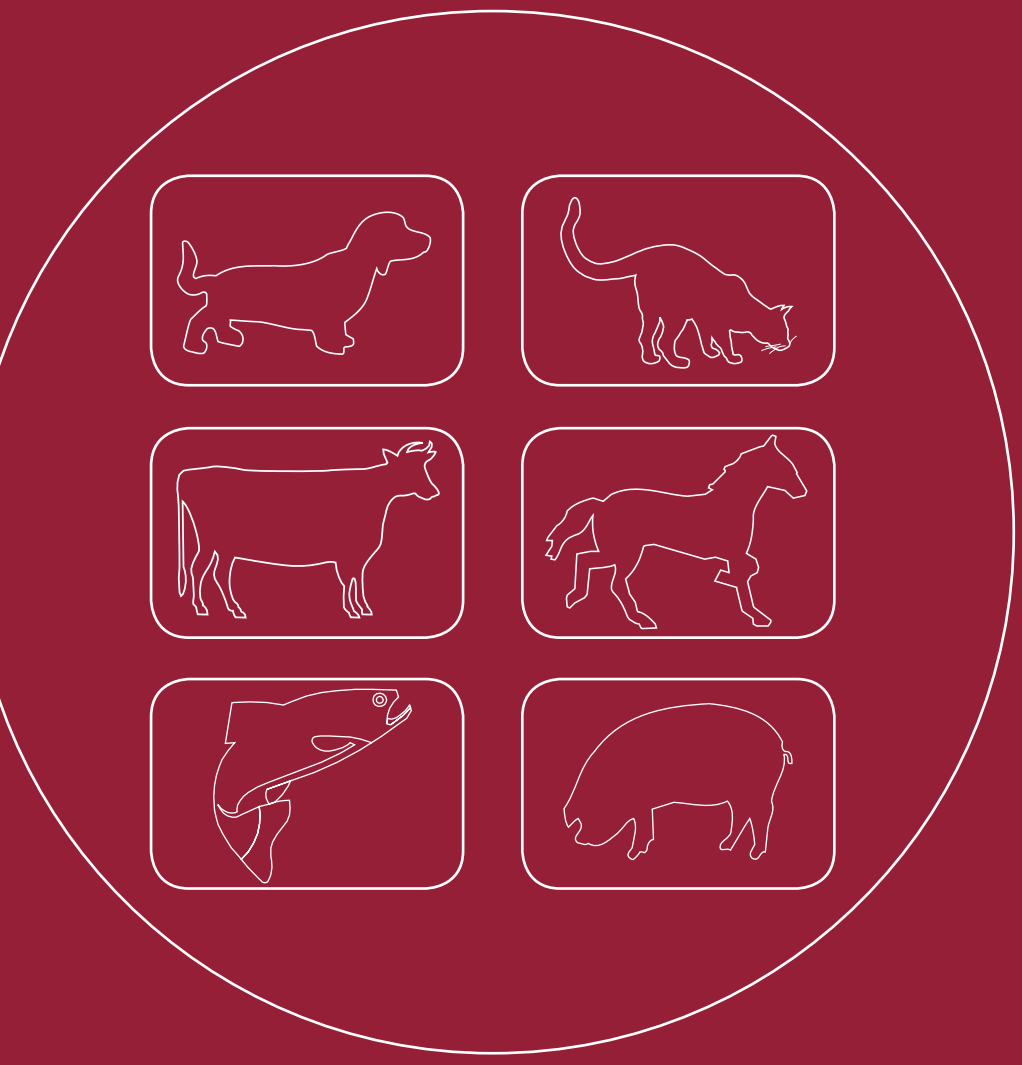
Swedish Veterinary Antimicrobial Resistance Monitoring

SVARM 2003



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Editors
Björn Bengtsson, Christina Greko and Märit Karlsson
Department of Antibiotics, National Veterinary Institute, SVA
SE-751 89 Uppsala
Sweden

Authors
Department of Antibiotics, National Veterinary Institute,SVA
Björn Bengtsson, Anders Franklin, Christina Greko and Märit Karlsson
Apoteket AB (National Corporation of Swedish Pharmacies)
Kristina Odensvik
Fiskhälsan FH AB (Fish Health Control Program)
Ulf-Peter Wichhardt

SVARM laboratory working group
Department of Antibiotics, National Veterinary Institute, SVA
Maria Finn, Margareta Horn af Rantzien, Annica Landén and Verena Rehbinder

SVARM advisory committee
Björn Bengtsson, Anders Franklin, Christina Greko and Märit Karlsson,
Department of Antibiotics, SVA
Viveka Båverud, *Department of Bacteriology, SVA*
Desirée Jansson, *Department of Poultry, SVA*
Gudrun Orava, *Information Department, SVA*
Ivar Vågsholm, *Zoonosis Center, SVA*
Kristina Odensvik, *Apoteket AB*

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Reprints can be ordered from
Department of Antibiotics
National Veterinary Institute
SE-751 89 Uppsala
Sweden

Phone: +46 (0) 18 67 40 00
Fax: +46 (0) 18 30 91 62
e-mail: sva@sva.se

Preface

WELCOME TO THE SECOND Swedish report combining results from the monitoring of antimicrobial resistance and antimicrobial usage in both veterinary and human medicine: SVARM and SWEDRES. It is today generally accepted that all use of antimicrobials in different sectors contributes to the development of resistance. This joint report will facilitate comparisons of resistance levels and incidence of use in the two areas.

In Sweden human and veterinary medicine have collaborated and communicated over a number of years, not least within the Swedish Strategic Programme for The Rational Use of Antimicrobial Agents and Surveillance of Resistance (STRAMA). Based on this experience, we are convinced that collaboration and joint efforts between human and veterinary medicine are essential in order to counteract the threat that antimicrobial resistance poses to both human and animal health.

Data in this report indicate that the Swedish strategies in human and veterinary medicine have been successful in containing resistance. The general concept is to use antimicrobials only when needed, on prescription by a professional only, and that the choice of treatment is based on relevant information.

Notwithstanding, some of the presented results in both veterinary and human fields are cause for concern. Examples of unfavourable development of resistance indicate that the antimicrobial arsenal available is becoming more and more limited. Further efforts must be made to prevent infectious diseases both in human and in veterinary medicine by other means.

Our hope is that this report will serve as a basis for policy recommendations and intervention strategies, and that it will increase our understanding of the dynamics of resistance. The ultimate goal is to preserve the effectiveness of available antimicrobials for man and animals.

Summary

THE RESULTS PRESENTED in this fourth report from SVARM concur with previous reports and other Swedish studies, showing that the situation regarding antimicrobial resistance in bacteria of animal origin is stable. Resistance does occur but the proportions are low, viewed from an international perspective. Likewise, data in the corresponding report covering human medicine, SWEDRES (http://www.strama.se or http://www.smittskyddsinstitutet.se) generally indicate a favourable situation.

Notwithstanding, some of the presented results in both human and veterinary fields are cause for concern. Examples of unfavourable development of resistance indicate that the antimicrobial arsenal available is becoming more and more limited. Further efforts must be made to prevent infectious diseases both in human and in veterinary medicine by other means.

Use of antimicrobials

Antimicrobials for use in animals in Sweden are only available on veterinary prescription and guidelines emphasising judicious use have been issued. Use for growth promotion was banned in year 1986. In 2003, a total of 16 metric tons of antimicrobials were used for animals. This represents a decrease by 7% compared with year 2002, and is at least partly explained by a true decrease in use of products for in-feed or water medication. Further, a decrease in sales of products sold with mastitis as one indication is paralleled by a decrease in the number of dairy cows.

The sales of products formulated for treatment of groups or flocks (in-feed or water medication) have decreased over the 90s. This is true also for the use of antimicrobials in aquaculture, where the total amounts prescribed (in kg active substance) have decreased from 259 kg in year 1994 to 40 kg in 2003. The reduction of use of antimicrobials for treatment of fishes is correlated with an increased use of vaccines.

Today, most of the antimicrobials sold for use in animals are products formulated for treatment of individual animals (87%). The use of most groups in this subset has decreased or been relatively unchanged over the last five years. However, the use of fluoroquinolones for treatment of individual animals has increased. Notably, the sales of tablets for treatment of companion animals have increased by 29% since 1999. When calculated to defined doses per 1 000 individuals and day, the current incidence of use of fluoroquinolones for pets is considerably higher than outpatient use for humans. The increased selective pressure has not yet been reflected as increased resistance among pathogens of dogs or cats. Nonetheless, the current usage level is cause for concern as fluoroquinolones are used for treatment of critical conditions in animals as well as people.

Resistance in zoonotic bacteria

Antimicrobial resistance in *Salmonella* from Swedish animals is rare and the situation has been stable since the late 70s, when monitoring of resistance began. The overall prevalence of resistance in each year's material is greatly influenced by the occurrence of multiresistant isolates of *S.* Typhimurium, i.e. resistant to at least three antimicrobials. As these phagetypes (DT104, DT193 and DT120) are rare among food-producing animals, probably a result of the strategies in the Swedish Salmonella control programme, the overall prevalence of resistance is low. Nor is there any indication of spread of such clones among the notified incidents in wild animals and pets.

Year 2003 *Campylobacter* spp. from pigs were studied. The majority of isolates were hippurate-negative thermophilic *Camplyobacter*, most likely *C. coli*. Generally the antimicrobial resistance among the isolates tested was low except for a high proportion of resistance to nalidixic acid (18%) and enrofloxacin (16%). This resistance is difficult to explain in relation to the assumed low use of fluoroquinolones in pigs in Sweden.

Resistance in indicator bacteria

In SVARM, antimicrobial resistance in indicator bacteria is monitored, i.e. in *Escherichia coli* and *Enterococcus* spp. from the normal enteric microflora of healthy animals. This year, data on indicator bacteria from pigs is reported.

Although usually harmless, these bacteria can form a reservoir of resistance genes that can be transferred to bacteria that cause disease in animals or humans. Moreover, resistance among indicator bacteria reflects the selective pressure exerted by use of antimicrobials in specific animal populations. Hence, recommendations on use can be based on trends in resistance and effects of interventions can be evaluated. If harmonised methodology is used, resistance in indicator bacteria can be compared on an international level.

In year 2003, prevalence of resistance in both *E. coli* and *Enterococcus* is low in an international perspective and has, with few exceptions, been stable since 2000 when monitoring commenced. Resistance occurred mostly to antimicrobials used as therapeutics in pig production. Tetracycline resistance in both *E. coli* and *Enterococcus*, erythromycin resistance in *Enterococcus* and sulphonamide resistance in *E. coli* were the most common traits.

In both *E. coli* and *Enterococcus*, there are indications of linked resistance genes, which imply that use of one antimicrobial could select for resistance also to other unrelated substances. The prevalence of streptomycin resistance in *E. coli* and *E. faecalis* is higher than expected, considering the limited use of this substance, but can be the result of such co-selection by use of tetracyclines, sulphonamides or macrolides.

Since monitoring of indicator bacteria in SVARM commenced, no vancomycin-resistant (VRE) and only two ampicillin-resistant *E. faecalis* or *E. faecium* (ARE) have been isolated from samples from pigs. These findings show that in Sweden, enterococci in pigs are no reservoir of VRE or ARE.

Resistance in animal pathogens

Data on antimicrobial susceptibility in animal pathogens are mainly from routine bacteriological examinations of clinical or post-mortem samples and are probably biased towards treatment failures or otherwise problematic cases.

The proportions of resistance among the pathogens included in the monitoring in year 2003 are largely similar to figures reported in previous reports. Viewed from an international perspective, the situation is favourable. However, the susceptibility to tiamulin in *Brachyspira hyodysenteriae*, measured as minimum inhibitory concentrations (MIC), is gradually decreasing and among *Brachyspira pilosicoli*, 14% of the isolates were classified as resistant (MIC > 2 mg/L) to that drug. Tiamulin is the drug of choice for treatment of the diseases associated with these pathogens, and few or no effective alternatives are available. The current situation is therefore cause for concern. Further, multiresistance is observed among 6-15% of investigated *E. coli*, depending on animal species, and among 29% of *Staphylococcus intermedius* from dogs. This means that in individual cases, it may be difficult to find effective antimicrobials for treatment of infections with these bacteria. The finding of penicillin resistance among *Pasteurella* spp. from the respiratory tract of calves can also have implications for therapeutic alternatives in the future. Such resistance, due to beta-lactamase production, has previously not been demonstrated in respiratory pathogens from Swedish calves. To contain these problems, efforts should be made to minimise the risk for spread of tiamulin resistance among *Brachyspira* spp., penicillin resistance among *Pasteurella* spp. and of multiresistance among other pathogens.

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Sammanfattning

RESULTATEN I DENNA FJÄRDE rapport från SVARM stämmer väl med de från tidigare år, och med andra svenska studier. Rapporten bekräftar att läget är stabilt. Resistens förekommer, men andelen är i ett internationellt perspektiv låg. Ett jämförelsevis gott läge redovisas också i motsvarande rapport över läget inom humansjukvården i Sverige, SWEDRES (http://www.strama.org eller http://www.smittskyddsinstitutet.se).

Inom både human- och veterinärmedicinen observeras likväl en del oroande trender. Dessa exempel på en ogynnsam utveckling antyder att den terapeutiska arsenalen blir allt mer begränsad. Det är därför viktigt att ytterligare ansträngningar görs för att förebygga infektionssjukdomar inom såväl human- som veterinärmedicin.

Användning av antibiotika

I Sverige får antibiotika användas till djur endast när en veterinär har skrivit recept. Riktlinjer för förskrivning av antibiotika har utarbetats och där betonas vikten av omdömesgillt bruk. Användning i tillväxtbefrämjande syfte förbjöds 1986. Under 2003 användes totalt 16 ton antibiotika till djur. Detta är 7% mindre än under 2002. Nedgången förklaras till en del av en sann minskning av försäljningen av produkter för inblandning i foder eller vatten. Försäljningen av produkter som är godkända för behandling av juverinflammation (och för andra sjukdomar) har också minskat, men den minskningen är proportionell till en nedgång av antalet mjölkkor i landet.

Försäljningen av produkter för behandling av grupper av djur (behandling via foder eller vatten) har minskat under 90-talet. Detta gäller även användningen av antibiotika i fiskodlingar, där den totala mängden som använts (mätt i kg aktiv substans) minskat från 259 kg år 1994 till 40 kg år 2003. Minskningen förklaras av en ökad användning av vacciner för att förebygga infektionssjukdomar.

Idag är huvuddelen av den mängd antibiotika som används produkter för behandling av enskilda djur (87%). Försäljningen av flertalet antibiotikagrupper av den typen har minskat eller varit oförändrad under de senaste fem åren. Användningen av fluorokinoloner för behandling av enskilda djur har dock ökat markant. Särskilt anmärkningsvärt är att försäljningen av tabletter för behandling av sällskapsdjur har ökat med 29% sedan 1999. Omräknat till definierade doser per 1 000 individer och dag så är användningen av fluorokinoloner till sällskapsdjur betydligt mer omfattande än till människa i öppenvård. Det ökande selektionstrycket har ännu inte avspeglats i ökad resistens hos de bakterier från hund och katt som övervakas. Trots detta är den ökade användningen oroande eftersom fluorokinoloner används för behandling av svåra infektioner hos djur och människor.

Resistens hos zoonotiska bakterier

Resistens mot antibiotika hos *Salmonella* från svenska djur är ovanligt. Läget har varit stabilt sedan slutet av 1970-talet, då övervakning av resistens hos *Salmonella* från djur påbörjades. Förekomst av resistens under enskilda år påverkas i stor utsträckning av om multiresistenta S. Typhimurium (resistenta mot tre eller fler antibiotika) förekommer eller inte. Infektion med fagtyper som ofta är multiresistenta (DT104, DT120 och DT193) förekommer sällan hos livsmedelsproducerande djur i Sverige, troligen som ett resultat av det svenska salmonellakontrollprogrammet. Detta gör i sin tur att resistens hos *Salmonella* sällan förekommer hos livsmedelsproducerande djur. Det finns heller inga tecken på spridning av multiresistenta kloner bland sällskapsdjur eller vilda djur.

