

Memorandum 2003:9a

**Recommendations for the use of  
antimicrobial agents in the treatment of  
the most significant infectious diseases  
in animals**

Helsinki 2003

To: The Ministry of Agriculture and Forestry

The Ministry of Agriculture and Forestry appointed a working group on 6<sup>th</sup> March 2002 the objective of which was to renew the Recommendations for the use of antimicrobial agents in the treatment of the most significant infectious diseases in animals, and propose as to how the update of recommendations should be undertaken in the future. Furthermore, the working group investigated how the recommendations for the use of antimicrobial agents in the treatment of animals issued by the working group of 1996 have been implemented. The working group was to complete their task by 31<sup>st</sup> December 2002. The Ministry of Agriculture and Forestry granted an extension until 30<sup>th</sup> June 2003.

Docent of Domestic Animal Reproduction Olli Peltoniemi from the Finnish Association for Food Animal Practitioners was appointed chairman of the group. Appointed members were Professor Satu Pyörälä from the Faculty of Veterinary Medicine of the University of Helsinki, Veterinary Practitioner Merja Rantala from the Veterinary Teaching Hospital of the University of Helsinki, Docent Liisa Kaartinen from the National Agency for Medicines, Veterinary Practitioner Anna-Liisa Myllyniemi from the National Veterinary and Food Research Institute, Veterinary Practitioner Ritva Kaikkonen from the Horse Section of the Finnish Association of Veterinary Practitioners, and Specialist in Small Animal Diseases, DVM Minna Rinkinen from the Small Animal Section of the Finnish Association of Veterinary Practitioners. Secretaries for the group were Veterinary Officer Katariina Kivilahti-Mäntylä up until 24.9.2002 and Veterinary Officer Henriette Helin starting from 17.10.2002.

Prior to the update work, the 1996 recommendations were circulated to the following authorities for comments regarding the required changes: the Faculty of Veterinary Medicine of the University of Helsinki, the National Veterinary and Food Research Institute, Pharma Industry Finland, the National Food Agency, the Veterinary Association, the National Public Health Institute and the National Agency for Medicines.

During the course of the work the following experts were consulted: Veterinary Practitioners Henry Kuronen, Vuokko Puurula, Eija Rimaila-Pärnänen, Laila Rossow and Pia Vennerström from the National Veterinary and Food Research Institute, Clinical Teacher Mari Heinonen, Professor Terttu Katila, Director of Animal Hospital Outi Laitinen, Specialist in Small Animal Diseases, DVM Minna Rajamäki, Veterinary Practitioner Tita Saukko, DVM Anssi Tast, Specialist in Small Animal Diseases, DVM Tarja-Riitta Vuorikoski from the Faculty of Veterinary Medicine of the University of Helsinki, Veterinary Practitioners Lassi Kauko and Helena Kuntsi-Vaattovaara and Specialists in Small Animal Diseases, DVM Anu Lappalainen and DVM Leena Saijonmaa-Koulumies.

The proposal for the Memorandum was widely circulated for comments which were submitted by the following authorities: the National Veterinary and Food Research Institute, The State Provincial Office of Southern Finland, the Faculty of Veterinary Medicine of the University of Helsinki, the State Provincial Office of Eastern Finland, the National Public Health Institute, Leo Animal Health, the National Agency for Medicines, Pharma Industry Finland, The Central Union of Agricultural Producers and Forest Owners (MTK), the Finnish Game and Fisheries Research Institute, the Ministry for Social Affairs and Health, the Veterinary Association, the Ophthalmologist Veterinary Practitioners in Finland and the Institute of Biology of the Academy of Åbo.

The working group respectfully submits its unanimous memorandum Recommendations for the use of antimicrobial agents in the treatment of the most significant infectious diseases in animals to the Ministry of Agriculture and Forestry.

In Helsinki, 15th of May 2003.

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## **I CURRENT SITUATION IN FINLAND**

### **1. Preface – Why are the recommendations updated?**

In Finland recommendations for the use of antimicrobial substances in veterinary medicine were published for the first time in 1996. Already at that time it was considered important that the current animal disease and antimicrobial resistance situation in Finland, coupled with the range of available products, be taken into consideration when drafting the national recommendations for treatment. The Finnish recommendations for the use of antimicrobial substances in veterinary medicine can be considered as pioneer work in the world because similar, equally detailed recommendations had not been issued anywhere. Many countries and organisations as well as the pharmaceutical industry have now published their own recommendations for the controlled use of antimicrobial substances. More than six years later, it was time to bring the Finnish recommendations and practical illustrations up to date.

The new veterinary medicines entering the market are primarily broad spectrum antimicrobials. Pharmaceutical industry is largely responsible for the information regarding medicines aimed at veterinary practitioners, and new medicines often receive considerable emphasis in that information. The new recommendations to be published aim to offer veterinary practitioners information on the position of different medicinal substances in the Finnish veterinary practice today. The use of antimicrobial substances should continue to be prudent and the treatment of infections as specific as is practicable in both human and veterinary medicine: narrow spectrum antimicrobials should be used instead of broad spectrum ones.

Clinical recommendations for treatment should be based on published research on the efficacy of medicines. New studies are being published continuously and critical scrutiny is required to select the studies on which the new recommendations are based. The latest available information of the present local antimicrobial resistance situation and the consumption of antimicrobial substances were utilised in the update of the recommendations. Antimicrobial resistance situation in Finland is currently highly favourable, enabling us to influence this positive trend by making sensible choices in medication, thus maintaining the efficacy of the

medicines. The 1996 recommendations for the use of antimicrobial substances in animals are now revised and updated as part of the battle against the increasing resistance.

Maintaining the efficacy of antimicrobial substances is one of the biggest challenges of human and veterinary medicine in the next few years. Human and veterinary medicine experts all over the western world are concerned about the increased resistance to fluoroquinolones presented by zoonotic bacteria, such as salmonella and campylobacter. The problems caused by the increased resistance to antimicrobials and resistant bacteria cannot be overcome by developing new medicines. New medicines should possess new mechanisms of action, and the probability of discovering such medicinal substances is becoming extremely remote. Therefore, the only effective means remaining is the prudent use of antimicrobial substances coupled with preventative measures, such as improving the environmental conditions as well as vaccinations and other prophylactic measures.

## **2. The working group of 1996 – recommendations in practice**

In 1996 the working group concluded that the resistance to animal pathogens was still at a reasonable level in Finland. However, active measures were called for to maintain the favourable situation. Controlled use of antimicrobial substances both in veterinary medicine and as feed additives was considered the most important means in winning this objective.

To reach the target, the working group suggested that resistance surveillance be continued and expanded, residue surveillance be continued, and a programme be launched to monitor the consumption of antimicrobial substances. They also suggested recommendations for the use of antibiotic feed additives and more training and information.

### **2.1. Resistance follow-up**

Susceptibility testing of animal pathogens is carried out at the National Veterinary and Food Research Institute (EELA), municipal food laboratories and other laboratories. Susceptibility testing has been carried out for years, mainly for clinical purposes, but also for surveillance and research. For instance, the resistance of Salmonella against antimicrobial substances has been systematically monitored at the National Veterinary and Food Research Institute (EELA) since the early 1980s. The susceptibility of other zoonotic bacteria isolated from foodstuffs and food

industry, as well as so-called indicator bacteria, has been examined periodically. Indicator bacteria are bacteria isolated from the intestines of healthy animals. They can act as a reserve for resistance factors which in turn transfer into animal or human pathogenic bacteria. Information on the resistance situation in Finland of the clinically most significant bacteria both in human and veterinary medicine, as well as indicator bacteria isolated from animals, can be found in the FINRES 1999 publication.

A regular resistance monitoring programme, FINRES-Vet, was launched at the beginning of 2002. The programme monitors the antimicrobial susceptibility of animal pathogens isolated from production animals and pets, zoonotic bacteria and indicator bacteria. The indicator bacteria under inspection are collected from samples taken from the intestinal contents of cows, pigs or poultry according to an annual programme agreed upon separately. For the present, there have not been sufficient resources to implement the programme fully. Of the zoonotic bacteria *Salmonella* has been included in the programme. In future, other zoonotic bacteria will also be included. Antimicrobial susceptibility of animal pathogens is tested mainly for clinical purposes, but the results will also benefit the monitoring programme.

The antimicrobial substances to be tested are normally chosen according to the recommendations by the European Commission's ARBAO Project. Other antimicrobials may be included at need. The results of the programme will be published in the FINRES-Vet reports.

## **2.2. Monitoring the consumption**

In Finland no studies have been made so far to find out whether the recommendations for the use of antimicrobial substances of the 1996 working group have been implemented. However, the consumption of antimicrobial substances has been under investigation. Since 1995 the National Agency for Medicines has collected data on the consumption of antimicrobial substances authorised for use in animals utilising the wholesale statistics on veterinary medicine products. The last published data is from 1999 (The Finnish Veterinarian Journal 2000). The objective has been to publish these data annually, but this is yet to be achieved. The results for the years 2000 and 2001 will be published in the FINRES-Vet report and, in future, the data for the consumption will be monitored as a separate project within the FINRES-Vet.

The Plant Production Inspection Centre monitors the consumption of antimicrobial and coccidiostatic feed additives annually (Figure 1).

### **2.3. Residues and withdrawal periods**

When the previous working group carried out its work on antimicrobial treatment in animals in 1995, Finland had just joined the European Union. Within the EU, the therapeutics of food producing animals all through the 1990s was greatly influenced by Council Regulation (EEC) 2377/90, which states that for medicinal substances administered to food-producing animals a maximum residue limit (MRL) must be established.

The Committee of Veterinary Medicinal Products of the European Agency for the Evaluation of Medicinal Products makes the MRL assessments, which set the basis for the MRL value established by the Commission. Each product is authorised with a withdrawal period based on the MRL values and individual studies on residues. The adequacy of the withdrawal periods of medicinal substances for the use in animals has been investigated at the National Agency for Medicines since 1999. These investigations are still under way because some of the substances still have a provisional MRL value.

The residue studies of old products have been carried out using the recommended dosage, which is often quite low according to the latest knowledge in pharmacokinetics. Because no trial results with higher dosages are available, the recommended dosage for food-producing animals cannot be increased. This puts the practitioner in an awkward position when treatment requires a larger dosage than what has been approved. Increasing the dosage or prolonging the course of treatment thus requires that the practitioner issues a longer withdrawal period for the product. Information regarding prolonged withdrawal periods is extremely scarce. However, it is of paramount importance for the practitioners to acknowledge the problems in establishing a withdrawal period and to take into account the nature of the ailment as well as possible effects multiple medications may have on the way substances are being eliminated.

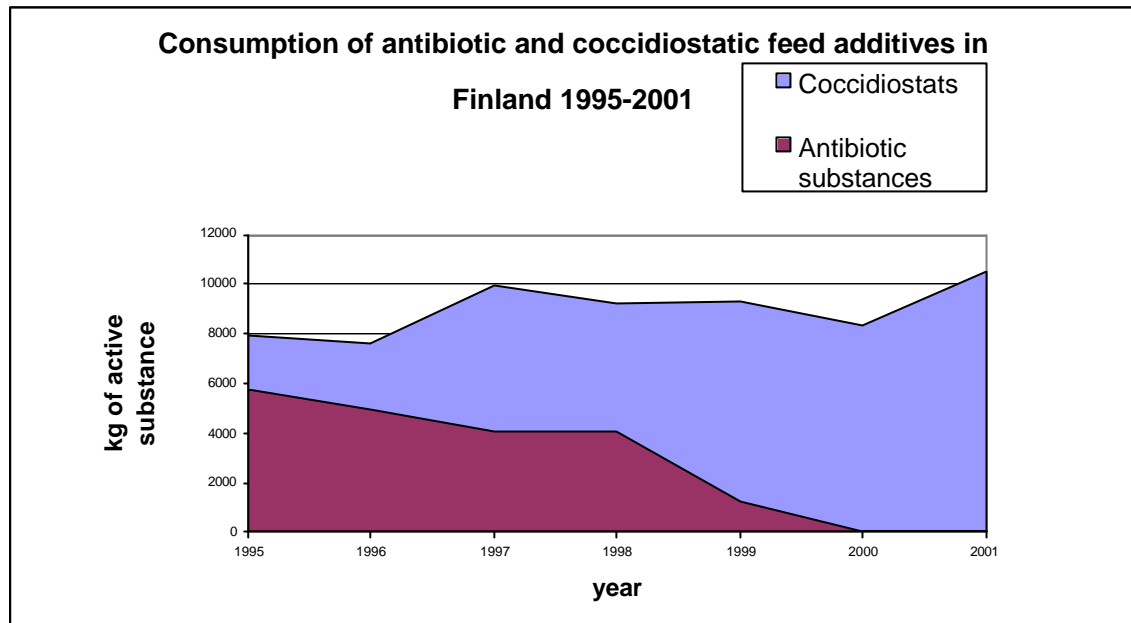
Monitoring of certain substances and residues in foodstuffs of animal origin takes place in all member states of the EU and is regulated by Council Regulation (EEC) 96/23, according to which the programme for sampling is made up and random samples are taken. Live animals as

well as foodstuffs of animal origin, i.e. meat, milk, fish, eggs and honey, have specific programmes of their own for sampling. The sampling is aimed at potential problem products.

