon

Practice area:
1. Province of Southern Finland
2. Province of Western Finland
3. Province of Eastern Finland
4. Province of Oulu
5. Province of Lapland
6. Province of Åland

Gender:
1. Male
2. Female

Year of graduation:

Specialist degree:
1. Yes
2. No

If yes, please specify:

Speciality area of practice (please select the most important):
1. Small animals
2. Cattle
3. Pigs
4. Horses
5. Mixed practice
6. Other. Please specify: ________________
7. I do not practice at present.

Total number of patients during the week of this survey

If you wish to participate in a prize draw and receive personal feedback, please provide your contact details below.

Name:
Veterinary surgeon's ID number:
Address:
Telephone:
Email:

1. Animal species
(For the group treatment of production animals, please indicate the number of patients.)

1. Dog
2. Cat
3. Horse
4. Cattle _____ patients
5. Pig _____ patients
6. Fur animals _____ patients
7. Fish _____ kg
8. Other. Please specify: ____________

2. Please select as appropriate:

1. Regular visit by appointment (surgery or farm)
2. Emergency call (surgery or farm)
3. Telephone prescription

3. Main diagnosis (please select the key diagnosis for the treatment decision)
Skin and ears, hypodermis
1. Skin infection (pyoderma or cellulitis)
2. Wound/abscess
3. Outer ear infection

Urinary tract
4. Acute urinary tract infection (uncomplicated)
5. Chronic or recurrent urinary tract infection
6. Obstruction of the lower urinary tract (cats)

Respiratory tract
7. Signs of upper respiratory tract infection (pharyngitis, rhinitis, sneezing, etc.)
8. Tracheobronchitis (including kennel cough)
9. Pneumonia

Mouth and digestive tract
10. Gingivitis or other oral infection
11. Acute intestinal infection
12. Chronic intestinal infection
13. Porcine diarrhoea or postweaning diarrhoea

Other indications
14. Endometritis/pyometra
15. Acute mastitis (cattle)
16. MMA syndrome/milk fever (pig)
17. Arthritis or tail biting

18. Antimicrobial medication associated with a surgical procedure.
Please specify the procedure: ____________
19. Other diagnosis. Please specify: ______________

4. Duration of signs before seeking medical advice (please select one)
1. 0–3 days
2. 4–7 days
3. 8–14 days
4. 15 or more days

5. Which diagnostic <u>examinations</u> or <u>procedures</u> were carried out (please select all applicable)?
1. Clinical examination
2. Urinary dipstick
3. Secretion microscopy
4. Leucocytes
5. Clavulanic acid test
6. Bacterial culture and resistance
7. X-ray or ultrasound examination
8. CMT
9. Other examination or procedure. Please specify: ____________

6. Please specify the <u>antimicrobial drug</u> administered to the patient by the veterinary surgeon *during the visit:*

Name of preparation and dosage form

Concentration

Administered dose

Name of preparation and dosage form

Concentration

Administered dose

7. Please specify the <u>oral</u> or <u>injected</u> antimicrobial drug prescribed or dispensed for the patient's *further treatment*:

Name of preparation and dosage form

Concentration

Duration of treatment ____________ days

Prescribed/dispensed dose

Name of preparation and dosage form

Concentration

Duration of treatment ____________ days

Prescribed/dispensed dose

8. Please specify the antimicrobial drug prescribed or dispensed to the patient as <u>local treatment</u> (e.g., intramammary infusions):

Name of preparation and dosage form

Concentration

Duration of treatment ____________ days

Prescribed/dispensed dose

9. Did any of the following factors influence your choice of antimicrobial drug?

1. Allergy (suspected)
2. Patient's other chronic illness
3. Owner's demand/request
4. Recurrent/chronic infection
5. Other. Please specify: ________________

10. Please select as appropriate:

1. First visit due to this infection period
2. Repeat visit

11. Completed by (please provide your veterinary surgeon's ID number, especially if you wish to receive feedback)