År 2003 undersöktes isolat av *Campylobacter* spp. från grisar. Majoriteten av isolaten identifierades som hippuratnegativa termofila *Campylobacter* spp., med största sannolikhet detsamma som *C. coli*. Andelen resistens hos de undersökta isolaten var generellt sett låg med undantag av resistents mot nalidixansyra (18%) och enrofloxacin (16%). Då förbrukningen av fluorokinoloner till grisar i Sverige antas vara låg, inget preparat finns registrerat för gruppbehandling, är den här resistensen svårförklarlig.

Resistens hos indikatorbakterier

I SVARM undersöks förekomsten av antibiotikaresistens hos indikatorbakterier, dvs *Escherichia coli* och *Enterococcus* spp. ur den normala tarmfloran från friska djur som provtagits i samband med slakt. År 2003 har resistensläget hos indikatorbakterier från slaktsvin undersökts.

Anledningen till att undersöka dessa vanligen harmlösa bakterier är att de kan utgöra en reservoar av resistensgener som kan överföras till bakterier med förmåga att framkalla sjukdom hos djur eller människor. Dessutom återspeglar resistensläget hos indikatorbakterierna effekten av det selektionstryck som användningen av antibiotika i en djurpopulation utgör. Rekommendationer om användning av antibiotika kan därmed baseras på trender i resistensläget och effekten av vidtagna åtgärder kan avläsas. Underökningar av indikatorbakterier möjliggör också jämförelser mellan länder, under förutsättning att metodologin harmoniserats.

Förekomsten av resistens hos såväl *E. coli* som *Enterococcus* är år 2003 låg i förhållande till vad som rapporteras från andra länder. Med få undantag är nivåerna jämförbara med vad som redovisats år 2000 och 2001. Resistens förekommer i huvudsak mot de antibiotika som används vid behandling av grisar. Vanligast är tetracyklinresistens hos såväl *E. coli* som *Enterococcus*, erythromycinresistens hos *Enterococcus* och sulfonamidresistens hos *E. coli*.

I materialet finns indikationer på att kopplad resistens

förkommer hos såväl *E. coli* som *Enterococcus*. Detta innebär att användning av en substans kan selektera för resistens även mot andra, obesläktade antibiotika. Eftersom streptomycin inte används i någon större utsträckning till grisar kan den relativt höga andelen streptomycinresistens hos både *E. coli* och *Enterococcus* bero på sådan ko-selektion genom användning av tetracykliner, sulfonamider eller makrolider.

Sedan undersökningen av indikatorbakterier påbörjades år 2000 har i prov från slaktsvin inget vankomycinresistent isolat av *E. faecalis* eller *E. faecium* (VRE) påvisats och endast två isolat av dessa species har varit resistenta mot ampicillin (ARE). Uppenbarligen utgör slaktsvin i Sverige ingen reservoar för VRE eller ARE.

Resistens hos sjukdomsframkallande bakterier

Uppgifterna om antibiotikakänslighet hos bakterier som framkallar sjukdom hos djur grundas i huvudsak på sammanställningar av resultat av rutinundersökningar av bakteriologiska prover som skickats till SVA. Urvalet är troligen vinklat mot särskilt svårbehandlade eller på annat sätt problematiska fall.

Andelen resistens hos de bakterietyper som ingår i övervakningen var under 2003 av samma storleksordning som tidigare år. Ur ett internationellt perspektiv är läget gynnsamt. Känsligheten för tiamulin hos *Brachyspira hyodysenteriae*, mätt som minsta hämmande koncentration (MIC), minskar dock gradvis. Bland *Brachyspira pilosicoli* kategoriserades 14% av isolaten som resistenta (MIC >2 mg/L) mot detta läkemedel. Tiamulin är förstahandsval vid behandling av sjukdomar som förknippas med dessa bakterier, och få eller inga effektiva alternativ finns. Läget är därför oroande. Vidare var 6-15% av *E. coli* från de olika djurslagen och 29% av *Staphylococcus intermedius* från hundar multiresistenta. Detta innebär att det i vissa fall är svårt att hitta antibiotika för behandling av infektioner med dessa bakterier. Påvisandet av penicillinresistens hos *Pasteurella* spp. från luftvägarna hos kalvar kan också innebära begränsningar av behandlingsalternativen i framtiden. Denna typ av resistens, orsakad av betalaktamas produktion, har tidigare inte påvisats bland dessa bakterier hos svenska kalvar. Det är angeläget att risken för spridning av tiamulinresistens hos *Brachyspira* spp., penicillin resistens hos *Pasteurella* spp. och av multiresistenta bakterier, minimeras för att problemet ska kunna begränsas.

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Use of antimicrobials

THROUGH AN INITIATIVE OF SVA and Apoteket AB (the National Corporation of Swedish Pharmacies), statistics on total sales of antibiotics for use in animals in Sweden are available since 1980. For a review of the figures from 1980-2000 as well as references to publications on which that review is based, see SVARM 2000. Up to and including the year 2002, data presented are sales from wholesalers to pharmacies. From 2003, the basis for the statistics has been changed to sales from pharmacies.

Material included

In Sweden, antimicrobials for use in animals are only available on veterinary prescription and all pharmaceuticals are dispensed by pharmacies. In 1986, the Feedstuffs Act restricted the use of antibiotics for veterinary medicinal purposes, i.e. their use as growth promoters was banned.

Drug statistics are based on sales figures provided by Apoteket AB and represent the total amount of antimicrobials authorised for veterinary use sold, calculated to kg active substance. These figures include antimicrobial formulations for systemic, intramammary and obstetric use, and intestinal anti-infectives, for all animal species (food producing animals, pets and horses etc). Up to and including year 2002, the source for the statistics has been sales of drugs from wholesalers to pharmacies. From year 2003, the statistics are based on the amount of drugs dispensed by pharmacies. As the pharmacies stock a limited amount of veterinary drugs, the figures from wholesalers´ statistics should be comparable to the figures of antimicrobials dispensed. In both cases, statistics represent an approximation on the actual usage of antimicrobials, assuming that the amount sold is also used during the observation period.

Drugs authorised for human use but prescribed for animals are not included. Such drugs are prescribed primarily in small animal medicine and their use is declining as the number of products authorised for veterinary use is increasing.

This year, statistics specifically on use of antimicrobials in aquaculture has also been included. The presented data are taken from the annual report by Fiskhälsan FH AB (Fish Health Control Program) and include prescriptions of antimicrobials for fish farmed for direct food production and for sports fishing (i.e. fish for stocking enhancement as well as recreation fishing).

Details on animal numbers are found in Appendix 1 and on methodology in Appendix 2.

Overall use of antimicrobials

The total use of antimicrobials is presented in table AC I. The potency of the different antimicrobials is not equal and therefore each substance group should be evaluated separately. Nonetheless, the total figures may indicate trends in the material. The total amount used has decreased since the mid 90s, but was roughly unchanged during year 2000-2002. In year 2003, an apparent decrease by 7% is noted. As noted above, from year 2003 the source of the statistics has been changed to amounts dispensed but it is unlikely that the change of source would result in changes of the observed

Table AC I. Yearly sales of antimicrobial drugs for veterinary use expressed as kg active substance (sales statistics from Apoteket AB).

ATCvet code	Antimicrobial class	1980	1984	1988	1992	1996	2000	2001	2002	2003
QJ01AA, QG01A	Tetracyclines[1]	9 819	12 955	4 691	8 023	2 698	1 754	1 453	1 415	1 307
QJ01B	Amfenicols	47	49	35	-	-	-	-	-	-
QJ01CE, QJ01R, QJ51	Penicillin G-and V[2]	3 222	4 786	7 143	7 446	8 818	8 254	8 414	8 179	7 579
QJ01CA, QJ01CR	Aminopenicillins	60	714	655	837	835	852	752	767	870
QJ01D, QJ51CA	Other betalactams	9	2	-	-	-	315	474	676	832
QA07AA, QJ01G, QJ01R, QJ51R	Aminoglycosides[3]	5 274	5 608	3 194	2 139	1 164	797	770	753	645
QA07AB, QJ01E	Sulphonamides	6 600	4 325	3 072	2 362	2 198	2 338	2 485	2 477	2 326
QJ01E	Trimetoprim & derivatives	134	186	250	284	339	390	414	414	381
QJ01F	Macrolides & lincosamides	603	887	1 205	1 710	1 649	1 352	1 510	1 412	1 124
QJ01MA	Fluoroquinolones	-	-	-	147	173	156	182	185	184
QJ01XX92, QJ01XX94	Pleuromutilins	-	-	124	268	1 142	871	841	988	744
QJ01MB	Quinoxalines	6 250	9 900	7 164	4 917	1 098	-	-	-	-
QJ01XX91	Streptogramins	-	8 800	1 088	1 275	525	-	-	-	-
QP51AA, QJ01BA	Other substances[4]	861	1 637	1 567	1 634	-	-	-	-	-
	Feed additives[5]	8 380	700	-	-	-	-	-	-	-
Total		41 259	50 549	30 189	31 043	20 639	17 079	17 295	17 266	15 992

[1] Includes drugs marketed with special marketing authorisation for years 2000-2003; [2] Calculated as benzyl-penicillin; [3] Includes drugs marketed with special marketing authorisation for 2002; [4] Mainly nitroimidazoles; [5] Avoparcin, bacitracin, nitrovin, oleandomycin and spiramycin.

magnitude. Changes in the number of animals may affect trends in statistics on use of antimicrobials. In year 2003, the number of dairy cows decreased by 3%, as did the number of broilers slaughtered while the number of pigs slaughtered remained roughly unchanged compared with year 2002 (see Appendix 1). About half of the decrease (594 of 1274 kg) derives from a decrease in use of products intended for medication via feed or water (see Table AC III). As that type of products are mainly used in pigs, and as the pig population is unchanged, at least part of the observed decrease in total consumption is a true decrease in incidence of use. By contrast, the observed decrease in use of penicillin may well to a large extent reflect the lower number of dairy cows, as injectable products are widely used for treatment of mastitis.

The use of specific antimicrobial classes is commented under 'Use for systemic treatment of individual animals' or 'Use for treatment of groups or flocks', as appropriate.

In chickens, ionophoric antibiotics are given to control coccidiosis. These substances are currently classified as feed additives, and are not included in the overall statistics based on sales from pharmacies. However, the sales of these products, based on data from feed mills, are discussed under the section on group treatment (see Table AC III).

Use for systemic treatment of individual animals

In table AC II, the volume sold in form of products formulated for use in individual animals, excluding topical, intrauterine and intramammary use is presented. The use of most groups has decreased or been relatively unchanged over the last five years. A large part of the injectables is probably used for treatment of bovine mastitis. Therefore, much of the decrease may be explained by a steadily decreasing number of dairy cows. It should be noted, however, that many of the drugs of concern are also used in horses. Annual changes in the number of horses (increases or decreases) can therefore have an influence on the figures. Currently, there are no reliable figures on number of horses so any interpretation of trends in sales of drugs of this category must be made with great caution.

The vast majority of the sales of cephalosporins are products formulated as tablets for oral use in dogs. The sales of such first-generation cephalosporins have increased steadily since 1997, when drugs of this class were introduced on the Swedish market for use in pets. In 1998, 73% of the total number of prescriptions of cephalosporins for dogs and cats were off-label prescription of products authorised for humans (Odensvik *et al.*, 2001). As drugs authorised for humans are

Table AC II. Yearly sales of antimicrobial drugs authorised for individual treatment expressed in kg active substance. Intramammaries (QJ51) and formulations for dermatological use (QD06), as well as local treatment of the genito-urinary tract (QG01) are not included (sales statistics from Apoteket AB).

ATCvet code	Antimicrobial class	1996	1997	1998	1999	2000	2001	2002	2003
QA07A	Intestinal anti-infectives[1]	863	706	649	607	587	614	594	594
QJ01A	Tetracyclines	596	663	656	695	634	623	628	606
QJ01C	Penicillins[2, 3]	9 560	9 530	9 287	9 424	9 037	9 095	8 894	8 406
QJ01D	Cephalosporins	-	53	133	245	315	474	676	832
QJ01E	Sulfonamides & trimethoprim	2 033	2 107	2 335	2 376	2 336	2 478	2 483	2 280
QJ01F	Macrolides & lincosamides	675	652	645	559	531	522	477	430
QJ01G	Aminoglycosides[2]	650	617	535	528	474	454	460	367
QJ01M	Fluoroquinolones	147	147	150	144	150	169	178	177
QJ01X	Pleuromutilins	73	65	64	52	56	48	49	77

[1] Drugs marketed with special marketing authorisation are included from year 2000; [2] Procaine-penicillin calculated as benzyl-penicillin; [3] The amount includes QJ01R, combinations.

Table AC III. Yearly sales of antimicrobial drugs authorised for group treatment and ionophoric anticoccidials sold expressed as kg active substance. Based on sale statistics from Apoteket AB and from the Board of Agriculture.

ATCvet code	Antimicrobial class	1980	1984	1988	1992	1996	2000	2001	2002	2003
QJ01A	Tetracyclines[1]	9 270	12 300	4 177	7 461	2 089	1 111	822	777	695
QJ01C	Penicillins	-	-	186	9	-	-	-	-	-
QJ01F	Macrolides and lincosamides	308	607	751	1 139	975	821	988	935	694
QJ01M	Fluoroquinolones	-	-	-	10	27	7	13	7	8
QJ01M	Quinoxalines	6 250	9 900	7 164	4 917	1 098	-	-	-	-
QJ01XX91	Streptogramins	-	8 800	1 088	1 275	525	-	-	-	-
QJ01XX92, QJ01XX94	Pleuromutilins	-	-	101	229	1 069	815	793	939	667
QP51AA	Nitroimidazoles	791	1 440	1 557	1 563	-	-	-	-	-
	Feed additives[2]	8 380	700	-	-	-	-	-	-	-
QP51AH	Ionophoric antibiotics (coccidiostats)[3]	390	7 900	6 991	8 267	11 643	9 368	10 019	8 439	10 920

[1] Drugs marketed with special marketing authorisation are included from year 2000; [2] Substances included are avoparcin, bacitracin, nitrovin, oleandromycin and spiramycin; [3] From 1999 regulated and classified as feed additives (dir 70/524/EEC). Figures from 1999 and onwards are from the Feed Control of the Board of Agriculture (www.sjv.se).

not included in the statistics in this report, the increasing trend partly reflects an increased prescription to pets of drugs authorised for veterinary use instead of off-label prescription of drugs of the same class authorised for humans rather than an increased incidence of use of the substance class as such. However, considering the magnitude of the increase, it is probable that there is also a true increase in use.

The use of fluoroquinolones for individual treatment has increased by 23% over the last five years. Sales of injectable products, used mainly for treatment of cattle and pigs, constitute approximately 60% of the figures on sales of fluoroquinolones in AC II. The sales of the subset composed of injectable fluoroquinolones have increased by 19%. It is unclear whether that increase derives from use in cattle or pigs, or both. The remainder of the sales are tablets for use in small animals. The sales of that subset have increased by 29%. Using a dose of 5 mg/kg, and an estimated average weight of dogs of 20 kg, the number of doses per 1 000 dogs and day can be calculated to 1.8. This use is considerably higher than what is used for outpatient care of people in Sweden (1.0 and 1.1 DDD/1 000 inhabitants and day for women and men, respectively). There are no apparent scientific of veterinary reasons for this recorded increase. Over the last years, several new products containing fluroroquinolones for use mainly in dogs have been launched on the Swedish market. It is probable that the increase of sales for dogs and cats reflects an active marketing, rather than a true change in need for the products. The increased use of fluoroquinolones for individual treatment of animals is of concern, as these drugs are used for treatment of critical conditions in both animals and man.

Use for treatment of groups or flocks

Of special interest when considering the risk for development of resistance is the consumption of antimicrobials intended for group or flock medication. Of the total sales of antimicrobials for animals, the proportion of drugs authorised for treatment of groups of animals via feed or water has decreased steadily over the years and is today but 13% of the total sales, measured as kg active substance (Table AC III). Only four classes of antimicrobials of this type remain on the market. All groups, except the pleuromutilins, show a declining trend since at least the mid 90s. Pleuromutilins (tiamulin, valnemulin) are only authorised for use in pigs, with swine dysentery as the main indication. A sudden increase in use was noted between year 2001 and 2002 but in 2003, the sales figures decreased notably. The reasons for this fluctuation remain unclear.