#### **2.4. Antibiotic feed additives**

The working group of 1996 proposed in their memorandum that the use of antibiotic feed additives should be reduced systematically and that antibiotic feed additives as growth promoters should be banned in the whole EU. Finland took an active role in the EU to impose the ban and the Council banned the use of zinc bacitracin, spiramycin, virginiamycin and tylosin phosphate as feed additives as of 1 July 1999 (Council Regulation 2821/98 of 17 December 2001). The use of antibiotic growth promoters carbadox and olanquidox as feed additives was banned in Finland as of 1 September 1999. Omitting these two substances has had no effect on the pigs' health. Antibiotic feed additives have not been compensated with increased use of antimicrobials either, but the consumption of antimicrobial substances has remained constant since 1999.

Some coccidiostats currently used as animal feed additives, however, have antimicrobial properties. The ban on the last four feed additives classified as antibiotic has been proposed to take effect from 2006. Substances to be banned are monensin, salinomycin, avilamycin and flavophospholipol, or flavomycin (Proposal for a Regulation of the European Parliament and of the Council on additives for use in animal nutrition COM (2002) 153 final). In Finland coccidiostats are currently used only in poultry feed.



**Figure 1.** Consumption of antibiotic and coccidiostatic feed additives in Finland 1995-2001. Source: Plant Production Inspection Centre.

## 2.5. Training and information

The importance of training and information was acknowledged already six years ago. The working group considered it important for veterinary practitioners, animal owners and other interest groups to receive sufficiently impartial and up-to-date information regarding the use of antimicrobial substances and changes in the resistance situation. Veterinarians were also urged to bring up different treatment practices for discussion.

Subjects relating to the use of antimicrobial substances have been dealt with nearly annually in the Annual Finnish Veterinary Congress and other veterinarian symposia and in post-graduate and further education since the publication of the first practical illustrations. Since 2000 it has been possible to take a specialist veterinary practitioner's degree at the Faculty of Veterinary Medicine where one of the subjects is the usage of antimicrobials and resistance to antimicrobial substances. However, no long-running, coordinated training scheme for veterinary practitioners has been organised. Contacts, discussion and information have, by and large, depended on the initiative of individual experts.

Animal owners as well as other professional groups within the industry (e.g. farming advisory organisations, dairies, abattoirs and animal feed industry) all play an active part in the antimicrobial treatment of animals. To date, no systematic training scheme has been provided for any of these groups.

Antimicrobial resistance was one of the important themes throughout Finland's Presidency in the EU in autumn 1999. Finland made proposals for improvement of the Community's legislation and guidelines in order to achieve a uniform judicial approach for the rational use of antimicrobial substances in the whole Community. The Council Decision of 14 December 1999 highlights the importance of preventive measures to reduce the consumption of antimicrobials.

In 1998-1999 the Ministry of Agriculture and Forestry was active in providing information on the use of antimicrobial substances for animals. General information was given out separately to veterinary practitioners and owners of both pets and food-producing animals. Particular attention was paid to the use of fluoroquinolones. The recommendations emphasised that the use of fluoroquinolones should be avoided, and this information was passed on to veterinary practitioners and owners of food-producing animals.

Other working groups have also emphasised the importance of further education and information. The most recent one was the joint working group on antimicrobial policy of the Ministry of Social Affairs and Health and the Ministry of Agriculture and Forestry in 2000, which proposed a systematic scheme of further education for all professionals working with antimicrobial medicines and substances in Finland. Despite the recommendations and proposals, further education directed at all relevant groups remains incoherent, and each group of professionals has channels of its own for information and education.

### **3. Finland today**

#### **3.1. Legislation**

By international standards, the use of antimicrobial substances is strictly regulated in Finland and the other Nordic countries. For instance, all antimicrobials administered internally are,

without exception, prescription only medicines in Finland. The Nordic practice has served as a model in reforming the pharmaceutical legislation in the EU.

The use of medicines and antimicrobial substances in animals is regulated with both national and EU legislation. The legislation can be broadly divided into following categories: provisions on the sales and distribution of medicines, provisions on the medicinal treatment of animals, provisions on residues, and legislation on feedingstuffs. In addition, the EU is reforming the zoonosis directive, which defines obligations for the member states to monitor the resistance situation of zoonotic organisms.

The objective, first and foremost, is to ensure the public health and the purity of foodstuffs. According to the directives concerning the medicinal treatment of animals, only medicines that have been approved by the National Agency for Medicines are permitted for treatment of food-producing animals. A veterinary practitioner is obliged to give sufficient information on an animal's medication to its owner or keeper who, in turn, must ensure that the withdrawal period established for the medicine in question is complied with.

### **3.2. Foreign substance and residue monitoring**

Every year a few sporadic antimicrobial positive milk or tissue samples are discovered in Finland. Each case is investigated in cooperation between veterinary practitioners and food producers, and most findings have been caused by human error. In 2001 four meat samples (0.04%) of all samples taken from foodstuffs from animal origin tested positive for a foreign substance, while 11 positive milk samples (0.55%) were discovered using microbiological screening methods. No samples exceeding the maximum residue limit were discovered in fish, eggs and honey. No traces of prohibited growth promoters or other prohibited substances were found from live animals or from samples taken at slaughter in meat and fish production.

The results of the national residue monitoring programme in Finland for 2001 can be found on the National Food Agency's (Elintarvikevirasto) website at <http://www.elintarvikevirasto.fi/> under 'Food control'.

### **3.3. Current resources for resistance and consumption monitoring, education and research**

The resources dedicated to monitoring the resistance of animal pathogens (FINRES-Vet) continue to be minimal. Currently there is one veterinary practitioner at the National Veterinary and Food Research Institute (EELA) responsible for the programme, in addition to other duties. Similarly, the laboratory staff involved in resistance monitoring also has other duties.

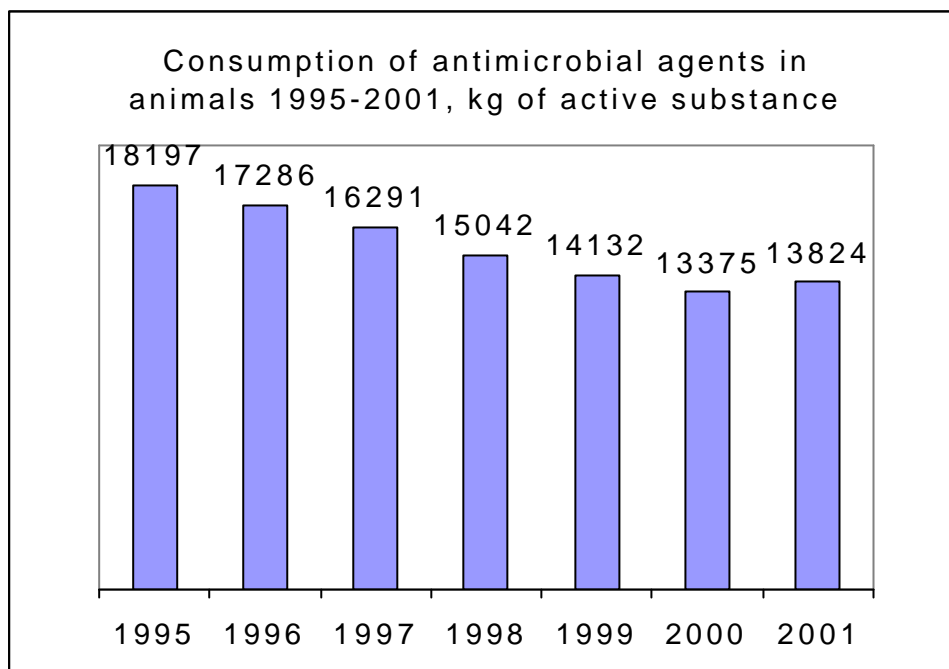
The National Agency for Medicines is responsible for monitoring the consumption of antimicrobial substances for use in animals, but it has not been possible to publish the results annually due to lack of resources.

There are no posts in clinical pharmacology or clinical microbiology at the Faculty of Veterinary Medicine of the University of Helsinki. The faculty has no resources dedicated to the research and education on antimicrobial resistance. Some research on the subject has been carried out at the faculty, chiefly at the Department of Clinical Veterinary Medicine, which has been funded externally.

At the Department of Food and Health of the Ministry of Agriculture and Forestry there is only one post in duties which include matters relating to resistance.

### **3.4. Consumption of antimicrobial substances authorised for treatment of animals**

The consumption of antimicrobials has been monitored since 1995. During the first five years, the annual consumption showed a steady decrease, but since then there has been very little change (Figure 2). The decrease in consumption of antimicrobials was partly due to the decrease in the number of animals, as well as the more moderate and controlled use of antimicrobial substances by veterinary practitioners.



**Figure 2.** Total consumption of antimicrobial substances in veterinary practice in 1995-2001. After the downward trend of the latter part of the 1990s the changes have been small. Data collected by the National Agency for Medicines.

The consumption of antimicrobials authorised for treatment of animals has also been examined according to different antimicrobial groups and methods of administration. These figures do not include antimicrobial products which are authorised for human use but used in small animal practice.

So far surveys on how the consumption of antimicrobials is divided between different species have been scarce. In the spring of 2001 a questionnaire regarding the use of antimicrobial substances was circulated among veterinary practitioners. The objective was to clarify how the consumption of antimicrobials is divided among different species and to what extent products authorised for human use are administered to different species in veterinary medicine. It was also investigated which antimicrobials are used for the most significant indications. The study showed the following distribution for the consumption of antimicrobial substances: cattle 60%, pigs 15%, dogs and cats 13%, horses 10% and fur animals 2%. Among other species the figure was less than 0.1% of the total consumption. Detailed information on this study will be published later on.

### 3.5. Use of antimicrobial substances in different animal species

In the therapeutic treatment of cattle, penicillins are by far the largest group of antimicrobials used, representing 80% of the total consumption of antimicrobial substances in cattle. The second largest groups are aminoglycosides (6%) and trimethoprim-sulphonamide combinations (5%). The large proportion of aminoglycosides is due to the fact that nearly all intramammary products contain an aminoglycoside.

In recent years the numbers of both dairy and beef cattle have decreased slightly in Finland. Improved health care on both dairy and beef farms promotes preventive medicine, which should be reflected as a diminished need for medicinal treatment. Mastitis is still the most common ailment and cause for antimicrobial treatment in dairy cattle. However, according to the surveys carried out by the National Veterinary and Food Research Institute, the development has been very positive in Finland and the mastitis prevalence continues a downward trend since the 1980s. In 1995 the mastitis prevalence was 38%, but in 2001 it was only 32%. The proportion of mastitis caused by the *Staphylococcus aureus* bacterium had decreased to 10% in 2001, which in turn reduces the therapeutic use of antimicrobial substances to treat this complicated type of mastitis which is difficult to cure. In beef cattle the most common causes for the therapeutic use of antimicrobials are respiratory infections and diarrhoeas. In recent years, Finland has suffered from several epidemics of respiratory tract infections, and it has been necessary to administer considerable amounts of antimicrobials for treating these.

According to the survey carried out in spring 2001, the most common antimicrobial substances for therapeutic use in pigs were penicillins (33%), tetracyclines (30%) and trimethoprim-sulphonamide combinations (20%). Oral trimethoprim-sulphonamide combinations as well as products containing tetracyclines are used mainly to treat food-producing animals, especially pigs. The consumption of these products has decreased markedly. The total consumption of trimethoprim-sulphonamide combinations was 2,882 kg in 1995 and 1,892 kg in 2001. Correspondingly, a total of 3,944 kg of tetracyclines were consumed in 1995 and 1,672 kg in 2001. The number of pigs has been about the same in recent years but the quantity of pigmeat produced has increased. In 1995, 2,066 million pigs were slaughtered, and six year later the number was almost the same, 2,061 million. Pigmeat production totalled 16,755 million kilos in 1995 and 17,576 million kilos in 2001.

Various programmes for the improvement of animal health have been quite efficient in reducing the consumption of antimicrobial substances on pig farms. The eradication programmes of enzootic pneumonia have also reduced the therapeutic use of antimicrobials on pig farms. Through the eradication programmes of enzootic pneumonia the prevalence of the infection per farm has been reduced to a fraction of the original figure. Now the national animal health care system aims to eradicate the disease from Finland altogether by means of national projects.