The observed decrease in use of tetracyclines is somewhat confounded by an increased use of doxycycline within that group. Doxycycline has a higher bioavbailability, and the dose is lower compared with that for, e.g. chlortetracycline. When the sales figures for 2003 are corrected for the lower dose of doxycycline, the use of tetracyclines has decreased by 60% since 1998 (when no doxycycline was used).

Coccidiostats of the ionophore group are used as feed additives to control coccidiosis in the production of chickens for slaughter. Since the late 80s, narasin is by far the most widely applied substance.

Use of products with mastitis as one authorised indication

In SVARM 2001, statistics on sales of drugs authorised for treatment of mastitis in cows as one indication were presented separately. Updated figures for that subset are found in Table AC IV. The unit of DDDcow per 1 000 cows and day was developed in collaboration between Norway and Sweden to correct for differences in dose and population size (Grave *et al.*, 1999, see also Appendix 2 for methodology).

Most of the drugs that are included are authorised not only for mastitis, but also for other indications, and for other animal species as well. However, estimates based on animal health records indicate that of the injectable drugs, 40-50% of the calculated DDDcow sold was used for treatment of mastitis. Therefore, the data is likely to reflect trends in usage for treatment of mastitis.

In Sweden, mastitis in dairy cows is mainly treated with injectable antimicrobials. The total use of the selected injcetables expressed as DDDcow/1 000 cows and day has increased since year 1990 an onwards (Table AC IV). The increase is probably, at least partly, explained by use of higher doses and longer duration of treatment for each case. The highest figures are recorded in 1994. In that year, the dairies lowered their limits for bulk-milk cell counts and this may have affected the number of treatments.

Among the different drug classes, the use of penicillins increased while the use of combinations of procaine penicillin and dihydrostreptomycin decreased. The relative proportion of penicillins of the total number of DDDcow increased from 60% to 75% between 1990 and 2001. Compared with year 2001, a slight decrease in use of benzyl-penicillin can be noted. One of the leading products in this class has been withdrawn from the market by the company, which probably explains the decrease of that group.

Enrofloxacin was introduced in 1989, which may explain that the figures for 1990 and 1991 are lower than the other years. However, an increase of this class between year 2000 and 2003 is noted. As discussed above, these products are also authorised for other indications and for other animal species, and the true reason for this increase therefore remains unclear.

In Table AC IV, figures on sales of intramammaries are also presented, expressed as DDDcow/1 000 cows. One single-dose applicator was defined as one daily dose. The products have been divided according to their indication, i.e. for therapy of mastitis during lactation or for dry cow treatment. For the former category, the incidence has decreased over the period studied. By contrast, the use of dry-cow treatment doubled in the 90s, but has since year 2000 remained relatively unchanged.

Use of antimicrobials in aquaculture

In Table AC V, statistics on yearly amounts of antimicrobials prescribed for use in farmed fish (fish for consumption and

Table AC IV. Antimicrobials for injection with mastitis in bovines as one indication and antimicrobials for intramammary use expressed as defined daily doses for cows (DDDcow) per 1 000 cows and day (DDDcow/1 000 cows at risk and day; according to Grave *et al*., 1999). Based on sale statistics from Apoteket AB and animal numbers from Official Statistics Sweden.

ATCvet	Drug class or indication	DDD cow (g)	1990	1992	1994	1996	1998	2000	2001	2002	2003
Injectables											
QJ01A	Oxytetracycline	5	0.5	0.5	0.7	0.6	0.7	0.7	0.5	0.5	0.5
QJ01C	Benzylpenicillin	12.6	0.1	0.1	1.9	1.7	1.3	1.0	1.0	1.0	0.8
QJ01C	Procaine penicillin	15	3.1	3.6	2.7	2.9	3.6	4.1	4.5	4.5	4.5
QJ01C	Penethamate hydroiodide	10	<0.1	-	-	-	-	-	-	-	-
QJO1E	Sulphonamide- trimethoprim	24	0.2	0.3	0.3	0.3	0.3	0.2	0.3	0.3	0.3
QJ01F	Spiramycin	5	0.3	0.4	0.8	0.4	0.3	0.2	0.2	0.2	0.2
QJ01M	Enrofloxacin	1.25	0.3	0.5	0.8	0.5	0.6	0.5	0.6	0.7	0.7
QJ01R	Procaine penicillin+DHS[1]	10	0.9	0.6	0.5	0.3	0.3	0.2	0.2	0.2	0.2
	Total injectables		5.3	6.0	7.6	6.6	7.1	6.9	7.3	7.4	7.2
Intramammaries											
QJ51	For therapy during lactation		1.9	1.8	1.8	1.5	1.3	1.1	1.1	1.0	1.0
QJ51	For dry cow treatment		0.9	1.4	2.4	2.1	2.0	1.8	1.9	1.7	1.8
	Total intramammaries		2.9	3.1	4.2	3.5	3.3	2.9	3.0	2.7	2.8

[1] DHS=dihydrostreptomycin

for sports fishing, i.e. fish for stocking enhancement as well as recreation fishing) are shown. Today, tetracyclines, amfenicols (florfenicol) and quinolones (oxolinic acid, flumequine) are the only antimicrobial classes used.

In most cases, antimicrobials for therapy of farmed fish are administered as medicated feed mixed at feed mills. All antimicrobial products used for this purpose were sold with a special marketing authorisation. The amounts used decreased notably in the beginning of the 90s and have during the last five years been around or below 50 kg active substance. The amount of fish produced has remained comparatively stable over the years, although the number of holdings has decreased. The reduction is correlated with an increased use of effective vaccines against two of the main indications (see below).

The vast majority of treatments are applied to fish weighing less than 100 g. In year 2003, 38% of the total amount prescribed was used for treatment of fish for consumption. Fiskhälsan FH AB estimates the total production of fish for consumption to 8 100 metric tons (live weight), and using that figure the use of antibiotics in 2003 was below 2 g per ton fish produced.

In some cases, antimicrobials may be administered to fish by injection or immersion. Injection is only used on rare occasions for treatment of breeders (salmonid fish) (Table AC V). Treatment by immersion is used particularly for eel, a species that rapidly become anorectic when subject to bacterial infections.

The main indications for antimicrobial therapy in Swedish fish farming are infections with *Aeromonas salmonicida* supsp. *salmonicida* (furunculosis), *A. salmonicida* subsp. achromogenes (infectious dermatitis), *Flavobacterium* spp.(flavobacteriosis) and *Listonella* (*Vibrio*) *anguillarum* (vibriosis). Vaccines against furunculosis and vibriosis are widely used, and in year 2003 flavobacteriosis and infectious dermatitis were the most commonly treated infections.

In year 2003, the amounts of antimicrobials used for Arctic char (*Salvelinus alpinus*) was in 2003 of a similar magnitude as that used for rainbow trout (*Oncorhyncus mykiss*) (Table AC VI). However, in year 2003, the amounts of char produced was approximately 800 metric tons, compared with 8 000 tons of rainbow trout. This means that the relative amounts of antimicrobials used in rearing of char is about 15 times higher than for rainbow trout. The production of char has increased markedly over the last years, and the relatively high antimicrobial use indicates that preventive measures are needed. This could be for example development of effective vaccines or other infection control strategies such as optimising the localisation of the rearing sites.

Table AC V. Yearly amounts (kg active substance) of antimicrobials prescribed for use in farmed fish per mode of administration and substance class (based on data from Fiskhälsan FH AB).

Administration route ATC vet code	Substance class	1990	1992	1994	1996	1998	2000	2001	2002	2003
In feed										
QJ01AA	Tetracyclines	992	108	128	47	32	2	4	16	12
QJ01BA	Amfenicols	0	0	0	0	3	5	5	10	5
QJ01EW	Trimethoprim-sulphonamides	0	130	19	87	-	-	-	-	-
QJ01MB	Quinolones	29	63	101	63	5	9	13	11	16
Intra-peritoneal										
QJ01EW	Trimethoprim-sulphonamides	-	<1	-	-	-	<1	-	-	-
Immersion										
QJ01AA	Tetracyclines	-	20	5	3	-	<1	-	<1	-
QJ01MB	Quinolones	-	-	6	-	16	20	8	3	7
Total		1 021	321	259	200	56	37	30	40	40

Table AC VI. Yearly sales of antimicrobials for in feed medication of farmed fish divided per fish species (based on data from Fiskhälsan FH AB)

Fish species	Latin name	1998	1999	2000	2001	2002	2003
Rainbow trout	*Oncorhynchus mykiss*	36.3	28.5	7.1	15.9	22.8	9.9
Brown trout	*Salmo trutta*	2.8	5.7	2.8	4.3	6.7	5.9
Arctic char	*Salvelinus alpinus*	0.8	3.1	5.9	2.0	5.2	11.8
Other species		0.1	1.0	0.1	0.2	2.1	4.5
Total		40.0	38.3	15.9	22.4	36.8	32.1

Resistance in zoonotic bacteria

THE MONITORING PROGRAM encompasses zoonotic bacteria isolated from animals of Swedish origin. This year data on antimicrobial susceptibility among *Salmonella enterica* and among *Campylobacter jejuni* and hippurate-negative thermophilic *Campylobacter* spp. are presented. More information regarding infections with these bacteria in Sweden is available in the yearly report, Zoonoses in Sweden 2002.

Note that some microbiological cut-off values defining resistance (breakpoints) used in previous SVARM-reports have been changed. To facilitate comparisons when data from previous years are presented, levels of resistance have been recalculated using the current cut-off values. For a summary of cut-off values used see Appendix 3.

Salmonella

Isolates included

Any finding of *Salmonella* in animals is notifiable in Sweden and confirmation at SVA of at least one isolate from each incident is mandatory. From these isolates, one from each animal species (warm-blooded wild and domesticated) involved in each notified incident year 2003 are included in the material, for more details see Appendix 3.

In Sweden, monitoring of antimicrobial susceptibility among *Salmonella* of animal origin has been performed regularly since 1978. Although the antimicrobials included in the test panels have varied, microdilution methods have been used in all these surveys. For comparison, data from previous years are therefore presented together with data for 2003.

Results and comments

A total of 101 isolates are included in the material (Table S I). Of subspecies I (enterica), 49 were *S.* Typhimurium, 28 *S.* Cubana, 4 *S.* Dublin and 17 isolates were other serovars. There were also 3 isolates of subspecies IIIb (diarizonae). The majority of isolates were from pigs (38%) and cats (39%) (Table S I). Of the isolates from pigs 74% were typed as the same clone of *S.* Cubana originating from an outbreak caused by contamination of pig feed in a feed mill. All isolates from cats, except one, were typed as Typhimurium and 56% as DT40. This is a common phagetype among non-migratory small birds and cats get infected eating birds easily caught at bird feeders during late winter. Both the *S.* Cubana clone and the *S.* Typhimurium isolates from cats were susceptible to all antimicrobials tested. The distributions of the MICs for the 101 isolates are given in Table S II and S III.

The low level of resistance among Salmonella enterica, as well as in the subset *S.* Typhimurium, year 2003 agrees with the results for previous years (SVARM 2000 to 2002). Further, among *S.* Typhimurium, levels of resistance have

Table S I. Number of isolates of *Salmonella enterica* included year 2003 presented by serovar and source.

Subspecies I	Cattle	Pig	Poultry	Dog	Cat	Wildlife	Total
Agona		1	1	1			3
Anatum			1				1
Cubana		28					28
Dublin	3	1					4
Enteritidis		1	1				2
Infantis	1	1					2
Kottbus		1					1
Livingstone			1				1
Muenster		1					1
Oritamerin	1					1	2
Senftenberg			1				1
Stanley		1					1
Tennessee	1						1
Typhimurium DT 15a			1				1
Typhimurium DT 40				1	22	2	25
Typhimurium DT 104	1	1					2
Typhimurium DT 120		1					1
Typhimurium NST		1	1				2
Typhimurium not phagetyped				1	16	1	18
Worthington			1				1
Subspecies IIIb	1				1	1	3
Total	8	38	8	3	39	5	101
Percent of total	8%	38%	8%	3%	39%	5%	

been stable, the only apparent trend is a lower level of resistance to streptomycin since 1999 compared to the preceding period (Table S IV).

It is apparent that the occurrence of multiresistant isolates, i.e. resistant to at least three antimicrobials, in each year's material greatly influences the prevalence of resistance. Among *S.* Typhimurium, five isolates were multiresistant in 1999 and two isolates in each of the years 2000 and 2001. These isolates were DT104, DT193 or DT120. The impact on the overall levels of resistance each year is demonstrated in Table S IV. The material from 2002 and 2003 did not include any multiresistant isolate. In 2002 resistance to a single antimicrobial (nalidixic acid) occurred in one isolate and 2003 one isolate was resistant to both streptomycin and sulphamethoxazole.

The material in the years 1997 to 2003 consists of one isolate from each notified incident of *Salmonella* in Sweden, including those detected in food-producing animals in the *Salmonella* control programme. From a public health perspective, the prevalence of resistance in *Salmonella* from food-producing animals is of greater importance than resistance in isolates from wild animals or pets. Therefore a subset of the 272 isolates from food-producing animals years 1997-2003 is presented in Table S V. In the whole material only 19 isolates (7%) were resistant to any of the antimicrobials tested and five isolates (2%) were multiresistant. All multiresistant isolates were *S.* Typhimurium, two each of DT104 and DT193 and one isolate of DT120. These isolates were resistant to ampicillin, streptomycin, tetracycline and sulphonamides. In addition, the DT104 and DT120 isolates were resistant to chloramphenicol.

In light of this, the overall situation of antimicrobial resist-

Table S II. Distribution of MICs for all *Salmonella enterica* (n=101) from animals in 2003.

Substance	Resistance (%)	Distribution (%) of MICs[1] (mg/L)																	
		≤0.03	0.06	0.12	0.25	0.5	1	2	4	8	16	32	64	128	256	512	1024	2048	>2048
Amoxi/clav.[2]	0							100.0											
Ampicillin	0					4.0	77.2	17.8	1.0										
Ceftiofur	0				2.0	5.0	88.1	5.0											
Chloramphenicol	0							2.0	73.3	23.8	1.0								
Enrofloxacin	2		25.7	69.3	3.0		2.0												
Florfenicol	0								76.2	21.8	2.0								
Gentamicin	0					14.9	59.4	21.8	4.0										
Nalidixic acid	2								56.4	41.6					2.0				
Neomycin	0							84.2	15.8										
Streptomycin	5								2.0	29.7	41.6	21.8	3.0			2.0			
Sulphamethoxazole	2											2.0	7.9	54.5	33.7				2.0
Tetracycline	1						3.0	73.3	21.8	1.0				1.0					
Trimethoprim	0				4.0	72.3	20.8	3.0											

[1] The white fields denote range of dilutions tested for each substance. MICs above the range are given as the concentration closest to the range. MICs equal to or lower than the lowest concentration tested are given as the lowest tested concentration. Bold vertical lines indicate cut-off values defining resistance; [2] Concentration of amoxicillin given, tested with clavulanic acid in concentration ratio 2/1.

Table S III. Distribution of MICs for the subset *Salmonella* Typhimurium (n=49) from animals in 2003.

Substance	Resistance (%)	Distribution (%) of MICs1 (mg/L)																	
		≤0.03	0.06	0.12	0.25	0.5	1	2	4	8	16	32	64	128	256	512	1024	2048	>2048
Amoxi/clav.[2]	0							100.0											
Ampicillin	0						73.5	24.5	2.0										
Ceftiofur	0					2.0	98.0												
Chloramphenicol	0								98.0	2.0									
Enrofloxacin	0		4.1	95.9															
Florfenicol	0								98.0	2.0									
Gentamicin	0					24.5	71.4	2.0	2.0										
Nalidixic acid	0								42.9	57.1									
Neomycin	0							93.9	6.1										
Streptomycin	2									6.1	65.3	26.5				2.0			
Sulphamethoxazole	2													42.9	55.1				2.0
Tetracycline	0							81.6	18.4										
Trimethoprim	0					75.5	22.4	2.0											

[1] The white fields denote range of dilutions tested for each substance. MICs above the range are given as the concentration closest to the range. MICs equal to or lower than the lowest concentration tested are given as the lowest tested concentration. Bold vertical lines indicate cut-off values defining resistance; [2] Concentration of amoxicillin given, tested with clavulanic acid in concentration ratio 2/1.

Table S IV. Occurrence of resistance (%) and source of isolates in *Salmonella* Typhimurium from animals 1978 to 2003.

Substance	Cut-off value (mg/L)	Resistance (%) 1978-86 (n=117)	1987-88[1, 2] (n=8)	1989-92 (n=79)	1993-96 (n=87)	1997-98 (n=50)	1999 (n=101)	2000 (n=46)	2001 (n=31)	2002 (n=31)	2003 (n=49)
Amoxi/clav.	>8/4	-	-	-	-	-	-	2	6	0	0
Ampicillin	>8	2	0	3	8	12	5	2	6	0	0
Ceftiofur	>2	-	-	-	-	-	-	0	0	0	0
Cephalotin	>16	-	-	1	0	0	3	-	-	-	-
Chloramphenicol	>16	4[3]	0[3]	3[3]	6[3]	12[3]	2[3]	2[3]	6[3]	0	0
Enrofloxacin	>0.25	-	-	1	1	0	1	0	0	0	0
Florfenicol	>16	-	-	-	-	-	-	2	6	0	0
Gentamicin	>8	-	-	0	0	0	0	0	0	0	0
Nalidixic acid	>16	-	-	-	-	-	-	4	3	3	0
Neomycin	>8	0	0	4	0	2	0	0	3	0	0
Streptomycin	>32	78	12	25	13	20	6	4	6	0	2
Sulphamethoxazole	>256	-	-	-	-	-	-	2	6	0	2
Tetracycline	>8	14	0	3	7	12	5	2	6	0	0
Trimethoprim	>8	-	-	-	-	-	-	0	0	0	0
Trim/sulph.	0.5/9.5	0	0	1	1	8	3	-	-	-	-
Percent of isolates from:											
Cattle, sheep, pigs, poultry		100	100	59	55	56	23	57	39	36	12
Horses, cats, dogs		-	-	15	22	16	53	37	38	32	82
Wildlife		-	-	26	23	28	24	7	23	32	6

[1] Only isolates from cattle; [2] 1988 includes isolates to September, isolates from October-December 1988 given under 1989; [3] Cut-off value defining resistance >8 mg/L.

Table S V. Distribution of MICs for all *Salmonella enterica* (n=272) from food-producing animals years 1997-2003. Due to change of panel design year 2000 some substances have only been tested for 145 isolates.

Substance	Resistance (%)	Distribution (%) of MICs[1] (mg/L) ≤0.25	0.5	1	2	4	8	16	32	64	128	256	512	1024	>1024
Amoxi/clav.[2]	0[3]				100.0										
Ampicillin	2		4.0	67.3	26.1	0.7			1.8						
Ceftiofur	0[3]	6.2	24.1	65.5	4.1										
Chloramphenicol	1				16.2	65.8	16.9		1.1						
Enrofloxacin	1	98.9		1.1											
Florfenicol	0[3]					75.9	23.4	0.7							
Gentamicin	0			55.1	19.5	25.4									
Nalidixic acid	2[3]					48.3	36.6	13.1	0.7			1.4			
Neomycin	0				69.9	29.0	1.1								
Streptomycin	6				0.4	2.2	21.7	34.2	35.3	3.3	1.8	1.1			
Sulphamethoxazole	1[3]									35.2	54.5	9.0		1.4	
Tetracycline	2			12.5	57.4	26.1	1.8			0.7	1.5				
Trimethoprim	0[3]	13.1	69.0	16.6	0.7	0.7									

[1] The white fields denote range of dilutions tested for each substance. MICs above the range are given as the concentration closest to the range. MICs equal to or lower than the lowest concentration tested are given as the lowest tested concentration. Bold vertical lines indicate cut-off values defining resistance; [2] Concentration of amoxicillin given, tested with clavulanic acid in concentration ratio 2/1. [3] 145 isolates tested.

ance in *Salmonella* is most favourable. There is no evident spread of multiresistant clones among food-producing animals within the country, probably as a result of the strategies in the Swedish *Salmonella* control programme. Nor is there among the notified incidents in wild animals any indication of spread of such clones as only one of the 75 *Salmonella enterica* isolates tested since 1997 was multiresistant.

Table S VI. Distribution of MICs for the subset *Salmonella* Typhimurium (n=105) from food-producing animals years 1997-2003. Due to change of panel design year 2000 some substances have only been tested for 54 isolates.

Substance	Resistance (%)	Distribution (%) of MICs[1] (mg/L)													
		≤0.25	0.5	1	2	4	8	16	32	64	128	256	512	1024	>1024
Amoxi/clav.[2]	0[3]				100.0										
Ampicillin	5		1.0	6.0	33.3	1.0			4.8						
Ceftiofur	0[3]		33.3	63.0	3.7										
Chloramphenicol	3				17.1	76.2	3.8		2.9						
Enrofloxacin	0	100.0													
Florfenicol	0[3]					96.3	3.7								
Gentamicin	0			52.4	21.0	26.7									
Nalidixic acid	2[3]					38.9	37.0	22.2	1.9						
Neomycin	0				72.4	27.6									
Streptomycin	6					1.0	5.7	41.9	45.7		2.9	2.9			
Sulphamethoxazole	2[3]									46.3	42.6	9.3		1.9	
Tetracycline	5			6.7	58.1	27.6	2.9			1.9	2.9				
Trimethoprim	0[3]	22.2	57.4	20.4											

[1] The white fields denote range of dilutions tested for each substance. MICs above the range are given as the concentration closest to the range. MICs equal to or lower than the lowest concentration tested are given as the lowest tested concentration. Bold vertical lines indicate microbiological cut-off values defining resistance; [2] Concentration of amoxicillin given, tested with clavulanic acid in concentration ratio 2/1; [3] 54 isolates tested.

Campylobacter

Isolates included

Samples for culture of *Campylobacter* spp. were selected from the total number of samples of colon content from healthy pigs collected at abattoirs with the purpose of isolating indicator bacteria.

Isolates were identified as *Campylobacter jejuni* or as hippurate-negative thermophilic *Campylobacter*, most likely *C. coli*. Antimicrobials included in the test panels and concentration ranges are given in Table Camp I. For details on methodology, including sampling strategy, see Appendix 3.

Results and comments

The majority of the isolates were identified as hippurate-negative thermophilic *Campylobacter* (n=100), and only five isolates were classified as *C. jejuni*. The distribution of the MICs for the hippurate-negative thermophilic *Campylobacter* isolates is given in Table Camp I. Among the five isolates of *C. jejuni*, one was resistant to erythromycin, nalidixic acid and enrofloxacin.

In SVARM 2001, a comparatively high proportion of resistance to nalidixic acid and enrofloxacin (30%) was reported for isolates of hippurate-negative thermophilic *Campylobacter* from pigs. In the material from 2003 such resistance was also found but at a lower level, enrofloxacin (16%) and nalidixic acid (18%). The decrease cannot be explained by different sampling strategies. Both years each sample was predominantly from unique herds representing several regions of Sweden. Despite the decrease this resistance is still surprisingly high. No fluoroquinolones are authorized for group treatment of pigs in Sweden. However, there are no figures available for the use of antimicrobials per animal species and consequently the proportion of fluoroquinolones for injection used in Swedish pig herds is not known. The only other resistance found was one isolate resistant to tetracycline.

Table Camp I. Distribution of MICs for hippurate-negative thermophilic *Campylobacter* spp. from pigs (n=100), 2003. Data for 1999 (n=91) are given for comparison (SVARM 2001).

Substance	Year	Resistance (%)	Distribution (%) of MICs[1] (mg/L)													
			≤0.03	0.06	0.12	0.25	0.5	1	2	4	8	16	32	64	128	>128
Ampicillin	-99	0					1.1	8.8	18.7	45.1	25.3	1.1				
	-03	0					3.0	9.0	16.0	39.0	32.0	1.0				
Enrofloxacin	-99	30	1.1	40.7	19.8	8.8			5.5	15.4	8.8					
	-03	16		30.0	44.0	8.0	1.0	1.0	1.0	8.0	7.0					
Erythromycin	-99	1					5.5	13.2	28.6	38.5	13.2		1.1			
	-03	0				1.0	5.0	21.0	34.0	33.0	6.0					
Gentamicin	-99	0					1.1	39.6	59.3							
	-03	0				1.0		5.0	68.0	23.0	3.0					
Nalidixic acid	-99	30							2.2	27.5	34.1	6.6		7.7	18.7	3.3
	-03	18							4.0	35.0	36.0	7.0	1.0	8.0	9.0	
Tetracycline	-99	2				56.0	20.9	15.4	3.3	2.2		1.1		1.1		
	-03	1				79.0	10.0	7.0	1.0	1.0	1.0		1.0			

[1] The white fields denote range of dilutions tested for each substance. MICs above the range are given as the concentration closest to the range. MICs equal to or lower than the lowest concentration tested are given as the lowest tested concentration. Bold vertical lines indicate cut-off values defining resistance.

Resistance in indicator bacteria

THE PREVALENCE of acquired resistance to antimicrobials among bacteria of the normal enteric microflora can serve as an indicator of the selective pressure exerted by use of antimicrobial agents in exposed populations. Although these bacteria are unlikely to cause diseases, they form a reservoir of transferable resistance determinants from which resistance genes can spread to bacteria that cause infections in animals or humans. Thus, surveillance of resistance among indicator bacteria in the normal enteric microbiota from healthy animals can be of great value to detect trends and to follow the effects of interventions. In SVARM, *Escherichia coli* and *Enterococcus* spp. from healthy animals serve as indicator bacteria. The report for year 2004 presents data on isolates from slaughter pigs.

Of special interest in monitoring antimicrobial susceptibility among indicator bacteria is the occurrence of specific patterns of resistance. Such patterns, or phenotypes, can indicate that resistance genes are located on the same genetic element. The danger of such elements is evident as a single transfer event conveys resistance to several antimicrobials to the recipient bacterium (co-transfer). Thereby, use of one antimicrobial can select for resistance to other unrelated antimicrobials (co-selection). In SVARM 2003, analyses of associations between resistance to different antimicrobials were performed on the combined data for years 2000, 2001 and 2003. To this end the Chi-Square test was used for statistical inference on the likelihood that isolates resistant to one antimicrobial also were resistant to another. The same test was used for analysis of differences in occurrence of resistance between years 2000, 2001 and 2003.

Some microbiological cut-off values defining resistance (breakpoints) used in previous SVARM-reports have been changed. To facilitate comparisons when data from previous years are presented, levels of resistance have been recalculated using the current cut-off values. For a summary of cut-off values used see Appendix 3.

Isolates included

Escherichia coli and *Enterococcus* spp. were isolated from ceacal or colon content from pigs sampled at slaughter. Each isolate originates from a unique herd. Antimicrobials included in the test panels and concentration ranges used are given in Table EC IV and ENT VII. For details on methodology, including sampling strategy, see Appendix 3.

Escherichia coli

The material includes 303 isolates of *E. coli* from pigs. Isolates were obtained from 83% of 367 samples cultured, a similar isolation frequency as in SVARM 2000 and 2001.

The majority of isolates (78%) were sensitive to all 14 antimicrobials tested but 67 isolates were resistant to at least one substance. Resistance to tetracycline, sulphonamides or streptomycin were the most common traits (9-12%) (Table EC I). Ampicillin or trimethoprim resistance was less common (3-4%) and only occasional isolates were resistant to amoxicillin/clavulanic acid, chloramphenicol, enrofloxacin, nalidixic acid or neomycin. No isolate was resistant to florfenicol, apramycin, ceftiofur or gentamicin. Thirty-four isolates (11%) were resistant to more than one antimicrobial

Table EC I. Occurrence of resistance (%) among isolates of *Escherichia coli* from pigs, 2003. Data for 2000 (pigs and cattle), 2001 (pigs) and 2002 (chickens) are given for comparison (SVARM 2000, 2001, and 2002).

		Resistance (%) (95% confidence interval inside brackets)									
		Pigs						Chickens		Cattle	
Substance	Cut-off value (mg/L)	2003 n=303		2001 n=308		2000 n=260		2002 n=306		2000 n=293	
Amoxi/clav.[1]	>16	<1	(0.0-1.8)	-[3]		-[3]		1	(0.2-2.8)	-[3]	
Ampicillin	>8	3	(1.6-6.0)	3	(1.6-5.9)	3	(1.3-6.0)	4	(2.3-7.2)	0	(0.0-1.3)
Apramycin	>32	0	(0.0-1.2)[2]	0	(0.0-1.2)	0	(0.0-1.4)	0	(0.0-1.2)	0	(0.0-1.3)
Ceftiofur	>2	0	(0.0-1.2)	0	(0.0-1.2)	0	(0.0-1.4)	0	(0.0-1.2)	0	(0.0-1.3)
Chloramphenicol	>16	<1	(0.1-2.4)	2	(0.5-3.8)	<1	(0.0-2.1)	0	(0.0-1.2)	0	(0.0-1.3)
Enrofloxacin	>0.25	<1	(0.1-2.4)	<1	(0.0-1.8)	0	(0.0-1.4)	3	(1.6-5.9)	<1	(0.0-1.9)
Florfenicol	>16	0	(0.0-1.2)	0	(0.0-1.2)	0	(0.0-1.4)	0	(0.0-1.2)	0	(0.0-1.3)
Gentamicin	>8	0	(0.0-1.2)	0	(0.0-1.2)	<1	(0.0-2.1)	<1	(0.0-1.8)	0	(0.0-1.3)
Nalidixic acid	>16	1	(0.2-2.9)	<1	(0.0-1.8)	0	(0.0-1.4)	5	(2.5-7.6)	<1	(0.1-2.4)
Neomycin	>8	1	(0.2-2.9)	<1	(0.0-1.8)	1	(0.2-3.3)	2	(0.7-4.2)	0	(0.0-1.3)
Streptomycin	>32	10	(6.8-13.8)	9	(6.4-13.2)	13	(9.2-17.8)	4	(1.8-6.3)	5	(2.9-8.3)
Sulphametoxazole	>256	9	(6.0-12.7)	10	(6.7-13.6)	7	(4.2-10.7)	10	(6.7-13.7)	1	(0.4-3.5)
Tetracycline	>8	12	(8.2-15.7)	8	(5.6-12.1)	7	(4.2-10.7)	6	(3.3-8.8)	1	(0.4-3.5)
Trimethoprim	>8	4	(2.3-7.2)	2	(0.9-4.6)	5	(2.4-7.9)	<1	(0.0-1.8)	0	(0.0-1.3)

[1] Concentration of amoxicillin given, tested with clavulanic acid in concentration ratio 2/1 (amoxicillin/clavulanic acid); [2] 220 isolates tested; [3] Not given due to uncertainties in the analysis years 2000 and 2001.

and 15 isolates (5%) were multiresistant, i.e. were resistant to three or more of the antimicrobials tested (Table EC II). The prevalence of multiresistant isolates has been similar in the three years studied (Table EC II).

Among the 871 isolates from years 2000, 2001 and 2003, resistance to any of the substances ampicillin, neomycin, streptomycin, sulphonamides, tetracycline or trimethoprim was associated with increased occurrence of resistance to the other substances mentioned (Table EC III). The associations between resistance to sulphonamides and tetracycline, between sulphonamides and streptomycin and between tetracyclines and streptomycin were statistically significant (P<0.001). Notably, all eight isolates resistant to chloramphenicol were resistant also to sulphonamides.

Four percent (38/871) of the isolates from years 2000, 2001 and 2003 were multiresistant (Table EC II). The most prevalent traits in these isolates were resistance to sulphonamides, streptomycin, tetracycline or ampicillin. Twenty-nine multiresistant isolates (76%) were resistant to both sulphonamides and streptomycin in combination with other traits. In 16 isolates (42%) resistance to sulphonamides and streptomycin was combined with resistance to

Table EC II. Number of *Escherichia coli* resistant to three or more antimicrobials, presented by year and resistance phenotype, pigs 2003. "R" in shaded fields indicates resistance. Data for 2000 and 2001 are from SVARM 2000 and 2001.