Although the use of antimicrobial substances for pigs is more controlled at present, the current positive trend should not be taken for granted. Pig industry has undergone a significant structural change in recent years. Along with the change in the production structure, animal health and well-being have changed in ways which are not always positive. Because of the concentration of the production and increased unit sizes, it is more and more important to pay critical attention to production conditions in the light of animal health and well-being. The prevention of infectious diseases on the farm level must also be optimal. For example, undersized loose housing with slotted floors may be cramped and hazardous to pigs' health. Poor living conditions may result in an increase in the consumption of antimicrobial substances.

Many different antimicrobial groups are used in the therapeutic treatment of small animals. The largest group of antibiotics used for dogs were first generation cephalosporins (48%), whereas cats were most commonly treated with aminopenicillins (68%). Unlike in other animal species, antimicrobial products authorised for humans are used in treating small animals (dogs 10% and cats 5%).

In the 21st century, the range of antimicrobial products for the treatment of small animals has grown by several products that contain fluoroquinolones. The first oral fluoroquinolones authorised for small animal therapeutics came on the market in the spring of 2000. At the end of 2002, four oral fluoroquinolone products authorised for small animals were available, together with one topical product that contains fluoroquinolone. Despite the greater choice in products, a veterinary practitioner should bear in mind that fluoroquinolones are not the primary choice in treating infections, but their use should always be based on susceptibility testing.

In small animal therapeutics random use of the latest products should be avoided. The choice of antimicrobial should be based on the current and true resistance situation. The main sources of information on small animal therapeutics are American, but when referring to foreign publications it should be borne in mind that, for instance, the antimicrobial resistance situation in the United States is very different from that in Finland.

Horses are mostly treated with penicillins and trimethoprim-sulfonamide combinations. Other antimicrobial substances are used far less frequently.

In poultry, the low infection prevalence and absence of many significant infections coupled with favourable production conditions have kept the incidence of secondary bacterial infections low. The need for antimicrobials is rare. The growing turkey industry may alter this favourable situation, unless particular attention is paid to the production conditions and the prevention of infections.

The need for antimicrobial treatment in fish has decreased. This can be attributed to a substantial increase in the use of fish vaccines against infections requiring antimicrobial treatment in fish. Vaccinating against furunculosis and vibriosis has been perceived more economical than antimicrobial therapeutics. The significance of vaccinations in general should be actively promoted in health care.

## II PROPOSALS AND COMMENTS OF THE WORKING GROUP

### 4. Principles of antimicrobial treatment of animals

The principles of antimicrobial treatment of animals have not changed since the recommendations of 1996. The objective is to promote the prudent use of antimicrobials in animal therapeutics to control the rise of antimicrobial resistance in animal pathogens. Animal infections and inflammations ought to be prevented, above all, by ensuring good production and living conditions. However, sometimes the use of antimicrobials is unavoidable, in which case the following principles should be complied with:

- The use of antimicrobial substances must be justified.
- Antimicrobial prophylaxis should be prescribed only when a veterinary practitioner considers it necessary due to the gravity of a single case or the situation in an entire animal unit.
- Alternative methods which have been proven equally efficient should be given precedence over antimicrobial treatment. Guidelines for treating the most significant diseases should be issued to standardise the treatment practice.
- The course of antimicrobial treatment should not exceed the length required by the nature of the disease.
- Preceding antimicrobial treatment, the veterinary practitioner should ascertain by clinical examination that the symptoms indicate a bacterial infection. If necessary, the veterinarian will take appropriate samples to determine the pathogen and its antimicrobial susceptibility.
- All information regarding the patient, the cause and the nature of the infection, and the range of available products must be taken into account when making a decision regarding antimicrobial treatment. The chosen antimicrobial and the correct dosage aim to kill the

microbe or inhibit its growth to enable the immune system to destroy it and be cured of the infection.

- The primary choice should be a narrow spectrum antimicrobial. The use of broad-spectrum antimicrobials and antimicrobial combination should be avoided. Pathogens susceptible to penicillin ought not to be treated with other beta-lactams or broad-spectrum antimicrobials unless the patient is allergic to penicillins.
- In salmonellosis, antimicrobial substances are used only in the case of a life-threatening systemic infection.
- In viral infections, antimicrobials ought not to be used as prophylaxis against secondary bacterial infections.
- If an animal unit suffers from recurrent infections that require antimicrobial treatment, efforts should be made to eradicate the diseases by altering the production conditions and methods.
- When treating food-producing animals, the cost of the treatment and the withdrawal periods of the intended medication must be taken into account.
- Antimicrobial substances prone to fast-developing resistance or proven to have detrimental effects on the environment must be avoided.
- Certain antimicrobial substances are reserved solely for human therapeutics and should be used in animal therapeutics only in exceptional cases. Such antimicrobial substances include:
  - antimicrobial substances intended for the treatment of multiresistant strains of staphylococci and enterococci, e.g. mupirocin and vancomycin,
  - antimicrobial substances prone to fast-developing resistance, e.g. rifampicin,
  - third and fourth generation cephalosporins,
  - broader spectrum fluoroquinolones and
  - new macrolides, e.g. azithromycin and roxithromycin

## **5. Objectives**

The recommendations and their occasional update alone are not enough to promote the prudent use of antimicrobial substances, but additional resources are needed. Currently sufficient resources are available only for the residue monitoring required by the EU. Sufficient resources must be guaranteed for the systematic monitoring of antimicrobial resistance and the consumption of antimicrobial substances (according to species and indications), for ongoing and coordinated training of different professional groups as well as for cooperation with other expert forums for promoting the prudent use of antimicrobials (e.g. FiRe and Mikstra networks together with the Nordic network on monitoring of antimicrobial resistance in the food chain).

### **5.1. Resistance monitoring**

Recommendations based on the current resistance situation should continue to be issued for the use of antimicrobial substances either as first-line treatment or as an alternative choice in the treatment of the most significant animal infections. The FINRES-Vet programme should be implemented in full. Studies within the programme should cover not only the antimicrobial susceptibility of animal pathogens and zoonotic bacteria but also the so-called indicator bacteria isolated from food-producing animals. Sufficient resources should be granted for the full-scale implementation of the programme.

Different groups should be informed about matters relating to antimicrobial resistance, and training on the subject should be organised. Discussion among veterinary practitioners and other parties working with animal therapeutics together with those working in the food-producing animal industry should be promoted.

### **5.2. Consumption monitoring**

Achieving the prudent use of antimicrobial substances requires more detailed information regarding the therapeutic use of antimicrobials in different species. The working group considers it essential that, in future, data could be collected on the consumption of antimicrobial substances according to species as well as the true total consumption in animal therapeutics, including products authorised for humans. Data on the consumption according to indication should also be available. All this calls for more resources.

Monitoring should be a continuous, long-term effort combined with the surveillance of antimicrobial resistance. This would help us find out the effect of the developing resistance and the consumption of antimicrobial substances on each other, enabling us to target the actions specifically at the problem areas.

In future, collecting this data will be easier due to computerised processing of data. This will help us collect this data, provided that the transfer of data from one system to another will be developed further.

### **5.3. Health care**

Preventive health care is the most effective means of promoting the prudent use of antimicrobial substances and maintaining a favourable resistance situation. Improving the production conditions and animal health helps to restrict antimicrobials to their proper use, instead of using them to compensate for poor conditions. Particular attention should be paid to the implementation of the antiparasitic treatment and vaccination programmes. A satisfactory animal disease situation must be maintained despite the increased demands on productivity and larger unit sizes.

Health care as opposed to the treatment of diseases will receive increasing emphasis in the duties of a veterinary practitioner, and the role of health care programmes will become greater in the future. The quality of health care must be assured. National standards for the health care of food-producing animals are now being drafted.

As the health care programmes of food-producing animals are being standardised, attention should also be paid to the health care of horses and dog kennels, and large catteries need the help of health care experts as well.

### **5.4. Training and information**

So far there has been no long-running, coordinated training or information scheme on the controlled use of antimicrobial substances aimed at veterinary practitioners, animal producers and owners, or other relevant groups. Further training is also needed for laboratory staff and

veterinary practitioners in sample-taking and interpreting the results. Due to the lack of resources, training and information have largely relied on voluntary work by individual experts.

The working group considers that both financial and other resources should be granted for training, information and creating information-producing networks. The working group proposes that a new post be created under the Department of Food and Health of the Ministry of Agriculture and Forestry for the coordination and development of antimicrobial training in our country and for contacts among organisations and experts who monitor the use of antimicrobial substances. Adequate remuneration should be paid to those whose expertise is utilised in training and information.

### **5.5. Residue monitoring**

The monitoring of residues must not be reduced. Prudent use of antimicrobial substances prevents the occurrence of animal drug residues in foodstuffs of animal origin. Domestic products will be faced with increasing international competition. Finnish agriculture has been founded on the principle "from farm to table" for years. The objective is to produce pure and safe, ethically produced foodstuffs of good quality. Purity of foodstuffs may not be taken for granted. The correct usage of medicines, including compliance with the established withdrawal periods, requires continuous and active information and training.

### **5.6. Updating recommendations in the future**

Thus far, recommendations have been issued mainly for the choice of antimicrobial substances for treating various infections in different animals. This alone is no longer adequate, but the recommendations should also cover the dosage and the length of the treatment period as well as other necessary treatments and preventive measures.

Recommendations for veterinary medicine covering at least the most significant infections should be drawn up to promote the controlled use of antimicrobial substances. The working group proposes that recommendations for treatment be outlined as a follow-up project to be published, for example, on the extranet pages of the Department of Food and Health of the Ministry of Agriculture and Forestry. The recommendations for treatment should cover such significant infections as MMA in sows, tail biting in pigs and bovine mastitis.

The working group proposes that the duties of the new post to be created under the Department of Food and Health of the Ministry of Agriculture and Forestry include the monitoring of the resistance situation and the consumption of antimicrobial substances, contacts with the experts in animal therapeutics of different species and, when necessary, convening a group of experts to update these recommendations. The need for update must be assessed at least every three years.

### III RECOMMENDATIONS ACCORDING TO SPECIES

When examining a patient and deciding upon a treatment, critical consideration should be given as to whether an antimicrobial is needed and, if this is the case, which one should be used. This sets considerable demands for infection diagnostics. In clinical examination, clear signs of a bacterial infection should be present, including at least two of the following: local signs of infection, fever, leukocytosis or left shift of leukocytes, and possible changes indicating an infection as seen by means of different imaging techniques. Direct microscopic examination of exudates and bacteriological samples also assist in infection diagnostics. The choice of an antimicrobial substance should more often be based on isolating the bacterium and susceptibility testing.

Knowledge on the antimicrobial spectrum of different antimicrobial substances as well as on pharmacokinetics and pharmacodynamics of the species requiring treatment is of paramount importance for the best possible outcome of the treatment. The chosen substance must be one that penetrates well to the site of the infection and the concentration of active substance in the tissue remains sufficiently high. Sufficient concentration, again, depends on the microorganism causing the infection and on the site of the infection. This means that no single dosage can be prescribed for each disease, but the dosage and the length of the treatment period should be optimised according to the gravity of the infection, the infection site and the cause of the infection. Increasing antimicrobial resistance threatens the utility of many antimicrobials in the long term, and therefore their use should be directed to where they are the most beneficial. Advertising and images also affect the veterinarians' choice of medication to a certain extent. It is highly desirable that the use of a new antimicrobial product is not based on advertising alone but information on the product should be looked for in literature and the latest research.

Recovery depends largely on the patient's own defence mechanisms and the surrounding conditions at the site of the infection: dead tissue and low pH together with poor circulation can prevent recovery despite the antimicrobial substance. Conquering an infection always requires a well-functioning immune system. In the case of a bacterial infection, a response to antimicrobial treatment can normally be seen in 2-3 days. Changing from one product to another is no solution, but reassessing the diagnosis is in order. If necessary, the patient should

be given a referral at an early stage to avoid getting into the vicious circle of recurrent courses of antibiotics.

The updated recommendations for the use of antimicrobial substances on most significant animal infections have been published using the same model as in the first recommendations issued in 1996. Specific recommendations have been issued for each essential animal species or group. Typical characteristics of antimicrobial treatment of a particular species have been outlined in the summaries. Recommendations for different species according to indication have been presented as tables. Recommendations for cats and dogs are given in one table.

The working group has divided the antimicrobial substances into first-line treatments and alternative treatments. The first-line treatments include such antimicrobials and groups of antimicrobials that the working group regards as the best choice in the treatment of an infection, considering the pathogen and the infection coupled with the resistance situation and the qualities of the antimicrobial substance in question. They are substances that are effective against the most common pathogens. Primary choice aims at specific treatment. In multiple pathogen infections, the treatment is directed at the most common pathogens.