Year			Resistance phenotype[1]								
2003 n=303	2001 n=308	2000 n=260	Sm	Su	Tc	Am	Tm	Cm	Nm	Nal	Ef
		1	R	R	R	R	R		R		
1	1	1	R	R	R	R	R				
1		1	R	R	R	R			R		
2			R	R	R		R				
1			R	R	R				R		
3	3	1	R	R	R						
1	1	3	R	R		R	R				
	1		R	R		R		R			
	2		R	R		R					
1	1	2	R	R			R				
		1	R	R				R			
		1	R				R		R		
1			R			R				R	R
1			R		R		R				
1				R		R	R				
1	2			R		R	R	R			
	1			R		R		R			
1					R	R				R	
15 (5%)	12 (4%)	11 (4%)	Total number of multiresistant isolates								

[1] Sm: streptomycin; Su: sulphonamides; Tc: tetracycline; Am: ampicillin; Tm: trimethoprim; Cm: chloramphenicol; Nm: neomycin; Nal: nalidixic acid; Ef: enrofloxacin.

Table EC III. Association between resistance traits in *Escherichia coli* isolated from pigs years 2000, 2001 and 2003 (n=871). For each substance the first line gives the resistance rates for susceptible isolates (S) and the second line rates for resistant isolates (R).

Single substance susceptibility		n	Resistance (%)[1]												
			Am	Ap[2]	Ce	Cm	Ef	Ff	Gm	Nal	Nm	Sm	Su	Tc	Tm
Ampicillin	S	843	0	0.0	0.0	0.4	0.2	0.0	0.1	0.2	0.4	9.3	6.4	8.5	2.1
	R	28	100.0	0.0	0.0	17.9	3.6	0.0	0.0	7.1	14.3	53.6	75.0	25.0	50.0
Apramycin[2]	S	788	3.0	0	0.0	0.9	0.3	0.0	0.1	0.3	0.9	10.6	8.9	9.4	3.7
	R	0	0.0	-	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Ceftiofur	S	871	3.2	0.0	0	0.9	0.3	0.0	0.1	0.5	0.8	10.7	8.6	9.1	3.7
	R	0	0.0	0.0	-	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Chloramphenicol	S	863	2.7	0.0	0.0	0	0.3	0.0	0.1	0.5	0.8	10.5	7.8	9.2	3.4
	R	8	62.5	0.0	0.0	100.0	0.0	0.0	0.0	0.0	0.0	25.0	100.0	0.0	37.5
Enrofloxacin	S	868	3.1	0.0	0.0	0.9	0	0.0	0.1	0.1	0.8	10.6	8.6	9.1	3.7
	R	3	33.3	0.0	0.0	0.0	100.0	0.0	0.0	100.0	0.0	33.3	0.0	0.0	0.0
Florfenicol	S	871	3.2	0.0	0.0	0.9	0.3	0	0.1	0.5	0.8	10.7	8.6	9.1	3.7
	R	0	0.0	0.0	0.0	0.0	0.0	-	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Gentamicin	S	870	3.2	0.0	0.0	0.9	0.3	0.0	0	0.5	0.8	10.7	8.6	9.1	3.7
	R	1	0.0	0.0	0.0	0.0	0.0	0.0	100.0	0.0	0.0	0.0	0.0	0.0	0.0
Nalidixic acid	S	867	3.0	0.0	0.0	0.9	0.0	0.0	0.1	0	0.8	10.6	8.7	9.0	3.7
	R	4	50.0	0.0	0.0	0.0	75.0	0.0	0.0	100.0	0.0	25.0	0.0	25.0	0.0
Neomycin	S	864	2.8	0.0	0.0	0.9	0.3	0.0	0.1	0.5	0	10.1	8.1	8.6	3.4
	R	7	57.1	0.0	0.0	0.0	0.0	0.0	0.0	0.0	100.0	85.7	71.4	71.4	42.9
Streptomycin	S	778	1.7	0.0	0.0	0.8	0.3	0.0	0.1	0.4	0.1	0	3.7	6.0	1.7
	R	93	16.1	0.0	0.0	2.2	1.1	0.0	0.0	1.1	6.5	100.0	49.5	34.4	20.4
Sulphametoxazole	S	796	0.9	0.0	0.0	0.0	0.4	0.0	0.1	0.5	0.3	5.9	0	7.3	1.3
	R	75	28.0	0.0	0.0	10.7	0.0	0.0	0.0	0.0	6.7	61.3	100.0	28.0	29.3
Tetracycline	S	792	2.7	0.0	0.0	1.0	0.4	0.0	0.1	0.4	0.3	7.7	6.8	0	3.0
	R	79	8.9	0.0	0.0	0.0	0.0	0.0	0.0	1.3	6.3	40.5	26.6	100.0	10.1
Trimethoprim	S	839	1.7	0.0	0.0	0.6	0.4	0.0	0.1	0.5	0.5	8.8	6.3	8.5	0
	R	32	43.8	0.0	0.0	9.4	0.0	0.0	0.0	0.0	9.4	59.4	68.8	25.0	100.0

[1] Am: ampicillin; Ap: apramycin; Ce: ceftiofur; Cm: chloramphenicol; Ef: enrofloxacin; Ff: florfenicol Gm: gentamicin; Nal: nalidixic acid; Nm: neomycin; Sm: streptomycin; Su: sulphametoxazole; Tc: tetracycline; Tm: trimethoprim; [2] 788 isolates tested.

Table EC IV. Distribution of MICs for *Escherichia coli* from pigs year 2003 (n=303). Data for years 2000 (n=260) and 2001 (n=308) are given for comparison (SVARM 2000 and SVARM 2001).

Substance	Year	Resistance (%)	Distribution (%) of MICs[1] (mg/L)															
			≤0.03	0.06	0.12	0.25	0.5	1	2	4	8	16	32	64	128	256	512	>512
Amoxi/clav.[2]	-03	<1							13.9	61.7	22.8	1.3	0.3					
	-01	-[3]																
	-00	-[3]																
Ampicillin	-03	3						6.6	68.0	21.5	0.7		0.7	2.6				
	-01	3					0.6	6.5	39.9	49.4	0.3			3.2				
	-00	3						0.4	31.2	64.6	0.8			3.1				
Apramycin	-03	0[4]							0.5	2.3	35.0	51.4	10.9					
	-01	0								3.2	41.2	44.5	11.0					
	-00	0					0.4		0.4	3.1	32.7	53.8	9.6					
Ceftiofur	-03	0				23.8	72.3	4.0										
	-01	0				31.5	65.6	2.9										
	-00	0				30.8	65.8	3.5										
Chloramph.	-03	<1							5.3	80.2	13.2	0.7	0.7					
	-01	2							2.9	69.5	25.3	0.6	1.6					
	-00	<1							1.9	50.0	47.7		0.4					
Enrofloxacin	-03	<1	11.9	78.9	8.3	0.3	0.3	0.3										
	-01	<1	36.0	62.3	1.3			0.3										
	-00	0	25.0	71.9	3.1													
Florfenicol	-03	0								67.7	31.7	0.7						
	-01	0							1.6	61.7	35.7	1.0						
	-00	0							1.2	43.8	54.2	0.8						
Gentamicin	-03	0					2.6	50.8	37.3	9.2								
	-01	0					0.6	17.2	51.6	28.2	2.3							
	-00	<1					1.5	19.6	55.0	21.9	1.5	0.4						
Nalidixic acid	-03	1						0.3	35.3	61.1	2.0	0.3		0.3	0.3	0.3		
	-01	<1							7.5	51.3	39.3	1.6				0.3		
	-00	0							1.9	26.2	68.8	3.1						
Neomycin	-03	1							59.1	34.7	5.3	0.3	0.7					
	-01	<1						3.9	53.6	36.7	5.5		0.3					
	-00	1						4.6	56.9	34.6	2.7				0.4	0.8		
Streptomycin	-03	10								5.3	47.5	34.3	3.0	2.0	2.0	3.3	2.6	
	-01	9								6.2	49.0	31.2	4.2	2.3	1.9	2.6	2.6	
	-00	13								6.9	53.1	24.2	2.7	3.5	3.8	3.1	2.7	
Sulphametoxazole	-03	9												71.0	19.1	1.0		8.9
	-01	10												61.0	28.9	0.3		9.7
	-00	7												57.7	35.4			6.9
Tetracycline	-03	12						19.8	53.1	14.9	0.7	0.3	1.0	0.7	9.6			
	-01	8						23.4	60.7	7.5		0.3	0.6	1.9	5.5			
	-00	7					0.8	8.1	70.0	13.5	0.8	0.4	0.8		5.8			
Trimethoprim	-03	4				19.8	59.1	15.2	1.7				4.3					
	-01	2			2.3	18.2	62.7	13.3	0.3	0.3	0.6		2.3					
	-00	5			0.8	10.0	59.2	23.5	1.2	0.8		0.4	4.2					
			≤0.03	**0.06**	**0.12**	**0.25**	**0.5**	**1**	**2**	**4**	**8**	**16**	**32**	**64**	**128**	**256**	**512**	**>512**

[1] The white fields denote range of dilutions tested for each substance. MICs above the range are given as the concentration closest to the range. MICs equal to or lower than the lowest concentration tested are given as the lowest tested concentration. Bold vertical lines indicate microbiological cut-off values defining resistance; [2] Concentration of amoxicillin given, tested with clavulanic acid in concentration ratio 2/1 (amoxicillin/clavulanic acid); [3] Data not included due to uncertainties in the analysis years 2000 and 2001; [4] 220 isolates tested.

tetracycline and in 14 isolates (37%) with ampicillin resistance. Six isolates (16%) had all four resistance traits in their phenotype.

In good agreement with the therapeutic use of tetracycline, sulphonamides, trimethoprim and ampicillin in pig production, resistance to these substances are among the most common traits. Moreover, the common occurrence of associations between resistance traits, in particular between the aforementioned substances, indicates the existence of linked resistance genes. This implies that co-selection for resistance could be of importance. For example, resistance to streptomycin, which is more common than anticipated from

the limited use of this antimicrobial, could be a consequence of co-selection by use of tetracycline or sulphonamides. Likewise, resistance to chloramphenicol might be retained among *E. coli* in pigs by use of sulphonamides.

Overall, frequencies of resistance are low in an international perspective and have been stable over the three years studied (Table EC I). One exception is resistance to tetracycline, which increased from 7-8% years 2000 and 2001 to 12% year 2003. The increase, although not statistically significant, is opposed to the trend among *E. coli* from diagnostic submissions where tetracycline resistance has decreased over the last years, in good agreement with a decrease in sales of tetracyclines (see Resistance in animal pathogens).

Enterococcus

The material includes 315 isolates from pigs. *Enterococcus hirae* (39%) was the predominant species followed by *E. faecalis* (28%) and *E. faecium* (23%) (Table ENT I). Other species of enterococci isolated were *E. durans* (6%) and *E. mundtii* (<1%). About four percent of the isolates could not be typed to species level.

All enterococci

Resistance to tetracycline was the most common trait (30%) followed by resistance to erythromycin (13%). Less common (3-5%) was resistance to streptomycin, neomycin, narasin, gentamicin, chloramphenicol or bacitracin. Only occasional isolates were resistant to ampicillin and no isolate was resistant to avilamycin or vancomycin (Table ENT II). Flavomycin and virginiamycin are not included in the overall comparison as the inherent susceptibility to these substances differs between species of enterococci.

No isolate of vancomycin resistant enterococci (VRE) was obtained from the selective cultures performed on all (510) samples. Likewise, no ampicillin resistant enterococci (ARE) were isolated from selective culture of 105 samples.

Enterococcus faecalis

Most isolates of *E. faecalis* (75%) were resistant to at least one antimicrobial. Resistance to tetracycline was the most prevalent trait (63%) but resistance to erythromycin (25%), streptomycin (16%) or neomycin (12%) was also common (Table ENT III). Resistance to chloramphenicol, gentamicin, flavomycin or narasin was less frequent (1-9%) and no isolate was resistant to ampicillin, avilamycin, bacitracin or vancomycin. Forty-four isolates (51%) were resistant to more than one antimicrobial and ten isolates (11%) were multiresistant (Table ENT IV).

Among the 195 isolates from years 2000, 2001 and 2003, resistance to any of the substances tetracycline, erythromycin, streptomycin, neomycin, gentamicin, or chloramphenicol was most often associated with increased occurrence of resistance to the other substances (Table EC V). The associations between resistance to erythromycin and tetracycline ($P<0.001$), between erythromycin and streptomycin ($P<0.01$) and between tetracycline and neomycin ($P<0.05$) were statistically significant. Interestingly, all eight isolates resistant to gentamicin were also resistant to neomycin, erythromycin and tetracycline. Moreover, all eight isolates resistant to chloram-

Table ENT I. Prevalence of enterococci in samples of caecal/colon content from pigs, 2003. Species not identified as *Enterococcus faecalis, E. faecium* or *E. hirae* are given as "other species". Data for years 2000 and 2001 are given for comparison (SVARM 2000 and SVARM 2001).

Year	Number of samples cultured	Percent positive cultures	Number of isolates tested for antimicrobial susceptibility	*Enterococcus* species isolated Number of isolates and percent of total isolates in brackets.			
				E. faecalis	*E. faecium*	*E. hirae*	*Other species*
2003	510	62%	315	87 (28%)	71 (23%)	124 (39%)	33 (10%)
2001	470	59%	279	52 (19%)	106 (38%)	77 (28%)	44 (16%)
2000	460	52%	241	56 (23%)	48 (20%)	106 (44%)	36 (13%)

Table ENT II. Occurrence of resistance (%) among isolates of *Enterococcus* spp. from pigs, 2003. Data for 2000 (pig and cattle), 2001 (pig) and 2002 (chickens) are given for comparison (SVARM 2000, 2001 and 2002).

Substance	Cut-off value (mg/L)	Percent resistant 95% confidence interval inside brackets									
		Pigs						Chickens		Cattle	
		2003 n=315		2001 n=308		2000 n=241		2002 n=332		2000 n=277	
Ampicillin	>8	<1	(0.0-1.8)	<1	(0.1-2.6)	<1	(0.0-2.6)	0	(0.0-1.1)	0	(0.0-1.3)
Avilamycin	>16	0	(0.0-1.2)	0	(0.0-1.3)	0	(0.0-1.7)	<1	(0.0-1.7)	<1	(0.0-2.0)
Bacitracin[1]	>32	3	(1.5-5.8)	1	(0.2-3.1)	2	(0.5-4.7)	22	(17.9-27.2)	<1	(0.1-2.6)
Chloramphenicol	>16	3	(1.1-4.9)	-		-		-		-	
Erythromycin	>4	13	(9.8-17.6)	12	(8.0-15.8)	11	(8.1-17.3)	20	(16.3-25.5)	3	(1.0-5.1)
Gentamicin	>512	2	(0.7-4.1)	1	(0.2-3.1)	0	(0.0-1.7)	0	(0.0-1.1)	0	(0.0-1.3)
Narasin	>2	3	(1.5-5.8)	3	(1.3-5.6)	2	(0.5-4.7)	72	(66.8-76.8)	1	(0.4-3.7)
Neomycin	>1024	4	(1.8-6.2)	2	(0.6-4.1)	3	(1.0-6.0)	0	(0.0-1.1)	<1	(0.0-2.0)
Streptomycin	>1024	5	(3.2-8.5)	7	(3.9-10.0)	4	(2.3-8.4)	1	(0.3-3.1)	<1	(0.1-2.6)
Tetracycline	>8	30	(24.5-34.9)	22	(17.5-27.6)	27	(23.9-36.5)	27	(22.4-32.2)	5	(3.1-8.8)
Vancomycin	>16	0	(0.0-1.2)	0	(0.0-1.3)	0	(0.0-1.7)	<1	(0.0-1.7)	0	(0.0-1.3)

[1] MIC in U/mL.

phenicol were resistant to tetracycline and seven also to erythromycin. Notably, 17 of the 21 multiresistant isolates had both erythromycin and tetracycline resistance in their phenotype.

Enterococcus faecium

Among *E. faecium* 35% of the isolates were resistant to at least one of the antimicrobials tested. The most prevalent traits were erythromycin, tetracycline or bacitracin resistance (13-18%) (Table ENT III). Occasional isolates were resistant to narasin and no isolate was resistant to the other substances tested. Eight isolates (11%) were resistant to more than one antimicrobial and three were multiresistant (4%) (Table ENT IV).

Among the 225 isolates from years 2000, 2001 and 2003, resistance to any of the substances tetracycline, erythromycin, or bacitracin was associated with increased occurrence of resistance to the other substances (Table EC VI). Notably six of the nine multiresistant isolates had both tetracycline and erythromycin in their resistance phenotype (Table ENT IV).

Enterococcus hirae

The majority of isolates were sensitive to all antimicrobials tested but 12% were resistant to at least one substance. Tetracycline was the most prevalent resistance trait (14%) followed by erythromycin (4%) (Table ENT III). Only occasional isolates were resistant to ampicillin, narasin or neomycin and no isolate was resistant to avilamycin, bacitracin, chloramphenicol, gentamicin or vancomycin.

Comments in relation to previous years

Resistance of noticeable magnitude occurred to the same antimicrobials as in years 2000 and 2001. Tetracycline resistance was the most common trait in *E. faecalis* as well as in *E. faecium* and *E. hirae*, although the prevalence among the latter two species was considerably lower. Resistance to erythromycin was common among both *E. faecalis* and *E. faecium*. The high prevalence of resistance to these antimicrobials is not surprising as both tetracyclines and macrolides are used for flock medication of pigs through feed or water.

In *E. faecalis* the prevalences of resistance to the aminoglycosides (neomycin, streptomycin and gentamicin) or chloramphenicol are higher than anticipated, as these antimicrobials are not used at all (chloramphenicol and gentamicin) or to a limited extent (streptomycin and neomycin). Resistance to these antimicrobials in *E. faecalis* is however often associated with resistance to tetracycline, erythromycin or both (Table ENT V). This indicates the existence of linked resistance genes and thereby use of tetracycline or erythromycin would co-select for resistance to the other drugs.

Among *E. faecalis* there are no statistically significant (P>0.05) trends in resistance, but the prevalence of erythromycin resistance is lower in 2003 than in previous years whereas prevalence of neomycin or gentamicin resistance is higher. Among *E. faecium* the prevalence of resistance to bacitracin and erythromycin has increased. For erythromycin the trend is statistically significant (P<0.05). No trend in resistance to tetracycline, as the increase observed for *E. coli*, is evident among *E. faecalis* and *E. hirae* but among *E. faecium* the prevalence of this resistance trait is higher 2003 than in previous years. The increase is however not statistically significant (P>0.05). As the number of isolates tested each year is small, interpretations of trends over time must be made with caution.

In three years studied, no vancomycin-resistant *E. faecalis* or *E. faecium* (VRE) were isolated from samples from pigs neither in direct cultures nor after the selective culture performed on all samples. Moreover, only two ampicillin-resistant *E. faecalis* or *E. faecium* (ARE) have been isolated in the three years studied, one isolate of each species. In addition, no ARE were isolated on selective cultures of 105 samples year 2003. These findings show that in Sweden, enterococci in pigs are no reservoir of VRE or ARE.

Table ENT III. Occurrence of resistance (%) among *Enterococcus faecalis*, *E. faecium* and *E. hirae* from pigs, presented by bacterial species and source of isolates, 2003. Data for 2000 (pigs and cattle) and 2001 (pigs) and 2002 (chickens) are given for comparison (SVARM 2000, 2001 and 2002). Cut-off values defining resistance are given in Table ENT II.

	E. faecalis					*E. faecium*					*E. hirae*				
	Pigs			Chickens	Cattle	Pigs			Chickens	Cattle	Pigs			Chickens	Cattle
Substance	2003 n=87	2001 n=52	2000 n=56	2002 n=57	2000 n=22	2003 n=71	2001 n=106	2000 n=48	2002 n=189	2000 n=71	2003 n=124	2001 n=77	2000 n=106	2002 n=45	2000 n=127
Ampicillin	0	2	0	0	0	0	1	0	0	0	<1	0	0	0	0
Avilamycin	0	0	0	2	0	0	0	0	0	1	0	0	<1	0	0
Bacitracin	0	0	0	35	0	13	3	4	24	1	0	0	0	2	0
Chloramph.	9	-	-	-	-	0	-	-	-	-	0	-	-	-	-
Erythromycin	25	27	36	26	5	18	11	2	11	6	4	0	4	40	0
Flavomycin	3	2	2	2	14	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR
Gentamicin	7	4	0	0	0	0	0	0	0	0	0	1	0	0	0
Narasin	1	4	2	39	0	3	4	2	78	1	2	3	2	87	2
Neomycin	12	6	7	0	0	0	2	2	0	0	<1	0	<1	0	0
Streptomycin	16	25	13	7	5	0	4	2	0	0	2	0	<1	0	0
Tetracycline	63	63	68	58	14	15	7	10	25	6	14	10	15	7	<1
Vancomycin	0	0	0	0	0	0	0	0	<1	0	0	0	0	0	0
Virginiamycin	NR[1]	NR	NR	NR	NR	2	3	2	11	1	0	0	0	7	0

[1] Not relevant as susceptibility in some species of *Enterococcus* is inherently low.

Table ENT IV. Number of isolates of *Enterococcus faecalis* (left panel) and *Enterococcus faecium* (right panel) resistant to three or more antimicrobials, presented by year and resistance phenotype, pigs 2003. "R" in shaded fields indicates resistance. Data for 2000 and 2001 from SVARM 2000 and 2001.

E. faecalis

Year			Resistance pattern[1]								
2003 n=87	2001 n=52	2000 n=56	Tc	Em	Sm	Na	Nm	Gm	Am	Fl	Cm
1			R	R	R	R	R	R			
	1		R	R	R	R					
	1	2	R	R	R		R				
1	1		R	R	R						
1			R	R	R		R				R
	1		R	R	R		R	R			
3			R	R	R		R	R			R
2			R	R			R	R			R
		1	R	R		R					
	1		R	R			R	R			
1			R	R							R
		1	R		R		R				
	1		R			R			R	R	
1		1		R	R		R				
10 (11%)	6 (11%)	5 (9%)	Total number of multiresistant isolates								

E. faecium

Year			Resistance pattern[1]						
2003 n=71	2001 n=106	2000 n=48	Tc	Em	Sm	Nm	Vi	Na	Ba
	1		R	R	R	R			
	1		R	R	R				
	1		R	R				R	R
2			R	R					R
1			R	R			R		
	1	1		R	R	R			
	1						R	R	R
3 (4%)	5 (5%)	1 (2%)	Total number of multiresistant isolates						

[1] Tc: tetracycline; Em: erythromycin; Sm: streptomycin; Na: narasin; Nm: neomycin; Gm: gentamicin; Am: ampicillin; Fl: flavomycin; Cm: chloramphenicol; Vi: virginiamycin; Ba: bacitracin.

Table ENT V. Association between resistance traits in *Enterococcus faecalis* isolated from pigs years 2000, 2001 and 2003 (n=195). For each substance the first line gives the resistance rates for susceptible isolates (S) and the second line rates for resistant isolates (R).

Single substance susceptibility		n	Resistance[1] (%)										
			Am	Av	Ba	Cm	Em	Fl	Gm	Na	Nm	Sm	Tc	Va
Ampicillin	S	194	0.0	0.0	0.0	4.1	28.9	2.1	4.1	1.5	8.8	17.5	64.4	0.0
	R	1	100.0	0.0	0.0	0.0	0.0	100.0	0.0	100.0	0.0	0.0	100.0	0.0
Avilamycin	S	195	0.5	0.0	0.0	4.1	28.7	2.6	4.1	2.1	8.7	17.4	64.6	0.0
	R	0	0.0	-	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Bacitracin	S	195	0.5	0.0	0.0	4.1	28.7	2.6	4.1	2.1	8.7	17.4	64.6	0.0
	R	0	0.0	0.0	-	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Chloramphenicol	S	79	0.0	0.0	0.0	0.0	19.0	3.8	1.3	1.3	5.1	12.7	59.5	0.0
	R	8	0.0	0.0	0.0	100.0	87.5	0.0	62.5	0.0	75.0	50.0	100.0	0.0
Erythromycin	S	139	0.7	0.0	0.0	0.7	0.0	3.6	0.0	0.7	2.2	12.9	54.7	0.0
	R	56	0.0	0.0	0.0	12.5	100.0	0.0	14.3	5.4	25.0	28.6	89.3	0.0
Flavomycin	S	190	0.0	0.0	0.0	4.2	29.5	0.0	4.2	1.6	8.9	17.9	65.8	0.0
	R	5	20.0	0.0	0.0	0.0	0.0	100.0	0.0	20.0	0.0	0.0	20.0	0.0
Gentamicin	S	187	0.5	0.0	0.0	1.6	25.7	2.7	0.0	1.6	4.8	15.5	63.1	0.0
	R	8	0.0	0.0	0.0	62.5	100.0	0.0	100.0	12.5	100.0	62.5	100.0	0.0
Narasin	S	191	0.0	0.0	0.0	4.2	27.7	2.1	3.7	0.0	8.4	16.8	63.9	0.0
	R	4	25.0	0.0	0.0	0.0	75.0	25.0	25.0	100.0	25.0	50.0	100.0	0.0
Neomycin	S	178	0.6	0.0	0.0	1.1	23.6	2.8	0.0	1.7	0.0	12.4	62.4	0.0
	R	17	0.0	0.0	0.0	35.3	82.4	0.0	47.1	5.9	100.0	70.6	88.2	0.0
Steptomycin	S	161	0.6	0.0	0.0	2.5	24.8	3.1	1.9	1.2	3.1	0.0	66.5	0.0
	R	34	0.0	0.0	0.0	11.8	47.1	0.0	14.7	5.9	35.3	100.0	55.9	0.0
Tetracycline	S	69	0.0	0.0	0.0	0.0	8.7	5.8	0.0	0.0	2.9	21.7	0.0	0.0
	R	126	0.8	0.0	0.0	6.3	39.7	0.8	6.3	3.2	11.9	15.1	100.0	0.0
Vancomycin	S	195	0.5	0.0	0.0	0.0	28.7	2.6	4.1	2.1	8.7	17.4	64.6	0.0
	R	0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	-

[1] Am: ampicillin; Av: avilamycin; Ba: bacitracin; Cm: chloramphenicol; Em: erythromycin; Fl: flavomycin; Gm: gentamicin; Na: narasin; Nm: neomycin; Sm: streptomycin; Tc: tetracycline; Va: vancomycin.

Table ENT VI. Association between resistance traits in *Enterococcus faecium* isolated from pigs years 2000, 2001 and 2003 (n=225). For each substance the first line gives the resistance rates for susceptible isolates (S) and the second line rates for resistant isolates (R).

Single substance susceptibility		n	Resistance[1] (%)											
			Am	Av	Ba	Cm	Em	Gm	Na	Nm	Sm	Tc	Va	Vi
Ampicillin	S	224	0.0	0.0	6.3	0.0	11.6	0.0	3.1	1.3	2.2	10.3	0.0	2.2
	R	1	100.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Avilamycin	S	225	0.4	0.0	6.2	0.0	11.6	0.0	3.1	1.3	2.2	10.2	0.0	2.2
	R	0	0.0	-	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Bacitracin	S	211	0.5	0.0	0.0	0.0	10.0	0.0	1.4	1.4	2.4	8.5	0.0	1.9
	R	14	0.0	0.0	100.0	0.0	35.7	0.0	28.6	0.0	0.0	35.7	0.0	7.1
Chloramphenicol	S	71	0.0	0.0	12.7	0.0	18.3	0.0	2.8	0.0	0.0	15.5	0.0	0.0
	R	0	0.0	0.0	0.0	-	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Erythromycin	S	199	0.5	0.0	4.5	0.0	0.0	0.0	3.0	0.0	0.5	8.5	0.0	2.0
	R	26	0.0	0.0	19.2	0.0	100.0	0.0	3.8	11.5	15.4	23.1	0.0	3.8
Gentamicin	S	225	0.4	0.0	6.2	0.0	11.6	0.0	3.1	1.3	2.2	10.2	0.0	2.2
	R	0	0.0	0.0	0.0	0.0	0.0	-	0.0	0.0	0.0	0.0	0.0	0.0
Narasin	S	218	0.5	0.0	4.6	0.0	11.5	0.0	0.0	1.4	2.3	10.1	0.0	1.8
	R	7	0.0	0.0	57.1	0.0	14.3	0.0	100.0	0.0	0.0	14.3	0.0	14.3
Neomycin	S	222	0.5	0.0	6.3	0.0	10.4	0.0	3.2	0.0	0.9	9.9	0.0	2.3
	R	3	0.0	0.0	0.0	0.0	100.0	0.0	0.0	100.0	100.0	33.3	0.0	0.0
Steptomycin	S	220	0.5	0.0	6.4	0.0	10.0	0.0	3.2	0.0	0.0	9.5	0.0	1.8
	R	5	0.0	0.0	0.0	0.0	80.0	0.0	0.0	60.0	100.0	40.0	0.0	20.0
Tetracycline	S	202	0.5	0.0	4.5	0.0	9.9	0.0	3.0	1.0	1.5	0.0	0.0	2.0
	R	23	0.0	0.0	21.7	0.0	26.1	0.0	4.3	4.3	8.7	100.0	0.0	4.3
Vancomycin	S	225	0.4	0.0	6.2	0.0	11.6	0.0	3.1	1.3	2.2	10.2	0.0	2.2
	R	0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	-	0.0
Virginiamycin	S	220	0.5	0.0	5.9	0.0	11.4	0.0	2.7	1.4	1.8	10.0	0.0	0.0
	R	5	0.0	0.0	20.0	0.0	20.0	0.0	20.0	0.0	20.0	20.0	0.0	100.0

[1] Am: ampicillin; Av: avilamycin; Ba: bacitracin; Cm: chloramphenicol; Em: erythromycin; Gm: gentamicin; Na: narasin; Nm: neomycin; Sm: streptomycin; Tc: tetracycline; Va: vancomycin; Vi: virginiamycin.

Table ENT VII. Distribution of MICs for *Enterococcus faecalis* from pigs year 2003 (n=87). Data for years 2000 (n=56) and 2001 (n=52) are given for comparison (SVARM 2000 and SVARM 2001).

Substance	Year	Resistance (%)	Distribution (%) of MICs[1] (mg/L)														
			≤0.12	0.25	0.5	1	2	4	8	16	32	64	128	256	512	1024	>1024
Ampicillin	-03	0		3.4	13.8	77.0	5.7										
	-01	2			5.8	59.6	30.8		1.9	1.9							
	-00	0				37.5	62.5										
Avilamycin	-03	0				13.8	63.2	12.6	10.3								
	-01	0				3.8	53.8	42.3									
	-00	0					48.2	51.8									
Bacitracin[2]	-03	0					2.3	4.6	50.6	39.1	3.4						
	-01	0					1.9	3.8	75.0	19.2							
	-00	0			1.8	1.8		1.8	17.9	64.3	12.5						
Chloramph.	-03	9					1.1	18.4	62.1	9.2	9.2						
	-01	-															
	-00	-															
Erytromycin	-03	25			9.2	27.6	26.4	11.5					25.3				
	-01	27		1.9	11.5	28.8	21.2	9.6				26.9					
	-00	36		1.8	7.1	3.6	33.9	17.9		1.8		33.9					
Flavomycin	-03	3					72.4	20.7	3.4					3.4			
	-01	2					5.8	61.5	30.8					1.9			
	-00	2					23.2	64.3	8.9		1.8			1.8			
Gentamicin	-03	7						3.4	11.5	40.2	31.0				6.9	6.9	
	-01	4							7.7	48.1	38.5				1.9	3.8	
	-00	0					1.8	3.6	8.9	69.6	16.1						
Narasin	-03	1	4.6	24.1	59.8	10.3					1.1						
	-01	4	1.9	11.5	73.1	9.6		1.9	1.9								
	-00	2	3.6	10.7	67.9	16.1				1.8							
Neomycin	-03	11							2.3	3.4	6.9	10.3	36.8			28.7	11.5
	-01	6								1.9	3.8	15.4	42.3			30.8	5.8
	-00	7								1.8	3.6	7.1	41.1			39.3	7.1
Streptomycin	-03	16									3.4	16.1	56.3			8.0	16.1
	-01	25									5.8	21.2	42.3			5.8	25.0
	-00	13									3.6	26.8	53.6			3.6	12.5
Tetracycline	-03	63			12.6	21.8	2.3			14.9	25.3	21.8	1.1				
	-01	63			3.8	5.8	23.1	3.8		5.8	23.1	34.6					
	-00	68		1.8	1.8	14.3	14.3			3.6	23.2	41.1					
Vancomycin	-03	0				9.2	74.7	14.9	1.1								
	-01	0				3.8	71.2	25.0									
	-00	0				5.4	80.4	14.3									
Virginiamycin	-03	NR[3]			2.3		5.7	2.3	18.4	69.0	2.3						
	-01	NR					1.9		3.8	67.3	26.9						
	-00	NR					1.8	3.6	7.1	80.4	7.1						
			≤0.12	**0.25**	**0.5**	**1**	**2**	**4**	**8**	**16**	**32**	**64**	**128**	**256**	**512**	**1024**	**>1024**

[1] The white fields denote range of dilutions tested for each substance. MICs above the range are given as the concentration closest to the range. MICs equal to or lower than the lowest concentration tested are given as the lowest tested concentration. Bold vertical lines indicate cut-off values defining resistance; [2] MIC in U/mL, see Appendix 3 for details; [3] Not relevant as susceptibility in *E. faecalis* is inherently low.