Some other useful medicinal substances or groups of substances are given as alternative treatments. In some cases the boxes have been left empty, which indicates that the working group had no opinion on the choice of a substance. In some cases the 'Remarks' column refers to the most essential preventive measures, like vaccinations.

## Ruminants

The antimicrobial treatment of ruminants is somewhat problematic compared with other domestic animals. The pharmacokinetics of many medicinal substances in ruminants, e.g. distribution volume, differs greatly from non-ruminants. Ruminants' liver has a highly developed xenobiotic metabolism, which means that ruminants rapidly eliminate substances that metabolise in the liver. A cow's rumen is large and has a low pH value compared with blood. Substances that ionise as alkali have a tendency to concentrate in the rumen.

Oral administration of antimicrobials in ruminants is highly problematic. Medicinal substances are diluted in a large quantity of fluid. In addition, ruminal microbes have an active xenobiotic metabolism which inactivates many medicinal substances. Trimethoprim, for instance, is eliminated fully in the rumen. The anaerobic nature of the rumen considerably decreases the activity of some antimicrobial substances, e.g. aminoglycosides. Ruminant's well-being depends on its ruminal microbes, while antimicrobial substances can damage the ruminal microflora or have an undesirable selective effect. Ruminants' urine is alkaline, which means that acidic substances are excreted in urine better than the alkaline ones.

The behaviour of medicinal substances in neonate ruminants differs from that of full-grown ones; in fact, a pre-ruminating individual resembles a non-ruminant. Many substances are still absorbed quite well from the gastrointestinal tract. On the other hand, young ruminants are susceptible to the adverse effects antimicrobials may have, and the oral administration of many antimicrobials may induce diarrhoea and malabsorption. The liver's ability to metabolise medicinal substances is often poor in the neonate ruminant. The half-life of medicinal substances is usually longer in young calves than in adult cows. For instance, the half-life of trimethoprim in a one-day-old calf is eight hours as opposed to one hour in an adult.

For sheep and goats, the principles of antimicrobial treatment are similar to those for cattle. Sheep and goats are more prone to tissue irritation, and thus intramuscular administration of irritant substances should be avoided. Pharmacokinetic aspects differ between the species and, consequently, recommendations for dosing should be based on studies on particular species. Unfortunately, there is very little published information available on the pharmacokinetics in sheep and goats. Not many products are authorised for the use on sheep and goats, and products authorised for the use on other species are frequently used to treat these.

The choice of an antimicrobial substance in the treatment of ruminants is still largely based on experience rather than on carefully planned clinical trials. Optimised doses and dosing schedules of most antimicrobial substances have not been studied for different indications. Clinical trials have been carried out in some infections, like aspiration pneumonia and mastitis, and recommendations can be based on these trials.

The following table (Table 1) shows the recommendations for the choice of a medicinal substance in treating microbial infections in ruminants under the current circumstances in Finland. All medicinal substances in the table were authorised or had a special licence in Finland in 2002. The principle has been that the primary choice is a specific treatment, i.e. an antimicrobial of as narrow a spectrum as possible. However, this may not always be possible, particularly in the case of a mixed infection caused by multiple pathogens. Attempts have been made to avoid recommending the use of antimicrobial substances in infections caused by a pathogen with increased resistance to the particular antimicrobial.

**Table 1. Ruminants**

Practical illustrations for alternative antimicrobial treatments in ruminants when the use of antimicrobials is indicated by the diagnosis. Unless otherwise stated, the method of administration is by injection. Explanations for the reference numbers after a pathogen or an antimicrobial substance can be found in the "Remarks" column.

The first-line treatments mentioned are antimicrobial substances or combinations of substances that are best suited for therapeutic treatment of a particular infection considering the pathogen, the disease, the resistance situation, and the properties of the antimicrobial substance. Some of the recommended treatments are scientifically proven for their clinical efficacy; for some, this is lacking and theoretic explanations have been complied with. First-line treatment aims at specific treatment. For instance, in infections where several bacteria are isolated, the treatment is directed at the most common pathogens.

Site of infection	Disease	Pathogen	First-line treatment	Alternative treatments	Remarks
Skin, ear and eye	Interdigital necrobacillosis	<i>Fusobacterium necrophorum</i> , <i>Bacteroides nodosus</i> .	Penicillin G.	Oxytetracycline.	Disinfectant hoof baths as well.
	Infective ceratoconjunctivitis	<i>Moraxella bovis</i> .  In sheep and goats chlamydiae, mycoplasmas.	Fucidic acid.	Oxytetracycline penicillin G.	Normally local treatment. Disease often self-limited.
Respiratory tract	Pneumonia in calves and lambs	<i>Mannheimia haemolytica</i> , <i>Hemophilus somnus</i> , viruses, mycoplasmas, Pasteurella.	Penicillin G or oxytetracycline.	Fluoroquinolones or trimethoprim - sulfonamide combinations.	
	Aspiration pneumonia	Multiple.	Penicillin G.	Oxytetracycline.	If symptoms severe, no treatment, culling recommended.
Gastrointestinal tract	Neonatal diarrhoea	<i>Escherichia coli</i> .	Trimethoprim - sulfonamide combinations .	Fluoroquinolones .	Confirm diagnosis. Rehydration essential. No antimicrobial substances orally.
	Peritonitis	<i>Arcanobacterium pyogenes</i> , <i>E. coli</i> , <i>Fusobacterium necrophorum</i> and other anaerobes .	Penicillin G + trimethoprim - sulfonamide combinations .	Penicillin G + fluoroquinolones or oxytetracycline.	Extremely poor prognosis, normally not treated.
	Salmonellosis	<i>Salmonella dublin</i> , <i>S. typhimurium</i> etc.	No antimicrobial substances.	Trimethoprim - sulfonamide combinations or fluoroquinolones .	Antimicrobial treatment only in life-threatening infections.
	Sheep enterotoxemia	<i>Clostridium perfringens</i>	No antimicrobial substances.	Penicillin G.	Rehydration. Vaccinating the flock recommended.

Gastrointestinal tract continued	Coccidiosis	<i>Eimeria</i> sp.	Trimethoprim - sulfonamide combinations .	Toltrazuril.	Rehydration.
	Cryptosporidiosis	<i>Cryptosporidium</i> sp.			No effective treatment available.
Genitals	Metritis	<i>Arcanobacterium pyogenes</i> , <i>E. coli</i> , anaerobes, Streptococci, Staphylococci.	Penicillin G or oxytetracycline.		Systemic treatment.
	Endometritis	Usually aseptic inflammation.	No antimicrobial substances.	Penicillin G.	Induction of estrus. If antimicrobials used, local treatment. In principle, uterine lavage only exceptionally.
Urinary tract	Cystitis	<i>Corynebacterium renale</i> , <i>Arcanobacterium pyogenes</i> , <i>E. coli</i> .	Penicillin G.	Subject to susceptibility testing.	Long treatment period.
	Pyelonephritis	<i>Corynebacterium renale</i> .	No antimicrobial substances.	As above.	Poor prognosis. Long treatment period.
Udder	Streptococcal mastitis	<i>Streptococcus agalactiae</i> , <i>S. dysgalactiae</i> , <i>S. uberis</i> .	Penicillin G.		Primarily local treatment. Prevention of essence: applies to all types of mastitis.
		Enterococci.	Subject to susceptibility testing.		Often resistant; prognosis of bacteriological recovery doubtful.
	Staphylococcal mastitis	<u><math>\beta</math>-lactam negative:</u> <i>Staphylococcus aureus</i> <sup>1</sup> , coagulase negative staphylococci (CNS).	Penicillin G.		Systemic or local treatment. <sup>1</sup> In acute <i>S. aureus</i> –infection systemic or combination treatment. Poor prognosis in chronic <i>S. aureus</i> –mastitis. In CNS mastitis primarily local treatment.

Udder continued	Staphylococcal mastitis continued	<u><math>\beta</math>-lactam positive:</u> <i>Staphylococcus aureus</i> , coagulase negative staphylococci (CNS).	Cloxacillin.	Subject to susceptibility testing.	Systemic or local treatment depending on medication. Poor prognosis if pathogen penicillin resistant <i>S. aureus</i> .
	Coli mastitis	<i>Escherichia coli</i>	No antimicrobial substances.	Enrofloxacin or trimethoprim - sulfonamide combinations .	Systemic treatment. Antimicrobial substance indicated only in postpartum and in serious cases. Large dose of trimethoprim - sulfonamide combination.
	Summer mastitis	<i>Arcanobacterium pyogenes</i> , <i>Streptococcus dysgalactiae</i> , anaerobes .	Penicillin G.	Macrolides .	Systemic treatment. Poor prognosis for resuming milk production.
	Other pathogens causing mastitis	<i>Klebsiella</i> sp.	Subject to susceptibility testing.	Enrofloxacin.	Prognosis of bacteriological recovery doubtful.
		<i>Pseudomonas</i> sp.	Subject to susceptibility testing.	Enrofloxacin.	Poor prognosis.
		Coryneforms (most common <i>Corynebacterium bovis</i> ).	No antimicrobial substances.	Penicillin G.	Improved sanitation essential.
		<i>Bacillus</i> sp.	Penicillin G.		
Yeasts .		No antimicrobial substances.		Confirm diagnosis. Supportive care. Doubtful prognosis.	
Musculo-skeletal system	Cellulitis, bursitis	<i>Arcanobacterium pyogenes</i> , anaerobes, streptococci, staphylococci.	No antimicrobial substances.	Penicillin G.	Normally chronic.
	Arthritis	<i>Arcanobacterium pyogenes</i> , <i>E. coli</i> , other bacteria	Penicillin G (+ trimethoprim - sulfonamide combinations or fluoroquinolones).	Oxytetracycline or trimethoprim - sulfonamide combinations .	Poor prognosis in polyarthritis.

Other infections	Calf's umbilical infection	Multiple pathogens .	Penicillin G.	Oxytetracycline or penicillin G + fluoroquinolones .	Prevention essential. In chronic cases draining of the abscess or surgical treatment.
	Tetanus	<i>Clostridium tetani</i> .	Penicillin G.		Poor prognosis.
	Listeriosis	<i>Listeria monocytogenes</i> .	Penicillin G.	Oxytetracycline.	Large dose.
	Malign oedema	<i>Clostridium septicum</i> .	Penicillin G.	Oxytetracycline.	Poor prognosis.
	Bovine tick borne fever	Rickettsiae.	Oxytetracycline.		Short treatment period.
	Tick borne fever, sheep	<i>Ehrlichia phagocytophila</i> .	Oxytetracycline.		
	Piroplasmosis	<i>Babesia</i> sp.	Imidocarb (special permit).		
Gastrointestinal tract (abomasal torsion or foreign body)		Penicillin G.		Antimicrobial started pre- or perioperatively. Abomasal surgery. No antimicrobials or short treatment period; foreign body: longer treatment period. If complications occur during the removal of foreign body, poor prognosis.	
Prevention of infection in surgical procedures	Caesarean section		Penicillin G.	Penicillin G + fluoroquinolones or oxytetracycline.	Antimicrobial treatment started preoperatively. Longer period of treatment and broader spectrum if contamination of peritoneal cavity occurs during procedure.
	Thelotomy		No antimicrobial substances if no mastitis .	Penicillin G + aminoglycoside.	Local treatment, frequent milking.

## Pigs

Many of the diseases treated in pigs are caused by microbial infections, and thus the most common medicinal treatments administered to pigs are antimicrobial substances. In recent years, increasing attention has been paid to prophylactic antimicrobial treatment, potential residues, the occurrence of resistant strains, and alternative treatments. The consumer expects that animals' well-being be taken into consideration in meat production, which includes minimising the use of antimicrobial substances. Antimicrobials administered routinely to every patch of fattening pigs arriving at a pig farm have no place in modern health care. A veterinarian's responsibility is to work out measures which are appropriate on each pig farm to maintain the health and prevent diseases, thus avoiding the use of antimicrobial substances. All medication should also be economically justified. In the case of the infectious swine diseases found in Finland, like enzootic pneumonia, atrophic rhinitis, dysentery and scab, the primary objective is to eradicate the pathogen from the production unit.

Medication is administered to pigs either by individual injections or by mass medication in feed or water. The 20% rule should be used as the criterion for mass medication, i.e. when morbidity exceeds 20 %, mass medication will be introduced, or alternatively, when mortality exceeds 2 %. Individual medication, i.e. treating only the sick animals, is difficult. The advantages of mass medication include its ease, and sometimes cost-effectiveness: less work is needed when there is no need to inject every animal individually and the animals will not be stressed by the treatment. The disadvantage is the fact that sick animals do not feed or drink in a normal manner and the amount of medicine ingested often remains too low, while perfectly healthy animals are being treated simultaneously. The consulting veterinarian decides case by case when the transition from individual medication to mass medication is feasible. If an antimicrobial substance is administered in the feed or water, the non-feeding animals must, nevertheless, be treated individually by injection.

The behaviour of medicinal substances in pigs has been studied very little. The absorption of medicines from the gastrointestinal tract of pigs is very similar to that of humans. In the case of parenteral administration of medication it should be kept in mind that the subcutaneous fat layer in a full-grown pig is thick and intramuscular injection requires a skilled technique. The absorption of medicinal substances from the fatty tissue is highly unpredictable. Some

substances may remain in the fat, resulting in too low a concentration at the focus of the infection. Correct dosing requires special attention in the case of newborn piglets: overdosing and concentrated products must be avoided. Procaine penicillin must not be administered to a pregnant sow for the risk of abortion.

One of the fundamentals in the choice of an antimicrobial substance is to maximise the accuracy of the diagnosis to choose the most suitable antimicrobial. If possible, the diagnosis includes the identification of the pathogen. To reach a diagnosis, an autopsy can be performed on some of the pigs that have died with typical signs or samples can be taken for laboratory testing.

A treatment plan should be worked out for every pig farm to minimise the number of antimicrobial substances used. It is imperative that the latest antimicrobials be reserved for use in pigs in exceptional cases only. They must not be used for prophylaxis. The following table (Table 2) presents the recommendations for the antimicrobial treatment of swine diseases.

**Table 2. Pigs**

Practical illustrations for alternatives of antimicrobial treatment in pigs when the use of antimicrobials is indicated by the diagnosis. Unless otherwise stated, the treatment is systemic treatment.

The first-line treatments mentioned are antimicrobial substances or combinations of substances that are best suited for therapeutic treatment of a particular infection when taking into consideration the pathogen, the disease, the resistance situation, and the properties of the antimicrobial substance. For first-line treatments, substances effective against the most common pathogens causing the infection have been chosen. First-line treatments aim at specific treatment. For instance, in infections where several bacteria are isolated, the treatment is directed at the most common pathogens.

Site of infection	Disease	Pathogen	First-line treatment	Alternative treatments	Remarks	
Respiratory tract	Atropic rhinitis	Toxic <i>Pasteurella multocida</i> .	Tetracyclines .	Trimethoprim - sulfonamide combinations .	Primarily implementation of eradication programme. Vaccination available.	
	Enzootic pneumonia	<i>Mycoplasma hyopneumoniae</i> .	Tiamulin or lincomycin.	Tetracyclines .	Primarily implementation of eradication programme. Penicillin G. for secondary infections in fattening pigs .	
	Necrotic pleuropneumonia	<i>Actinobacillus pleuropneumoniae</i> .	Penicillin G.	Tiamulin or tetracyclines .		
	Bronchopneumonia	Streptococci.	Penicillin G.	Trimethoprim - sulfonamide combinations .		
	Pneumonia	<i>Mannheimia haemolytica</i> .	Penicillin G.	Tetracyclines or aminopenicillins .		
	Rhinitis (bordetella rhinitis) and pneumonia		<i>Pasteurella multocida</i> .	Penicillin G.	Trimethoprim - sulfonamide combinations .	Treatment determined by pathogen.
			<i>Bordetella bronchiseptica</i> .	Trimethoprim - sulfonamide combinations .	Tetracyclines .	
Gastrointestinal tract	Necrobacillosis	<i>Fusobacterium necrophorum</i> .	Penicillin G.	Trimethoprim - sulfonamide combinations .		
	Enteritis, diarrhoea	<i>Escherichia coli</i> .	Trimethoprim - sulfonamide combinations or aminopenicillins .	Subject to susceptibility testing.	Vaccination recommended.	
	Piglet dysentery	<i>Clostridium perfringens</i> , type C.	Aminopenicillins .	Tiamulin or lincomycin.	Vaccination recommended.	

Gastrointestinal tract continued	Dysentery	<i>Brachyspira hyodysenteriae</i> .	Tiamulin.	Tylosin or lincomycin following susceptibility testing.	Bacteriological sample recommended. Primarily implementation of eradication programme.
	Diarrhoeas by other brachyspirae	Brachyspirae.	Tiamulin.	Tylosin or lincomycin following susceptibility testing.	Bacteriological sample recommended.
	Salmonellosis	Salmonellae.	No antimicrobials.		
	Oedema disease	<i>Escherichia coli</i> .	Trimethoprim - sulfonamide combinations .	Aminopenicillins .	
	Proliferative enteritis	<i>Lawsonia intrasellularis</i> .	Tylosin.	Tiamulin, tetracyclines .	New disease.
Kidneys and urinary tract	Cystitis	<i>Escherichia coli</i> .	Trimethoprim - sulfonamide combinations .	Aminopenicillins .	Good sanitation of essence, prevention of pooling of urine.
	Cystopyelonephritis	<i>Actinobaculum suis</i> .	Penicillin G.	Aminopenicillins .	
		<i>Escherichia coli</i> .	Trimethoprim - sulfonamide combinations .	Aminopenicillins .	
Genitals	Endometritis	Coliform .	Trimethoprim - sulfonamide combinations.	Subject to susceptibility testing.	
		Gram -positive bacteria.	Penicillin G.		
	Balanoposthitis	<i>Actinobaculum suis</i> .	Penicillin G.	Aminopenicillins .	
Mammary glands	Milk fever, acute mastitis	Gram -negative bacteria (usually <i>E. coli</i> ).	Trimethoprim - sulfonamide combinations.	Aminopenicillins.	Feeding, surroundings and water to be checked.
		Gram -positive bacteria.	Penicillin G.	Aminopenicillins .	
Central nervous system	Meningoencephalitis	Streptococci, listeria <i>Escherichia coli</i> (rarely).	Penicillin G.	Aminopenicillins .	Large dose.

Musculoskeletal system	Arthritis	Streptococci, <i>Haemophilus parasuis</i> , <i>Erysipelothrix rhusiopathiae</i> .	Penicillin G.	Aminopenicillins or tetracyclines .	
		<i>Mycoplasma hyosynoviae</i> .	Tylosin or lincomycin or tiamulin .		
	Glasser's disease	<i>Haemophilus parasuis</i> .	Penicillin G.	Trimethoprim - sulfonamide combinations or aminopenicillins or tetracyclines .	Vaccination available.
	Interdigital necrobacillosis	<i>Fusobacterium necrophorum</i> , <i>Actinomyces pyogenes</i> + others .	Penicillin G.	Tetracyclines .	
Skin	Greasy pig (exudative epidermitis)	<i>Staphylococcus hyicus</i> .	Penicillin G.	Subject to susceptibility testing.	
	Swine erysipelas	<i>Erysipelothrix rhusiopathiae</i> .	Penicillin G.	Tetracyclines or aminopenicillins .	Prophylactic vaccination recommended.
Ear	Otitis media	Streptococci .	Penicillin G.	Trimethoprim - sulfonamide combinations .	
Others	Tail biting	Multiple (mouth's microbial flora).	Penicillin G.		Improvement in surrounding conditions of essence.

## Horses

The use of antimicrobials in horses is limited by many factors. An adult horse is totally dependent on its intestinal microbes. Several antimicrobial substances have an adverse effect on the microbial flora of the colon because they alter its balance and may thus induce, for instance, fatal diarrhoea in the horse. Due to their undeveloped intestinal microflora, foals are less sensitive to the negative effects of antimicrobial substances, which means that the selection of antimicrobials appropriate for use in foals is wider. The horse is also highly sensitive to tissue irritation caused by medicinal products. The treatment of horses may be very expensive due to their large size.

According to the EU provisions, horses belong to food-producing animals, and thus the medicinal products used must have been licensed for the use in food-producing animals since the beginning of 1997. Very few products licensed particularly for horses exist in Finland. Products licensed for other food-producing animals can be used for horses by virtue of the so-called cascade principle, whereby the minimum withdrawal period for slaughter is 28 days. Many products licensed for use in small animals and humans can also be used for horses. These products can only be used for registered horses. The veterinary practitioner makes an entry of the use of such products in the horse's passport or registration book. The withdrawal period for slaughter is six months.

Certain products which are prohibited for use in other food-producing animals because they leave residues harmful to human health (e.g. metronidazole) in foodstuffs are approved for use in horses. These products can only be used for horses that are registered and whose identification document shows that slaughtering the horse for food production is prohibited. The owner of the horse confirms with his signature that the slaughter of the horse for food production is prohibited. This information is then confirmed by a representative of Suomen Hippos r.y (the Finnish Trotting and Breeding Association) at trotting tracks and horse-breeding societies or by sending the identification document to Suomen Hippos. At slaughter, a horse must be accompanied by an appropriate identification document (the horse's passport or registration book.)

The treatment of an infection should always be based on identifying the pathogen and on antimicrobial susceptibility testing when samples can be taken. More attention should be paid to taking samples, because it is the only means of discovering which types of pathogens exist in Finland and whether new types of pathogens are to be found among the horse population. Taking of samples and handling of specimens must be performed in an appropriate manner.

The information found in literature regarding the role of different pathogens in the infections of different organs can only be used as guidelines, because geographical location and use of medicinal substances select the pathogens. For example, in previously unmedicated mares streptococci are a common cause for metritis, whereas in mares treated with penicillin, coliform are the most common. Particularly if an animal has undergone antimicrobial treatment in the past, it is essential to isolate the pathogen and test it for antimicrobial susceptibility. Puerperal metritis is a most serious condition, whose therapeutic treatment should combine oxytocin, an anti-inflammatory analgesic and uterine lavage with an antimicrobial substance. In uterine lavage the uterus is aseptically filled with several litres of physiological saline (4-5 l) using a tube, after which the fluid and purulent discharge is drained via a tube. Local treatment of the uterus may also be necessary. Following lavage either water-soluble penicillin or gentamycin buffered with sodiumbicarbonate diluted in physiological saline may be inserted into the uterus. A violent endotoxemia resulting in laminitis may set in as a complication of puerperal metritis. These types of patients usually require aggressive rehydration and supportive care. Conditions other than puerperal metritis are also treated with uterine lavage, local treatment of the uterus and oxytocin, either with or without an antimicrobial treatment. Uterine lavage is always performed during estrus when the cervix is dilated.

Many bacteria causing lower respiratory tract infections show poor response to systemic antimicrobial treatment because the concentration of the antimicrobial substance in the lungs remains low. Horses may suffer from an infection for a relatively long period of time, and particularly in young horses respiratory infections with mild symptoms may last for months. In these horses the infection often goes unnoticed until the horse wears out easily under strenuous exercise. At this point mere rest and allowing time for recovery may be insufficient. Conditions in the stable, such as adequate ventilation, the quality of hay, dividing horses into different sections depending the use of the horse (racing, yearling, broodmare etc) and animal density, must also be attended to.

Penicillin is often the first-line treatment in horses as most pathogens causing equine diseases are susceptible to it and normally penicillin is well tolerated by horses. Trimethoprim-sulfonamide combinations can be considered the second-line treatment and they can also be administered orally. The treatment alternatives for equine diseases caused by different microbes listed in Table 3 are based on literature and practical experience.

**Table 3. Horses**

Practical illustrations for alternatives of antimicrobial treatment in horses when the use of antimicrobials is indicated by the diagnosis. Unless otherwise stated, the treatment is systemic treatment. Explanations for the reference numbers after a pathogen or an antimicrobial substance can be found in the "Remarks" column.

The first-line treatments listed are antimicrobial substances or combinations of substances that are best suited for therapeutic treatment of a particular infection when taking into consideration the pathogen, the disease, the resistance situation, and the properties of the antimicrobial substance. For first-line treatments, substances effective against the most common pathogens causing the infection have been chosen. First-line treatments aim at specific treatment. For instance, in infections where several bacteria are isolated, the treatment is directed at the most common pathogens.