Table ENT VIII. Distribution of MICs for *Enterococcus faecium* from pigs year 2003 (n=71). Data for years 2000 (n=48) and 2001 (n=106) are given for comparison (SVARM 2000 and SVARM 2001).

Substance	Year	Resistance (%)	Distribution (%) of MICs[1] (mg/L)														
			≤0.12	0.25	0.5	1	2	4	8	16	32	64	128	256	512	1024	>1024
Ampicillin	-03	0		12.7	9.9	32.4	36.6	8.5									
	-01	<1		17.0	17.0	32.1	28.3	3.8	0.9	0.9							
	-00	0		6.3	10.4	18.8	58.3	6.3									
Avilamycin	-03	0			1.4	4.2	36.6	56.3	1.4								
	-01	0			0.9	7.5	18.9	59.4	12.3	0.9							
	-00	0				2.1	16.7	39.6	39.6	2.1							
Bacitracin[2]	-03	13				2.8		4.2	7.0	29.6	43.7	5.6	7.0				
	-01	3			10.4	11.3	10.4	2.8	12.3	34.9	15.1	2.8					
	-00	4				6.3	2.1	4.2	12.5	12.5	58.3	4.2					
Chloramph.	-03	0						32.4	64.8	2.8							
	-01	-															
	-00	-															
Erytromycin	-03	18			26.8	5.6	16.9	32.4	9.9	7.0			1.4				
	-01	11		24.5	16.0	5.7	15.1	27.4	7.5	0.9		2.8					
	-00	2		2.1	14.6	6.3	25.0	50.0				2.1					
Flavomycin	-03	NR[3]						1.4					1.4	97.2			
	-01	NR						1.9				1.9	4.7	91.5			
	-00	NR						2.1				2.1		95.8			
Gentamicin	-03	0				1.4	4.2	38.0	38.0	14.1	2.8				1.4		
	-01	0					6.6	12.3	51.9	25.5	3.8						
	-00	0					4.2	39.6	39.6	14.6	2.1						
Narasin	-03	3		1.4	40.8	47.9	7.0	2.8									
	-01	4	2.8	12.3	23.6	53.8	3.8	3.8									
	-00	2	2.1	2.1	37.5	54.2	2.1		2.1								
Neomycin	-03	0						8.5	38.0	33.8	12.7	4.2	1.4			1.4	
	-01	2						4.7	25.5	34.9	23.6	6.6	2.8				1.9
	-00	2					2.1	2.1	37.5	35.4	10.4	8.3				2.1	2.1
Streptomycin	-03	0									32.4	62.0	4.2			1.4	
	-01	4					2.8		0.9	10.4	40.6	38.7	1.9			0.9	3.8
	-00	2								14.6	62.5	18.8	2.1				2.1
Tetracycline	-03	15			56.3	25.4	1.4	1.4			7.0	5.6	2.8				
	-01	7		6.6	2.8	63.2	18.9	1.9		0.9	2.8	2.8					
	-00	10			4.2	47.9	35.4	2.1		2.1		8.3					
Vancomycin	-03	0				81.7	15.5	2.8									
	-01	0				80.2	16.0	3.8									
	-00	0				77.1	22.9										
Virginiamycin	-03	1			29.6	18.3	32.4	16.9	1.4		1.4						
	-01	3			17.0	22.6	27.4	21.7	8.5	2.8							
	-00	2			20.8	16.7	25.0	12.5	22.9	2.1							
			≤0.12	**0.25**	**0.5**	**1**	**2**	**4**	**8**	**16**	**32**	**64**	**128**	**256**	**512**	**1024**	**>1024**

[1] The white fields denote range of dilutions tested for each substance. MICs above the range are given as the concentration closest to the range. MICs equal to or lower than the lowest concentration tested are given as the lowest tested concentration. Bold vertical lines indicate microbiological cut-off values defining resistance; [2] MIC in U/mL, see Appendix 3 for details; [3] Not relevant as susceptibility in *E. faecium* is inherently low.

Table ENT IX. Distribution of MICs for *Enterococcus hirae* from pigs year 2003 (n=124). Data for years 2000 (n=106) and 2001 (n=77) are given for comparison (SVARM 2000 and SVARM 2001).

Substance	Year	Resistance (%)	Distribution (%) of MICs[1] (mg/L)														
			≤0.12	0.25	0.5	1	2	4	8	16	32	64	128	256	512	1024	>1024
Ampicillin	-03	<1		44.4	24.2	16.1	13.7	0.8		0.8							
	-01	0		46.8	23.4	18.2	11.7										
	-00	0		46.2	15.1	17.9	17.9	2.8									
Avilamycin	-03	0			0.8	21.8	32.3	33.1	10.5	1.6							
	-01	0			3.9	18.2	24.7	49.4	3.9								
	-00	<1			1.9	11.3	31.1	34.0	20.8	0.9							
Bacitracin[2]	-03	0				23.4	60.5	11.3	0.8	3.2	0.8						
	-01	0			7.8	27.3	54.5	2.6	2.6	5.2							
	-00	0			1.9	33.0	45.3	16.0	0.9	1.9	0.9						
Chloramph.	-03	0					1.6	71.8	26.6								
	-01	-															
	-00	-															
Erytromycin	-03	4			95.2	0.8			2.4				1.6				
	-01	0		6.5	92.2	1.3											
	-00	4		32.1	61.3		2.8					3.8					
Flavomycin	-03	NR[3]										0.8	0.8	98.4			
	-01	NR						1.3		1.3		1.3		96.1			
	-00	NR								0.9			0.9	98.1			
Gentamicin	-03	0			0.8		0.8	17.7	43.5	29.8	6.5				0.8		
	-01	1						3.9	54.5	33.8	6.5					1.3	
	-00	0						7.5	54.7	35.8	1.9						
Narasin	-03	2	4.0	22.6	30.6	34.7	5.6	2.4									
	-01	3	14.3	18.2	31.2	33.8		2.6									
	-00	2	7.5	26.4	20.8	40.6	2.8	1.9									
Neomycin	-03	<1						1.6	11.3	34.7	34.7	12.9	4.0				0.8
	-01	0						1.3	2.6	32.5	33.8	24.7	5.2				
	-00	<1							4.7	33.0	28.3	31.1	1.9				0.9
Streptomycin	-03	2									6.5	71.8	20.2				1.6
	-01	0								1.3	11.7	68.8	18.2				
	-00	<1									25.5	66.0	6.6			0.9	0.9
Tetracycline	-03	14			55.6	30.6					4.8	6.5	2.4				
	-01	10			19.5	57.1	11.7	1.3			2.6	7.8					
	-00	15			12.3	39.6	32.1	0.9			0.9	14.2					
Vancomycin	-03	0				87.9	12.1										
	-01	0				76.6	22.1	1.3									
	-00	0				86.8	13.2										
Virginiamycin	-03	0			46.0	8.9	36.3	8.9									
	-01	0			49.4	16.9	24.7	7.8	1.3								
	-00	0			38.7	12.3	30.2	6.6	12.3								
			≤0.12	**0.25**	**0,5**	**1**	**2**	**4**	**8**	**16**	**32**	**64**	**128**	**256**	**512**	**1024**	**>1024**

[1] The white fields denote range of dilutions tested for each substance. MICs above the range are given as the concentration closest to the range. MICs equal to or lower than the lowest concentration tested are given as the lowest tested concentration. Bold vertical lines indicate microbiological cut-off values defining resistance; [2] MIC in U/mL, see Appendix 3 for details; [3] Not relevant as susceptibility in *E. hirae* is inherently low.

Resistance in animal pathogens

DATA ARE, if not otherwise stated, from routine bacteriological examinations of diagnostic submissions of clinical or post-mortem samples performed at SVA. Standard methods were used for isolation and identification, and isolates were tested for susceptibility by microdilution in broth except for *Brachyspira* spp. for which a modified broth method was used. Different types of panels (VetMIC™) were used depending on bacterial species or animal species. For further details, see Appendix 3.

Note that the microbiological cut-off values used to define resistance (breakpoints) were different in the reports from years 2000 and 2001. For reasons of comparability, data from previous years have been re-interpreted using the current cut-off values. A summary of currently used cut-off values is shown in Appendix 3.

Pig

Isolates included

Isolates of *Escherichia coli* for the years 1992-2003 are from diagnostic submissions of samples from the gastro-instestinal tract (intestinal content, faecal samples or mestenteric lymph nodes), while data from 1989-91 include all *E. coli* isolated from pigs, irrespective of type of material cultured. Isolates of *Brachyspira hyodysenteriae* and *Brachyspira pilosicoli* are from diagnostic submissions of faecal samples.

The investigated samples were from all parts of Sweden. No information on the indications for sampling was available, but the vast majority of *E. coli* and *Brachyspira* spp. are likely to derive from herds with diarrhoeal problems. For *Brachyspira* spp., efforts were made to exclude repeat isolates, but not for *E. coli*. Data are probably biased towards problem herds, where antimicrobials have been used previously and may not be representative for all cases of diarrhoea. Any assessment of trends is based on the assumption that this bias is inherent throughout the observation period.

Escherichia coli

Resistance to streptomycin, tetracycline, trimethoprim-sulphonamide or ampicillin was common, as in previous years (Table Pig I). An apparent decrease in the prevalence of resistance to tetracycline since year 2001 among the tested *E. coli* can be noted (P=0.0005, Chi-square for trend). Feed or water medicated with tetracyclines is used for group treatment of different conditions in pigs. The sales of tetracyclines formulated for in-feed or in-water medication has decreased by more than 90% since the beginning of the 80s. In the last years, doxycycline has been introduced on the Swedish market. As the dose of those products is about ¼ of that of chlortetracyclines, the current figures on total amount of the tetracycline class are not directly comparable with earlier figures. The sales figures for 2003 were therefore corrected for the lower dose of doxycycline. Since 1998 (when no doxycycline was used), the dose corrected sales of tetracyclines has decreased by 60%. Most of the sales of this type of products are for treatment of pigs, and consequently it is possible that the declining trend in resistance is associated with a decrease in tetracycline exposure. In contrast, a numeric, but not statistically significant, increase in prevalence of resistance among *E. coli* from healthy pigs is noted (see Resistance in indicator bacteria). The age of the sampled animals differ between the materials, and the geographical origin of the samples has not been matched. Thus, it is possible that the somewhat contradictory results are due to differences in the study populations. Further, the data on sales are on national level and the trends over time may differ between regions.

Trimethoprim-sulphonamides were introduced for use in pigs in 1974 and were initially widely used for treatment of diarrhoea in piglets (amongst other indications). In 1974-75, the MICs of trimethoprim were ≤1 mg/L for 93 isolates from piglet diarrhoea (Franklin, 1976). By 1981-82, the frequency of resistance to trimethoprim-sulphonamides among 200 isolates was 10% (breakpoint for resistance >8 mg/L; Franklin, 1984). The figures presented in Table Pig I are higher, but no significant trend can be demonstrated when data for individual years (1989-2003) are analysed.

Among isolates from the 70s and early 80s, resistance to ampicillin was 6 and 7%, respectively (Franklin, 1976; Franklin, 1984). The figures presented in Table Pig I are higher, and analysis of data from individual years from 1989-2003 indicates an increasing trend in proportion of resistance to ampicillin (P<0.00001, Chi-square for trend). It is uncertain whether this increase is related to an increased use of aminopenicillins for pigs. During 2001-2003, 86% of the isolates that were resistant to ampicillin were also resistant to at least one other antimicrobial, and 69% to three or more antimicrobials (multiresistance). Ampicillin resistance was associated with resistance to streptomycin (67%), tetracycline (63%) or trimethoprim-sulphonamides (51%) (P<0.001, Chi-square in all cases). It appears that the genes encoding ampicillin resistance are frequently carried together with other resistance genes, and co-selection by other antimicrobials is thereby likely to contribute to the maintenance and spread of this resistance trait.

Multiresistance was common (15%) among all isolates from years 2001-2003. Resistance to streptomycin was included in the pattern of most of the multiresistant isolates (91%). The association between streptomycin resistance and multiresistance was statistically significant (P<0.000001). Simultaneous resistance to streptomycin, ampicillin, tetracycline and trimethoprim-sulphonamides was observed in 31% of the multiresistant isolates (5% of all isolates).

Table Pig I. Occurrence of resistance among *Escherichia coli* from pigs during different years and distribution of MICs for the isolates from 2003. Isolates are from diagnostic submissions of faecal samples or samples taken post mortem from the gastro-intestinal tract..

	Years,% resistant isolates						Distribution (%) of MICs[1] (mg/L)									
Substance	1989-94 n=682	1995-97 n=1252	1998-00 n=1075	2001 n=330	2002 n=340	2003 n=340	≤0.12	0.25	0.5	1	2	4	8	16	32	>32
Ampicillin	9	9	11	16	19	14				14.4	63.2	8.5		13.8		
Ceftiofur	-	-	-	0	0	0		44.7	52.1	3.2						
Enrofloxacin	5	5	6	5	7	6	91.8	2.1	2.6	0.9	2.6					
Florfenicol	-	-	-	0	1	0					5.3	54.7	37.6	2.4		
Gentamicin	1	0	1	0	1	2					78.2	17.4	2.9	0.6	0.9	
Neomycin	6	6	5	5	4	6						85.6	8.2	0.3		5.9
Streptomycin	44	32	30	30	33	26						13.2	37.1	17.6	5.6	26.5
Tetracycline	32	31	33	35	28	23				37.6	30.3	8.2	0.6	23.2		
Trim-Sulph.[2]	16	13	14	16	21	19			78.2	1.8		0.6	19.4			

[1] The white fields denote range of dilutions tested for each substance. MICs above the range are given as the concentration closest to the range. MICs equal to or lower than the lowest concentration tested are given as the lowest tested concentration. Bold vertical lines indicate cut-off values defining resistance; [2] Concentration of trimethoprim given, tested in concentration ratio 1/20 (trimethoprim/sulphametoxazole).

Table Pig II. Occurrence of resistance and distribution of MICs for *Brachyspira hyodysenteriae* from pigs years 2001 (n=75), 2002 (n=109) and 2003 (n=100). Isolates are from diagnostic submissions of faecal samples.

		Resis-tance	Distribution (%) of MICs[1] (mg/L)														
Substance	Year	(%)	≤0.016	0.031	0.063	0.125	0.25	0.5	1	2	4	8	16	32	64	128	>128
Tiamulin	-01	0	2.7	13.3	44.0	37.3	1.3	1.3									
	-02	0		17.4	21.1	38.5	10.1	8.3	4.6								
	-03	0			9.0	54.0	25.0	10.0	2.0								
Tylosin	-01	83								4.0	8.0	5.3					82.7
	-02	73								1.8	18.3	7.3		0.9			71.6
	-03	89									3.0	5.0	3.0				89.0

[1] The white fields denote range of dilutions tested for each substance. MICs above the range are given as the concentration closest to the range. MICs equal to or lower than the lowest concentration tested are given as the lowest tested concentration. Bold vertical lines indicate cut-off values defining resistance.

Table Pig III. Occurrence of resistance and distribution of MICs for *Brachyspira pilosicoli* from pigs year 2002-2003 (tiamulin n=93, tylosin n=86). Isolates are from diagnostic submissions of faecal samples.