Site of infection	Disease	Pathogen	First-line treatment	Alternative treatments	Remarks
Skin, subcutaneous tissue	Dermatitis, cutaneous	<i>Staphylococcus aureus</i> , <i>Staphylococcus</i> spp.	Disinfective washes e.g. iodine, chlorhexidin or benzyl peroxide.	Penicillin G, trimethoprim - sulfonamide combinations .	Diagnosing and avoiding the predisposing factors most important.
	Dermatitis, subcutaneous (furunculosis)	<i>S. aureus</i> , <i>Staphylococcus</i> spp., <i>Streptococcus</i> spp., <i>Corynebacterium</i> spp.	Disinfective washes as in cutaneous dermatitis. Penicillin G.	Trimethoprim - sulfonamide combinations .	Diagnosing and avoiding the predisposing factors most important. Susceptibility testing advisable, treatment thereafter. Prone to mixed growth in samples, to be taken aseptically relatively deep in exudate or subcutaneous skin biopsy. Often requires long treatment period, 3-4 weeks.
	Lymphangitis	<i>S. aureus</i> , <i>Staphylococcus</i> spp., <i>Streptococcus</i> spp., <i>Corynebacterium pseudotuberculosis</i> .	In distal parts iodine compress or similar. Penicillin G if necessary.	Trimethoprim - sulfonamide combinations .	Diagnosing the cause for lymphangitis. Supportive care.
	Deep penetrating wounds (often forming an abscess)	Mixed infection.	Penicillin G.	Penicillin G + metronidazole <sup>1</sup>  (Trimethoprim - sulfonamide combination or gentamycin combined with penicillin, if gram-negative bacteria present. Gentamycin with special permit).	Draining and hydrotherapy of abscess. Tetanus to be considered in penetrating wounds.  <sup>1</sup> Metronidazole, when <i>Bacteroides fragilis</i> bacterium is suspected. When using metronidazoles, slaughtering the horse for food production to be prohibited.

Eye	Corneal ulcer, bacterial keratitis	<i>S. aureus</i> , <i>Streptococcus</i> spp., <i>Staphylococcus</i> spp., <i>Pseudomonas</i> spp.	Local treatment: Fucidic acid, if pathogen gram-positive.	Neomycin + polymyxin + gramicidin.  Tobramycin.  (Chloramphenicol).	Culture recommended, particularly in prolonged cases. Always check for corneal damage. If ulceration is discovered, no corticosteroids are to be used. When using chloramphenicol slaughtering the horse for food production to be prohibited. Also remember possibility of viral and fungal keratitis.
Respiratory tract	Upper respiratory tract infection	<i>Streptococcus</i> spp.	Penicillin G.	Trimethoprim - sulfonamide combinations.	Usually viral, best treatment is rest.
	Sinusitis	Mixed infection.	Draining and lavage of the sinus. Penicillin G.	Metronidazole.	Often of tooth origin, thus prerequisite for recovery is extraction or root canal treatment.
	Lower respiratory tract infection	<i>Str. pneumoniae</i> (pneumococcus), <i>Str. zooepidemicus</i> , <i>Actinobacillus</i> / <i>Pasteurella</i> spp., <i>Mannheimia haemolytica</i> , <i>Mycoplasma</i> spp.	Penicillin G.	Trimethoprim - sulfonamide combinations, penicillin G + aminoglycoside.	Transtracheal sample to determine pathogen. In young horses (2-4 yrs old) infections often produce mild symptoms, duration depending on pathogen 2-3 months. Response to antimicrobial treatment may be poor. Rest is optimal treatment. Combination treatment only in severe cases.
		Staphylococcus, $\beta$ -lactamase negative.	Penicillin G.		
		Staphylococcus, $\beta$ -lactamase producing.	Subject to susceptibility testing.	Trimethoprim - sulfonamide combinations or cephalosporin.	

Respiratory tract continued	Pleuropneumonia	Mixed infection, e.g. <i>Str. zooepidemicus</i> , <i>Streptococcus</i> spp., <i>Pasteurella</i> spp., <i>E. coli</i> , <i>Bacteroides</i> spp., <i>Clostridium</i> spp., <i>Pseudomonas</i> spp.	Penicillin G + gentamycin (+metronidazole).	Penicillin G + trimethoprim - sulfonamide combination (+ metronidazole).	Culture of pleural fluid. Immediate and aggressive treatment. Draining of fluid.
	Lower respiratory tract <i>Rhodococcus</i> -infections, foals up to one year old.	<i>Rhodococcus equi</i> .	Erythromycin + rifampicin (Rifampicin must not be used alone, develops resistance easily).		Immediate and aggressive treatment, delaying worsens the prognosis considerably. Observe response to treatment and changes in lungs. Treatment period from several weeks to months. Utmost care must be exercised in medication, to be ensured that medicine travels to foal. Erythromycin may induce fatal diarrhoea in adult horse.
	Strangles	<i>Streptococcus equi</i> .	Fomentation and draining of the abscesses .	Fomentation and draining of the abscesses . Penicillin G, if systematic symptoms severe.	With antimicrobial treatment only the abscesses often encapsulate and symptoms return following the treatment. Horse may carry the bacteria for a long period of time for example in guttural pouches . Also atypical forms occur. Contagious disease.
Gastrointestinal tract	<i>Clostridium</i> diarrhoea	Clostridia.	Penicillin G.	Metronidazole.	Supportive care essential. May turn fatal quickly.

Gastrointestinal tract continued	Salmonellosis	Salmonellae.	No antimicrobial substances.	Trimethoprim - sulfonamide combinations, gentamycin.	Blood culture in serious infections. Zoonosis; hygiene instructions to prevent spreading. Antimicrobial treatment only in life-threatening cases (systemic infection, arthritis). Susceptibility testing paramount.
	Anterior enteritis (duodenitis -proximal jejunitis)	Unknown, suspected etiologic factors among others <i>Clostridium</i> spp., <i>Salmonella</i> spp.	Penicillin G + gentamycin.	Penicillin G + trimethoprim - sulfonamide combination.	Supportive care: rehydration, removal of reflux.
Genitals	Retained placenta and puerperal metritis	Mixed infection.	Penicillin G + gentamycin.	Penicillin G + trimethoprim - sulfonamide combination.	See introduction.
	Endometritis	Streptococci.	Penicillin G.	Trimethoprim - sulfonamide combination.	See introduction.
		Coliform .	Gentamycin.	Trimethoprim - sulfonamide combination.	See introduction.
Others	Peritonitis	Mixed infection, often with <i>Bacteroides fragilis</i> .	Metronidazoles + penicillin G + medication that destroys gram - negative bacteria (trimethoprim - sulfonamide combination or gentamycin).		Doubtful prognosis. Discover primary cause.
	Neonatal illnesses: umbilical and joint infections, osteomyelitis, infective osteitis, respiratory tract infections, sepsis	In pneumonia e.g. <i>Str. equisubsp. zooepidemicus</i> . Others: <i>E. coli</i> , <i>Actinobacillus</i> spp., <i>Klebsiella</i> spp., <i>Salmonella</i> spp., <i>S. aureus</i> , <i>Clostridium</i> spp.	Penicillin G + gentamycin (or trimethoprim - sulfonamide combination).	Third generation cephalosporin.	Culture prior to starting treatment (blood, synovial fluid etc.). Immediate and aggressive start of treatment. Supportive care vital! Third generation cephalosporin only following susceptibility testing or poor response to other treatment. Surgical treatment, joint lavages .

Others continued	Sepsis	<i>E. coli</i> , <i>A. equuli</i> , <i>Salmonella</i> spp., <i>Klebsiella</i> , <i>Staphylococcus</i> spp., <i>S. aureus</i> , <i>Streptococcus equi</i> , <i>Clostridium</i> spp.	Penicillin G + gentamycin (or trimethoprim-sulfonamide combination).	Trimethoprim-sulfonamide combinations .	Immediate and aggressive start of treatment, specimen for culture prior to treatment.
	Joint infections in adult horses (traumas, iatrogenic)	<i>Staphylococcus</i> spp., <i>S. aureus</i> , <i>Actinobacillus</i> spp., <i>Streptococcus</i> spp., enterobacteria.	Start treatment with penicillin G + gentamycin, continue following susceptibility testing.	Penicillin G + trimethoprim-sulfonamide combination.	Synovial fluid culture. Joint lavage essential to successful treatment.
	Infective osteitis and osteomyelitis in adults (traumas, iatrogenic).	Enterobacteria, <i>Streptococcus</i> spp., <i>Staphylococcus</i> spp., <i>S. aureus</i>	Start treatment with penicillin G + gentamycin, continue following susceptibility testing.	Penicillin G + trimethoprim-sulfonamide combination.	Surgical treatment.
	Hoof abscess		Drain abscess, iodine compresses .	Penicillin G.	In serious cases an antimicrobial can be combined with draining and compresses. Remember tetanus.
	Mastitis	<i>Str. zooepidemicus</i> most common pathogen, others e.g. <i>Staphylococcus</i> spp., <i>Actinobacillus</i> spp., enterobacteria	Penicillin G.	Subject to susceptibility testing.	Milk sample prior to treatment.
Treatment in connection with surgical procedures (start pre-operatively)	Operations on gastrointestinal tract		Penicillin G + gentamycin.	Penicillin G + trimethoprim-sulfonamide combination.	Start intravenously 15-30 mins prior to operation. The postoperative period of treatment depends on the level of contamination during the surgery; 1-2 days may be sufficient.
	Bone operations, arthroscopy		Not necessary in clean operations.	Penicillin G or trimethoprim-sulfonamide combination.	Need for antimicrobial treatment to be assessed individually.

## **Fish**

This review examines the therapeutic treatment of fish farmed for food production only. Preventive health care is essential in fish farming as water – the immediate environment of fish – constantly harbours copious amounts of bacteria. High density of fish coupled with many other physico-chemical stress factors in water rapidly lead to serious infections causing diseases in fish.

Antimicrobial substances were not used to treat fish diseases until the 1980s. Most of the antimicrobials, estimated at 80 %, are used to treat fry, while less than 20 % of antimicrobials are used for 2-year-old fish at the time of slaughter. These treatments are important in terms of residual monitoring: other uses of antimicrobial substances do not leave residues in the fish used in food production. However, the risk of antimicrobial resistance is imminent in all treatment of infectious fish diseases. The majority of the pathogens causing infections in the fish are gram-negative bacteria, which means that the range of antimicrobial substances that can be used is small and the increased occurrence of resistance is worrying. Oxolinic acid was not introduced until the 1990s, and resistant strains of bacteria were found soon after this. However, the licence for the only veterinary proprietary product containing oxolinic acid was not revoked until 2001. Increased resistance has also been detected in the case of oxytetracycline. This has been in use since the early 1980s, but the development has been slower. The most recently introduced antimicrobial substance for fish is florphenicol, which is available on a special permit.

Increased resistance has forced the fish farmers to be more vigilant in the prevention of infections. Improved farming conditions and vaccinations have altered the situation, making it possible to reduce the consumption of antimicrobials. The need for antimicrobial substances in the therapeutic treatment of fish has decreased markedly, particularly due to the oil-based double-vaccines (against furunculosis and vibriosis), the use of which increased rapidly in 2000-2001.

The therapeutic treatment of fish used for food is always mass medication. This means that besides the therapeutic aspects also the detrimental effect on the environment must be taken into consideration. Fish affected by the disease become anorexic and the antimicrobial

substance mixed in feed inevitably ends up in the water and the sediment. Particularly substances that are poorly absorbed in the gastrointestinal tract end up in the environment unchanged, which may increase the resistance in different strains of microbes. Attempts are made to avoid the environmental problems related to antimicrobials in feed by controlled feeding, i.e. improving the utilisation ratio of the feed.

**Prior to starting the treatment, some dead or destroyed fish must be sent to the National Veterinary and Food Research Institute (EELA) for analysis to confirm the diagnosis.**

Recommendations for the therapeutic treatment of fish are shown in Table 4.

**Table 4. Fish**

Practical illustrations for alternatives of antimicrobial treatment in fish when the use of antimicrobials is indicated by the diagnosis.

The first-line treatments mentioned are antimicrobial substances or combinations of substances that are best suited for therapeutic treatment of a particular infection when taking into consideration the pathogen, the disease, the resistance situation, and the properties of the antimicrobial substance. For first-line treatments, substances effective against the most common pathogens causing the infection have been chosen. First-line treatments aim at specific treatment. For instance, in infections where several bacteria are isolated, the treatment is directed at the most common pathogens.

Site of infection	Disease	Pathogen	First-line treatment	Alternative treatments	Remarks
General infection or wound	Vibriosis	<i>Listonella anguillarum</i> (formerly <i>Vibrio anguillarum</i> ).	Oxytetracycline.	Trimethoprim - sulfonamide combinations .	Warm water disease. Vaccination available.
	Furunculosis (ASS)	<i>Aeromonas salmonicida</i> subsp. <i>salmonicida</i> .	Oxytetracycline.	Trimethoprim - sulfonamide combinations , florphenicol (special permit) following susceptibility testing.	Warm water disease. Vaccination available.
	ASA, Contagious skin infection	<i>Aeromonas salmonicida</i> subsp. <i>achromogenes</i> .	Oxytetracycline.	Trimethoprim - sulfonamide combinations .	Warm water disease.
	Yersiniosis	<i>Yersinia ruckeri</i> .	Oxytetracycline.		Warm water disease.
	Columnaris disease, Bacterial gill disease (formerly flexibacteriosis)	<i>Flavobacterium columnare</i> (formerly <i>Flexibacter columnaris</i> ).	Oxytetracycline.	Florphenicol following susceptibility testing.	Warm water disease.
	Bacterial cold water disease and rainbow trout fry syndrome (formerly flexibacteriosis)	<i>Flavobacterium psychrophilum</i> (formerly <i>Flexibacter psychrophilus</i> ).	Oxytetracycline.	Florphenicol following susceptibility testing.	Cold water disease.
Chronic nephritis, systemic infection	BKD, bacterial kidney disease	<i>Renibacterium salmoninarum</i> .	No antimicrobials .		Cold water disease. No effective treatment available.

## Poultry

In this review, poultry means broilers, chickens and turkeys as breeding and food-producing animals. In poultry infections, we are always concerned with an entire infected flock, which means that a rapid decision regarding the treatment is required. The decision depends on various factors. One of the most important ones is the cause of the infection and whether it is one that responds to treatment. The age of the birds, the stage of production, losses caused by the disease and the cost of medication all influence how the problem is to be dealt with. **Prior to starting the treatment, some dead or destroyed birds must be sent to the National Veterinary and Food Research Institute (EELA) for analysis to confirm the diagnosis.**

Health care in poultry is mainly based on preventing infections. Often the cause of an infection can be traced to poor sanitation, quality of the animal population, substandard living conditions, poor care of the animals, or poor quality of feed and water. Bacterial infections in poultry are largely secondary infections which are normally not treated with antimicrobials.

Not many products are licensed for use in poultry in Finland, which makes antimicrobial treatment of poultry quite problematic. Medication is usually administered in drinking water. Some substances may be mixed in feed and some valuable birds may be treated parenterally by individual injections. Average mortality among poultry during their first week of life is less than 1% and thereafter approximately 0.5% per month. On different farms the mortality varies very little, only 1-2 %.

When planning to administer the medication in drinking water, it must be ensured that the water contains no substances which may reduce the efficacy of the medication: chloride has been reported to inactivate at least fluoroquinolones. High iron, calcium and magnesium contents as well as metal containers and metal piping can inactivate tetracyclines. Measuring the water consumption in order to reach the correct medicine concentration is essential, as water consumption may differ considerably from the official mean values. If there are leaks in the water system the water consumption may be overestimated, followed by insufficient medicine concentration in the water. The water supply systems must always be examined prior to starting the treatment.

Arthritis and tenosynovitis occur to a certain extent in parent broilers during breeding (at the age of 10-14 weeks). The causative pathogen is usually *Staphylococcus aureus*. These are normally treated with phenoxymethyl penicillin (penicillin V), which is usually administered in drinking water. The National Veterinary and Food Research Institute (EELA) has been monitoring the development of resistance, but so far the strains have remained susceptible to penicillin. Occasionally arthritis and tenosynovitis also occur in broilers. In most cases these are not treated but the sick birds are culled.

Coccidiosis is an intestinal infection caused by the unicellular *Eimeria* parasite. In practice, coccidiosis is not treated, but the treatment is prophylactic. Ionophoric coccidiostats are mixed in feed and fed to broilers (monensin, salinomycin, lasalocid sodium) and turkeys (lasalocid sodium). All parent broilers and often laying hens raised in barns with no cages are given a coccidiosis vaccination at the age of about a week. So far coccidiosis has not occurred in vaccinated birds. Toltrazuril can be used to treat coccidiosis and oxytetracycline for the secondary bacterial infections. Antimicrobial substances can be used to treat necrotic enteritis (*Clostridium perfringens*) occurring in broilers and sometimes in other birds used in the food industry.

Turkeys and chickens may be infected with swine erysipelas (*Erysipelothrix rhusiopathiae*) or pasteurellosis (*Pasteurella multocida*). Both infections are triggered by stress and poor hygiene. Both swine erysipelas and pasteurellosis can be treated with antimicrobials (penicillin and oxytetracycline). However, these infections are often recurrent, following the course of treatment. Turkeys can be vaccinated against swine erysipelas if the infection incidence is high and improvements to the living conditions have failed to eradicate it.

No medicinal products for the treatment and prevention of blackhead disease, or histomoniasis (*Histomonas meleagridis*), in turkeys are available in Finland, and thus controlling the spread of the disease is based on good sanitation and the “all in, all out” method. If necessary, oxytetracycline can be used for secondary bacterial infections.

Recommendations for the antimicrobial treatment of poultry are given in Table 5.

**Table 5. Poultry**

Practical illustrations for alternatives of antimicrobial treatment in poultry when the use of antimicrobials is indicated by the diagnosis.

The first-line treatments mentioned are antimicrobial substances or combinations of substances that are best suited for therapeutic treatment of a particular infection when taking into consideration the pathogen, the disease, the resistance situation, and the properties of the antimicrobial substance. For first-line treatments, substances effective against the most common pathogens causing the infection have been chosen. First-line treatments aim at specific treatment. For instance, in infections where several bacteria are isolated, the treatment is directed at the most common pathogens.

Site of infection	Disease	Pathogen	First-line treatment	Alternative treatments	Remarks
Gastrointestinal tract	Coccidiosis of chicken and turkey	Eimeriae.	Toltrazuril (special permit).	Tetracyclines .	
	Blackhead disease in turkey (histomoniasis)	<i>Histomonas meleagridis</i> .		Tetracyclines .	No antimicrobial treatment available, tetracyclines effective only in secondary bacterial infections.
	Necrotic enteritis	<i>Clostridium perfringens</i> .	Penicillin V (phenoxymethyl penicillin, fixed term special permit).	Tetracyclines or tylosin.	
Musculoskeletal system	Arthritis and tenosynovitis in parent broilers	<i>Staphylococcus aureus</i>	Penicillin V.	Tetracyclines .	Subject to susceptibility testing.
	Arthritis in turkey		Tetracyclines		Subject to susceptibility testing.
Others	Swine erysipelas	<i>Erysipelothrix rhusiopathiae</i>	Penicillin V.	Tetracyclines .	Turkey most susceptible.
	Pasteurella infection in adult chickens and turkeys	<i>Pasteurella multocida</i>	Penicillin V.	Tetracyclines .	Rare.

## Bees

At present, the only antimicrobial substance of practical significance licensed for therapeutic use on bees in Finland is fumagillin. According to the pharmaceutical legislation regarding the veterinary use of medicinal products, however, the use of an antimicrobial substance that has been licensed for one species of food-producing animals may be used for another species of food-producing animals (B17 or Decree of the Ministry of Agriculture and Forestry 23/EEO/2002). In such cases, the veterinary practitioner must establish an adequate withdrawal period for the product.

### Adult bees

Not much is known about bacterial infections in adult bees, because these are difficult to diagnose and often secondary. In many cases the situation is over and treatment is no longer required when the test results come through. On the whole, very little research has been done on the antimicrobial treatment of communicable diseases in bees. The increased occurrence of varroosis might also subject bees to increased secondary infections. The aforementioned fumagillin is used to treat a disease caused by the *Nosema apis* microsporidian in adult bees.

### Larvae and pupae

The use of antimicrobial substances is not recommended for therapeutic use in bacterial infections of bee larvae such as American foulbrood and European foulbrood. In Europe (e.g. Sweden, Denmark, Germany and Great Britain), antimicrobials are generally not used to treat diseases of the pupae. During the American foulbrood eradication procedures, positive results have been reported with over 95 % success rate using the artificial swarming technique without therapeutic use of antimicrobials. Practical guidance aims at avoiding the use of antimicrobial treatment in standard eradication procedures of American foulbrood. Antimicrobials ought not to be used as prophylaxis, either. The use of oxytetracycline as prophylaxis has resulted in the discovery of resistance to oxytetracycline in, for example, Argentina, Canada and the United States. If antimicrobial treatment is required, the primary choice is oxytetracycline. The elimination time for oxytetracycline in honey and syrup is some weeks. Hence, if necessary, the treatment is renewable every two weeks. The treatment can be renewed 2-3 times, providing the brood is still open in the hive. Thus far, the withdrawal period for oxytetracycline has been two months, but in future it will be three months.

Larvae may also become infected with fungal diseases (chalkbrood, stonebrood) which can be diagnosed but no effective antimicrobial cure is known.

**Dosing**

Antimicrobials are administered to bees orally. In late summer and in the autumn medicines are mixed with syrup to be fed to the bees as winter food. In the spring antimicrobial substances are more effectively administered to bees by mixing the medication into different types of pastes (icing sugar or invert sugar, oil-based paste). Particularly in chilly weather bees tend not to feed on liquids from the standard feeding supply. It is recommended that medication against nosema to very weak colonies be also administered in the spring by spraying the bees with medicated sugar solution. However, the effectiveness of this method is often doubtful. In the Finnish conditions, it is almost impossible to save hives which are gravely infected with nosema in the spring. The method of administration affects the concentration of antimicrobial substances in the food supply, i.e. honey. The concentration of medical substances is the highest when administered by sugar solution and lowest when administered in oil-based paste. Oil-based paste is not bee food, which is why the bees attempt to clear it away rather than storing it in the combs.

## Dogs and cats

Antimicrobial substances are the most frequently used medicines in dogs and cats. The recommendations in Table 6 are intended as guidelines for the choice of first-line treatment for the most common infections in dogs and, where applicable, in cats. Quite deliberately a quite concise list has been given, aimed at encouraging to more specific treatment rather than mentioning all the available choices for substance. It is also hoped that the recommendations will standardise the treatment practice of infections in our country. The choice of different alternatives has been based on scientific literature, experts' recommendations and the prevailing resistance situation in Finland. In bacterial infections, a response to antimicrobial treatment should be seen in 2-3 days. Should this not happen, the diagnosis ought to be reassessed or the patient referred onwards.

In many cases the use of antimicrobial substances in dogs and cats can be decreased. Such cases are, for example, acute disorders of the gastrointestinal tract (vomiting, diarrhoea), small cuts and skin damage, certain respiratory tract infections, diseases of lower urinary tract in cats, and many surgical procedures. Courses of antimicrobial treatment are often willingly used in connection with surgical procedures for psychological reasons, but no scientific or practical foundation exists to justify it. Antimicrobial substances should to an increasing extent be administered intravenously prior to the procedure. We have reached the end of an era when antimicrobial substances were used as a precaution or as prophylaxis to secondary infections. Prudent use of antimicrobial substances also entails refraining from their use unless they are absolutely necessary.

Even if products authorised for humans occasionally must be used for pets, the use of certain substances, such as the new generation macrolides (e.g. azithromycin, clarithromycin) and mupirosin, should be avoided because their use instigates serious threats of developing resistance. Furthermore, mupirosin is the only substance available at present to eradicate methicillin resistant *S. aureus* from the mucous membranes in humans. In the case of the latest medicines released to the market, careful consideration should be given to whether there is actual need to employ them for widespread use. They should be kept as reserve medicines for as long as possible.

**Table 6. Dogs and Cats.**

Practical illustrations for alternatives of antimicrobial treatment in dogs and cats when the use of antimicrobials is indicated by the diagnosis. The information in the table has been compiled mainly with regard to canine diseases but, where applicable, it can also be used when making choices for the treatment of cats. Unless otherwise stated, the treatment is systemic treatment. Explanations for the reference numbers after a pathogen or an antimicrobial substance can be found in the "Remarks" column.

The first-line treatments mentioned are antimicrobial substances or combinations of substances that are best suited for therapeutic treatment of a particular infection when taking into consideration the pathogen, the disease, the resistance situation, and the properties of the antimicrobial substance. For first-line treatments, substances effective against the most common pathogens causing the infection have been chosen. First-line treatments aim at specific treatment. For instance, in infections where several bacteria are isolated, the treatment is directed at the most common pathogens .

Site of infection	Disease	Pathogen	First-line treatment	Alternative treatments	Remarks
Skin and ear	Localised cutaneous infection (e.g. hot spot, skinfold infection)	<i>Staphylococcus intermedius</i> .	Local treatment fucidic acid and corticosteroid.	In extensive infections, systemic antimicrobial treatment as in cutaneous dermatitis .	Clearing the area of exudate essential (e.g. chlorhexidin). In skin fold infections, the possibility of <i>Malassezia</i> -infection to be noted.
	Superficial dermatitis	<i>Staphylococcus intermedius</i> .	Clindamycin or lincomycin or trimethoprim - sulfonamide combinations .	First generation cephalosporin <sup>1</sup> or amoxicillin + clavulanic acid.	Clearing the area of exudate essential (e.g. chlorhexidin washes). Determine primary cause in recurrent cutaneous infections. <sup>1</sup> Dosage from the upper limit of recommended range.
	Deep pyoderma	<i>Staphylococcus intermedius</i> ,  (secondary in complicated cases <i>Escherichia coli</i> , <i>Proteus</i> group, <i>Pseudomonas</i> ).	Clindamycin or lincomycin.	1 <sup>st</sup> generation cephalosporin <sup>1</sup> or amoxicillin + clavulanic acid <sup>1</sup> .	Long treatment period (several weeks). Determine primary cause, removal of predisposing factors of essence. <sup>1</sup> Dosage from the upper limit of recommended range.
	Bites, abscesses	Pasteurellae, staphylococci, streptococci, anaerobic bacteria .	Penicillin or aminopenicillin.	Amoxicillin + clavulanic acid <sup>1</sup> or clindamycin (also metronidazole if necessary).	Draining, removal of dead tissue and local treatment of the wound important. <sup>1</sup> Dosage from the upper limit of recommended range.

Skin and ear continued	Otitis externa	Staphylococci, <i>Malassezia pachydermatis</i> , streptococci (gram-negative rods in complicated cases).	Local treatment: Polymyxin B + miconazole or fucidic acid + framycetin + nystatin.	Local treatment: Aminoglycoside or fluoroquinolones only based on susceptibility testing.	Rarely an independent disease. Primary cause and perpetuating factors to be determined and tested for yeast. In <i>Malassezia</i> infection treatment period up to 30 days. For optimised response to treatment, cleansing of the ear canal is essential. Systemic treatment following bacteriological results and susceptibility testing; see pyoderma.
	Otitis media	See otitis externa.	Amoxicillin + clavulanic acid or cephalosporins .	Fluoroquinolones only based on susceptibility testing.	Treatment following susceptibility testing (sample from the middle ear, not the ear canal). Cleansing of the ear canal and middle ear essential. Long treatment period, dosage from the upper limit of recommended range. No potentially ototoxic or cortisone products.
Respiratory tract and pleural cavity	Infective tracheobronchitis "kennel cough"	Viruses , <i>Bordetella</i> spp.	No antimicrobials .	Amoxicillin- clavulanic acid or doxycycline <sup>1</sup> .	Primarily acute viral infection; recovery in uncomplicated infections without treatment in 7-14 days.  <sup>1</sup> Large dose.
	Feline chlamydial infection	<i>Chlamydia psittaci</i> .	Doxycycline or tetracycline .		Treatment period minimum of 3-4 weeks.
	Pneumonia	<i>Bordetella</i> spp., <i>Escherichia coli</i> , pasteurellae staphylococci, streptococci, <i>Klebsiella</i> spp., <i>Proteus mirabilis</i> , anaerobes	Amoxicillin + clavulanic acid or trimethoprim - sulfonamide combinations .	Serious cases: i.v. treatment with 1 <sup>st</sup> generation cephalosporins or fluoroquinolones; (+ metronidazole).	In aspiration pneumonia, treatment of anaerobic bacteria combined with first- line antimicrobial.

Respiratory tract and pleural cavity continued	Pyothorax, pleuritis	Often mixed infection with anaerobic bacteria.	Aminopenicillin or penicillin.	Clindamycin.	Draining most important; often requires hospitalisation and parenteral medication.
Mouth and gastrointestinal tract	Gingivitis, periodontitis	Anaerobe and facultatively anaerobe bacteria, mixed infection.	Primarily no antimicrobial treatment.	Aminopenicillin, amoxicillin-clavulanic acid, clindamycin or metronidazole.	Removal of plaque and tartar first-line treatment. No antimicrobial as the sole treatment. Prophylactic antimicrobial treatment interoperatively (e.g. extraction, removal of tartar): prolonged cases: systemic disease or stomatitis. Medication is continued orally in stomatitis patients and immunosuppressed patients. Local treatment chlorhexidine gluconate both pre- and postoperatively.
	Root canal abscess	Anaerobic and facultatively anaerobic bacteria, mixed infection.	Primarily no antimicrobial treatment.	Aminopenicillins, amoxicillin-clavulanic acid, clindamycin or metronidazole.	First-line treatment extraction, root canal treatment or draining of abscess. Antimicrobial only if systemic symptoms appear.
	Enteritis	Bacteria are very rarely primary cause for acute enteritis. Several pathogens suspected, e.g. campylobacteria, clostridia, <i>E. coli</i> , Salmonellae. However, these are frequently isolated from healthy animals as well.	No antimicrobial treatment unless invasive <sup>1</sup> with the risk of sepsis.	Trimethoprim-sulfonamide combinations.	Supportive care most important (re-hydration, fasting). <sup>1</sup> Invasive = bacteria penetrate the mucous membrane and intestinal wall. When medication necessitated, choice is based on the assumed pathogen. Treatment to be started parenterally, sufficient treatment period normally under 5 days.
	Abnormal bacterial growth in small intestine	Several.	No antimicrobials, determine primary cause.	Tylosin or metronidazole.	Primarily other than bacterial disease.

Mouth and gastrointestinal tract continued	Inflammatory bowel disease	Etiology immunological, e.g. dietary hypersensitivity can be discovered at the background. Significance of bacteria unclear.	Tylosin or metronidazole.	Immunomodulatory medication or sulphasalazin.	Primary cause to be determined; effectiveness of aforementioned products most likely due to other than their antimicrobial nature.
	Anal sacculitis	<i>Escherichia coli</i> , protea, clostridia, enterococci.	Local treatment, no systemic antimicrobials.	Trimethoprim - sulfonamide combinations or aminopenicillins.	Expression of anal sacs essential.
	Feline suppurative cholangiohepatitis	Several.	Aminopenicillins.	Amoxicillin + clavulanic acid.	Following susceptibility testing, minimum treatment period 6-8 weeks.
	Peritonitis	Several, depending on the cause (e.g. <i>E. coli</i> , enterococci, <i>Fusobacterium</i> ).	Aminopenicillin + gentamycin.	Clindamycin + gentamycin <u>or</u> fluoroquinolones + metronidazole.	Treatment always started parenterally. Normally surgical treatment also necessary.
Genitals	Prostatitis	<i>Escherichia coli</i> , klebsiellae, pasteurellae, pseudomonas, staphylococci, streptococci.	Trimethoprim - sulfonamide combinations.	Fluoroquinolones.	In acute cases, treatment period 2-3 weeks, 3-6 weeks if recurrent or chronic. Antitestosterone treatment or castration may also be considered.
	Pyometra, metritis	<i>Escherichia coli</i> , staphylococci, streptococci, anaerobes.	Trimethoprim - sulfonamide combinations.	Amoxicillin + clavulanic acid.	Surgical treatment most important. Evacuation of the uterus if no surgery undertaken.
Urinary tract	Cystitis	<i>Escherichia coli</i> , staphylococci, streptococci, protea, enterococci.	Trimethoprim - sulfonamide combinations or aminopenicillins.	Amoxicillin + clavulanic acid.	Susceptibility testing recommended. Acute uncomplicated cystitis 7-10 days. Complicated cystitis 30 days.
	Pyelonephritis	See cystitis above.	Amoxicillin + clavulanic acid or trimethoprim - sulfonamide combinations.	1 <sup>st</sup> generation cephalosporins or fluoroquinolones.	Susceptibility testing paramount, 3-6 week treatment period, large dose.

Musculoskeletal system	Myositis or phlegmon	Staphylococci, clostridia.	Clindamycin or amoxicillin + clavulanic acid.	$\beta$ -lactamase + metronidazole.	Draining and culture. Varying flora according to initial cause (deep penetrating wound, bite, iatrogenic).
	Infective osteitis, osteomyelitis	Staphylococci, <i>E. coli</i> , also others.	Clindamycin.	Trimethoprim - sulfonamide combinations or 1 <sup>st</sup> generation cephalosporins (+metronidazole).	Draining and culture (if applicable), restoring blood circulation, removal of sequestra. Treatment period several weeks with a large dose.
	Infective arthritis	Staphylococci, streptococci.	Clindamycin.	1 <sup>st</sup> generation cephalosporin.	Diagnosis based on synovial fluid sample, joint lavage.
Surgical prophylaxis	Clean operations : e.g. removal of skin tumor, castration, laparotomy	Dependent on the site of the operation.	Procedures: < 60 min in duration: normally no antimicrobial, > 60 min in duration: 1 <sup>st</sup> generation cephalosporins or penicillin.	Aminopenicillins .	Prophylaxis administered i.v. approximately 30 mins preoperatively. To be continued maximum of 12-24 hours postoperatively. Prophylaxis to target the most probable pathogen.
	Clean-contaminated operations: e.g. ovariectomy, Caesarean section, uncomplicated pyometra, removal of uroliths, operations of the GI-tract		Trimethoprim - sulfonamide combinations or 1 <sup>st</sup> generation cephalosporin with a large dose.	Aminopenicillins .	Treatment continued orally only in the case of pre-existing infection at the site of operation.
Eye	Conjunctivitis	Staphylococci, streptococci.	Fucidic acid.	Chloramphenicol.	
		<i>Chlamydia</i> spp, common pathogen in the cat.	Tetracycline or doxycycline systemically or locally. Long treatment period.		Viruses are common cause in cats, if necessary antimicrobial treatment for secondary bacterial infection.

Eye continued	Keratitis	Staphylococci, streptococci, also <i>Pseudomonas</i> spp.	Chloramphenicol.	Polymyxin - neomycin – gramicidin only as a result of susceptibility testing.	NB! Patient to be referred onwards if no clear response to treatment in a matter of days. No corticosteroids to be used if ulcerated cornea.  Herpes virus common in cats, antimicrobial treatment may be necessitated by a secondary bacterial infection.
	Blepharitis	Staphylococci, streptococci.	Fucidic acid.		May need systemic treatment; for alternative treatments see superficial dermatitis.
Others	Borreliosis or ehrlichiosis	<i>Borrelia</i> sp.	Doxycycline or tetracycline.	Aminopenicillins .	Long treatment period.
	Leptospirosis	<i>Leptospira</i> sp.	Penicillin.	$\beta$ -lactamase + aminoglycoside.	Large dose.

## **Fur animals**

In this report fur animals refer to farmed foxes, raccoon dogs, minks and polecats. Very few research findings are available regarding the therapeutic use of antimicrobial substances for microbial infections in fur animals, but the treatment is largely based on practical experience together with antimicrobial susceptibility testing in certain infections. Feed hygiene must be of a high standard, particularly in the summer, in order to avoid intestinal infections.

The entire farm is often treated simultaneously, but some individual treatments may also be used. Medication is either mixed in feed or given by injections. Sick animals often become anorexic and thus injections bring the best results. The range of antimicrobials available for use must be kept as narrow as possible. Only few medicinal products are licensed for use in fur animal therapeutics. When using products licensed for other animals, the dosing for foxes and raccoon dogs should follow that of dogs and cats.

Recommendations for the antimicrobial treatment of fur animals are given in Table 7.

**Table 7. Fur animals.**

Practical examples for alternatives of antimicrobial treatment in fur animals when the use of antimicrobials is indicated by the diagnosis.

The first-line treatments mentioned are antimicrobial substances or combinations of substances that are best suited for therapeutic treatment of a particular infection when taking into consideration the pathogen, the disease, the resistance situation, and the properties of the antimicrobial substance. For first-line treatments, substances effective against the most common pathogens causing the infection have been chosen. First-line treatments aim at specific treatment. For instance, in infections where several bacteria are isolated, the treatment is directed at the most common pathogens.

Site of infection	Disease	Pathogen	First-line treatment	Alternative treatments	Remarks
Gastrointestinal tract	Gingivitis, periodontitis	Streptococci.	Penicillin G.	Lincomycin.	In connection with changing of teeth.
	Enteritis, diarrhoea	See Remarks .	Subject to susceptibility testing.		Feed hygiene problem. Determine bacteria.
Skin, subcutaneous tissue, joints	Abscesses, phlegmona, arthritis	Streptococci.	Penicillin G.	Lincomycin.	
Urinary tract	Cystitis of blue fox	Often streptococci.	Penicillin G.	Trimethoprim - sulfonamide combinations .	In winter.
	Cystitis of silver fox	<i>Escherichia coli</i> .	Trimethoprim - sulfonamide combinations .		In winter.
Genitals	Purulent metritis post-breeding	Streptococci, staphylococci, <i>Escherichia coli</i> .	Penicillin G or following susceptibility testing.	Trimethoprim - sulfonamide combinations .	
	Metritis of blue fox	<i>Pseudomonas aeruginosa</i> .	Subject to susceptibility testing.		Susceptibility varies.
Mammary gland	Mastitis	Streptococci, <i>Escherichia coli</i> .	Penicillin G.	Trimethoprim - sulfonamide combinations .	

ISBN 952-453-164-X  
ISSN 0781-6723