	Resistance	Distribution (%) of MICs[1] (mg/L)														
Substance	(%)	≤0.016	0.031	0.063	0.125	0.25	0.5	1	2	4	8	16	32	64	128	>128
Tiamulin	14		11.8	21.5	26.9	7.5	8.6	5.4	4.3	3.2	1.1	2.2	3.2	4.3		
Tylosin	50								2.3	18.6	24.4	4.7	1.2	1.2	2.3	45.3

[1] The white fields denote range of dilutions tested for each substance. MICs above the range are given as the concentration closest to the range. MICs equal to or lower than the lowest concentration tested are given as the lowest tested concentration. Bold vertical lines indicate cut-off values defining resistance.

Resistance to these antimicrobials was also demonstrated in *E. coli* isolated from healthy pigs at slaughter (see Resistance in indicator bacteria). The overall frequency of resistance was, however, considerably higher among the isolates from diagnostic submissions. This is expected, and is probably explained by a combination of different factors. Firstly, the material from diagnostic submissions is mostly composed of isolates from herds with diarrhoeal problems where there is a high likelihood of antimicrobial use, whereas the indicator bacteria are from randomly selected herds. Secondly, strains associated with disease are likely to carry virulence determinants, and to spread both within and between herds. Last, the material from diagnostic submissions is mostly from pigs under four months of age (mostly piglets), compared with the material collected at slaughter when the pigs are approximately six months.

Brachyspira hyodysenteriae

Resistance to tiamulin, defined by microbiological cut-off values, has not been observed in Sweden. However, a comparison of the distributions of MIC for years 2001, 2002 and 2003 indicates a progressive decrease in susceptibility (Table Pig II). Similar patterns have been observed in other countries, and have there preceded emergence of truly resistant strains (Karlsson *et al.*, 2002; Cizek *et al.*, 2002). This development is therefore of great concern, since no effective alternatives are licensed for treatment of swine dysentery. In the current situation, it is imperative that all herds where treatment failure is suspected are investigated thoroughly. If tiamulin resistant *B. hyodysenteriae* are demonstrated, efforts should be made to minimise the risk of spread of the infection to other herds.

As in previous years, the percentage of resistance to tylosin

among *B. hyodysenteriae* was high (89%), defined by microbiological cut-off values (Table Pig II). Resistance appears to have increased over the last decade, as in 1988-90 only 20% of the isolates were classified as resistant when tested with an agar dilution technique (Gunnarsson *et al.*, 1991).

Brachyspira pilosicoli

In the fall of 2001, failure of treatment with tiamulin in a Swedish pig herd with spirochaetal diarrhoea associated with resistance to this antimicrobial in *B. pilosicoli* was reported (Karlsson *et al.*, 2002). As no previous information was available on resistance to antimicrobials in this species, a special project was initiated in 2003. The presented data are preliminary findings from that study. The frequency of resistance to tiamulin, defined by microbiological cut-off values, was 14% (Table Pig III). For tylosin, results for 7 isolates were excluded due to uncertainties in the reading of MICs. Among the remaining isolates, the frequency of resistance was 50%. The majority of the isolates resistant to tiamulin (8/13) were also resistant to tylosin. Although such isolates may be susceptible to other antimicrobials, only tiamulin and tylosin are licensed for this indication in pigs in Sweden. The findings stress the need for susceptibility testing of *B. pilosicoli* isolated from pigs in herds where tiamulin is to be used.

Tiamulin resistance in Swedish *Brachyspira pilosicoli* isolates

TREATMENT FAILURE of porcine intestinal spirochetosis (PIS) with tiamulin in a Swedish pig herd was reported in 2002 (Karlsson *et al.*, 2002). The etiologic agent of PIS is *Brachyspira pilosicoli*, an anaerobic spirochete (Trott *et al.*, 1996] and the disease is characterized by nonfatal diarrhea in growing pigs causing reduction in growth rate. Isolates of *B. pilosicoli* from the herd were susceptibility tested and the tiamulin MICs varied between 32-64 mg/L.

Only sparse information is available regarding antimicrobial susceptibility in porcine *B. pilosicoli*. In 2003 a study was performed to investigate the Swedish situation through susceptibility testing of field isolates of *B. pilosicoli*. Isolates with a tiamulin MIC >2 mg/L were retested with a high range panel.

Using the clinical breakpoint for *B. hyodysenteriae* proposed by Rønne & Szancer, 1990 (>4 mg/L) 11% of the 93 *B. pilosicoli* isolates in the study were resistant to tiamulin. In the SVARM reports a lower microbiological cut-off value of >2 mg/L is used. With this cut-off, 14% of the isolates would be designated as resistant. The tendency towards a trimodal MIC distribution (fig Pig I) makes it difficult to set microbiological cut-off values. The mechanisms of tiamulin resistance in *B. pilosicoli* are not known. In vitro, tiamulin resistance develops in a stepwise manner in *B. pilosicoli* (Karlsson *et al.*, 2001) and the situation in vivo could be the same, which would explain the MIC distribution. Probably more than one change is needed in the bacteria before an MIC of 32-64 mg/L is reached and perhaps several different changes can cause the slight increase of MIC to around 0.5 mg/L. Studies to define a clinical breakpoint are needed. However, for monitoring purposes a lower cut-off value is preferred to detect the low level resistance (or decreased susceptibility), as this might be the first step towards clinical resistance.

Due to withdrawal of drugs authorized for use in pigs the antibiotic arsenal against PIS is diminishing. In many countries tiamulin is the drug of choice for treatment of the disease. Tiamulin resistance in *B. pilosicoli* is a threat to the pig industry, especially as there are no other real control alternatives.

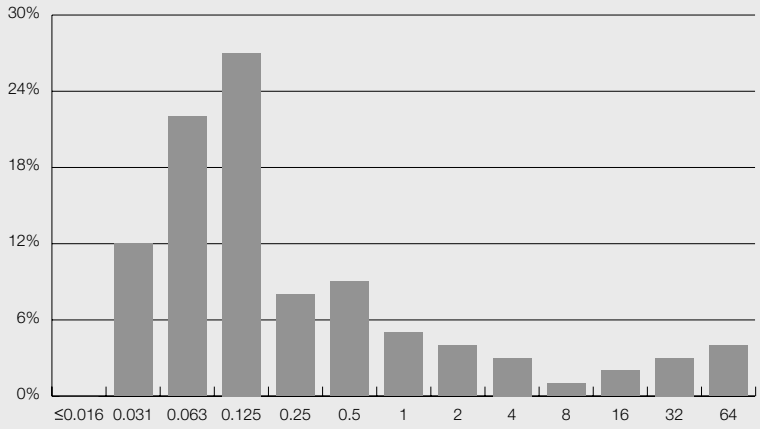

Figure Pig I. Distribution of MICs for 93 isolates of *Brachyspira pilosicoli* from 87 different Swedish pig herds from the years 2002 and 2003.

Cattle

Isolates included

Udder pathogens (*E. coli* and *Klebsiella* spp.) were isolated from samples of acute mastitis. The data presented are preliminary results from a project where milk samples from cases of acute mastitis were collected and cultured by practising veterinarians from May 2002 until April 2003. The practitioners taking part in the study and the number of samples collected by each veterinarian were determined to get a sample representing dairy cows in Sweden.

Escherichia coli

Resistance to antimicrobials in *E. coli* from mastitis was uncommon, and 89% of the isolates were susceptible to all tested antimicrobials (Table Cattle I). This is in accordance with data presented in previous Swedish investigations of similar materials (Nilsson *et al.*, 1997; Robertsson & Franklin, 1987). However, when resistance occurred it was frequently to more than one antimicrobial and 7% of the isolates were resistant to at least three of the tested antimicrobials (counting nalidixic acid and enrofloxacin as one).

Resistance to ampicillin, streptomycin and sulphonamides were the most common resistance traits, and 6% of the isolates were resistant to all these substances. Five isolates (3%) were resistant to nalidixic acid and four of these were resistant to at least two other unrelated antimicrobials. This type of resistance was not reported in previous investigations.

Klebsiella

The material was composed of 33 *K. pneumoniae*, 10 *K. oxytoca* and 1 *Klebsiella* sp. Resistance to ampicillin is inherent in *Klebsiella* spp., but one isolate had an MIC of 4 mg/L. The susceptibility test was repeated three times, and identification (using API 20E) twice with the same result. Still, the identification of that isolate must be considered dubious in view of the high susceptibility to ampicillin.

Apart from ampicillin, the isolates were susceptible to most of the tested antimicrobials. Resistance to streptomycin, sulphonamides and tetracycline were the most commonly encountered traits (Table Cattle II) Excluding ampicillin, only one isolate was multiresistant.

Of the tested antimicrobials, only enrofloxacin, teracycline and the combination trimethoprim-sulphonamides are licensed for treatment of mastitis in cattle in Sweden. The results of treatment of mastitis caused by *Klebsiella* sp. are generally considered poor, even though resistance is rare. Factors related to the bacterium and to the pharmacodynamics of these antibiotics may explain the poor treatment results.

Table Cattle I. Occurrence of resistance among *Escherichia coli*, (n=169) isolated from clinical mastitis in dairy cows and distribution (%) of MICs.

Substance	Resistance (%)	Distribution (%) of MICs[1] (mg/L)															
		≤0.03	0.06	0.12	0.25	0.5	1	2	4	8	16	32	64	128	256	512	>512
Ampicillin	7					0.6	12.4	62.7	16.6	0.6	0.6		6.5				
Apramycin	0								3.0	27.8	55.0	14.2					
Ceftiofur	0				21.9	74.0	3.6	0.6									
Chloramphenicol	2							3.0	84.6	10.7		1.8					
Enrofloxacin	2	11.2	77.5	8.3	1.2		0.6			1.2							
Florfenicol	0							1.8	66.3	31.4	0.6						
Gentamicin	0					1.2	48.5	42.0	8.3								
Nalidixic acid	3						1.2	29.0	65.1	1.2	0.6	0.6	0.6		1.8		
Neomycin	1						1.2	44.4	45.0	8.3				0.6	0.6		
Streptomycin	9								4.1	39.6	45.6	1.2	0.6	1.2	0.6	7.1	
Suphamethoxazole	8												80.5	11.2			8.3
Tetracycline	5						11.8	67.5	15.4	0.6				4.7			
Trimethoprim	3			4.7	29.0	53.3	9.5	0.6				3.0					

[1] The white fields denote range of dilutions tested for each substance. MICs above the range are given as the concentration closest to the range. MICs equal to or lower than the lowest concentration tested are given as the lowest tested concentration. Bold vertical lines indicate cut-off values defining resistance.

Table Cattle II. Occurrence of resistance among *Klebsiella* spp.[1] (n=44) isolated from clinical mastitis in dairy cows and distribution (%) of MICs.

Substance	Resistance (%)	Distribution (%) of MICs[2] (mg/L)															
		≤0.03	0.06	0.12	0.25	0.5	1	2	4	8	16	32	64	128	256	512	>512
Ampicillin	NR[3]								2.3		4.5	15.9	77.3				
Apramycin	0								63.6	29.5	6.8						
Ceftiofur	0				20.5	68.2	9.1	2.3									
Chloramphenicol	0							29.5	56.8	13.6							
Enrofloxacin	0	2.3	45.5	43.2	9.1												
Florfenicol	0							18.2	63.6	18.2							
Gentamicin	0					59.1	38.6	2.3									
Nalidixic acid	0							15.9	70.5	11.4	2.3						
Neomycin	0						50.0	45.5	4.5								
Streptomycin	14								65.9	18.2		2.3	4.5	4.5		4.5	
Suphamethoxazole	9												50.0	40.9			9.1
Tetracycline	7						18.2	50.0	25.0					6.8			
Trimethoprim	2			2.3		31.8	54.5	9.1				2.3					

[1] 33 *K. pneumoniae*, 10 *K. oxytoca* and 1 *Klebsiella* spp.; [2] The white fields denote range of dilutions tested for each substance. MICs above the range are given as the concentration closest to the range. MICs equal to or lower than the lowest concentration tested are given as the lowest tested concentration. Bold vertical lines indicate cut-off values defining resistance; [3] Not relevant as the genus is inherently resistant to ampicillin.

Penicillin resistance in *Pasteurella* from Swedish cattle

IN 2003 THE FIRST Swedish isolates of beta-lactamase producing *Pasteurella* spp. from cattle were confirmed. The isolates were from a herd specialised in purchasing 1-2 months old calves from dairy farms and rearing them for slaughter. The first isolate was obtained from the lung of a pneumonic calf sent for routine post mortem examination to the National Veterinary Institute. Subsequently, beta-lactamase producing *Pasteurella* spp. were isolated from two of 20 nasal swabs from calves in the group of about 200 animals from where the pneumonic calf came. The isolates had MICs of >4 mg/L for penicillin and 8- >32 mg/L for ampicillin.

In Sweden, penicillin is the recommended first-line antimicrobial in therapy of pneumonia in cattle. Previous studies have shown that the choice is well founded. In years 1979-84, 60 isolates of *Pasteurella multocida* and 17 of *Mannheimia haemolytica* from calves with acute respiratory disease were all susceptible to penicillin and ampicillin (MIC ≤0.5mg/L) (Franklin *et al.*, 1988). In the same study, one of 42 isolates of *Pasteurella multocida* obtained on post mortem examination had elevated MICs to penicillin and ampicillin (2 mg/L and 4 mg/L, respectively) and one of 30 *Mannheimia haemolytica* had an elevated MIC to ampicillin (4 mg/L). None of these isolates produced beta-lactamase. In a similar study conducted 1997-2000, all 254 isolates of *Pasteurella* spp. from tracheal washes or nasal swabs from calves were susceptible to penicillin and ampicillin (Bengtsson & Viring, 2000).

In contrast, penicillin/ampicillin resistance in *Pasteurella* and *Mannheimia* from the respiratory tract of cattle is a common finding in many countries. In a four-year study in North America, 1988-1992, susceptibility to penicillins in *Mannheimia haemolytica* and *Pasteurella multocida* isolated from lungs of cattle that died of respiratory disease was 50-71% and 83-89, respectively (Watts *et al.*, 1994). In the Netherlands, resistance to amoxicillin in *Pasteurella multocida* and *Mannheimia haemolytica* from veal calves in 1996-2000 was 17 and 39%, respectively (MARAN-2002) and in France 50 and 79% of *Pasteurella multocida* and *Mannheimia haemolytica* tested were resistant to penicillin in 1995-2000 (Tardy *et al.*, 2001).

Thus, in many countries resistance in respiratory pathogens in cattle has reduced the therapeutic usefulness of penicillin, which in some textbooks no longer is recommended as a first line-antimicrobial in pneumonia in cattle (Bateman, 2000). In the light of this, it is important to monitor resistance in *Pasteurella* and *Mannheimia* from Swedish cattle and if possible reduce the spread of resistant clones and/or genetic resistance determinants. To this end, a nationwide study to determine the prevalence of beta-lactamase producing *Pasteurella* and *Mannheimia* among Swedish dairy calves was started in the spring of 2004. To effectively counteract the spread of resistance, however, bacteriological diagnosis and subsequent susceptibility testing of isolates to guide measures taken by practitioners in the control of respiratory diseases on herd level should be used to a greater extent than hitherto.

Horse

Isolates included

Isolates of *E. coli* are from the genital tract of mares, while isolates of *Streptococcus zooepidemicus* are from the respiratory tract. For both these bacterial species, the number of isolates tested has increased during the study period.

All isolates are from diagnostic submissions and exclusion of repeat isolates from the same individual or horses in the same stable was not possible. The southern part of Sweden is probably underrepresented in the materials. Further, data are likely to be biased towards treatment failures and recurrent infections. Any assessment of trends relies on the assumption that these biases are inherent throughout the study period.

Escherichia coli

In *E. coli* from horses, the percentage of resistance to the tested antimicrobials was of the same magnitude as in previous years (Table Horse I). The two most common traits were resistance to streptomycin and to the combination trimethoprim-sulphonamides. Interestingly, only one isolate of 48 from the years 1992-1994 was classified as resistant to trimethoprim-sulphonamides compared with 15-19% during the more recent years. No similar observations can be made among *E. coli* from other animal species tested at the same laboratory with the same method (see other *E. coli* from other animal species in this report). Methodological errors are therefore not a likely explanation for this observation. Oral formulations of trimethoprim-sulphonamides for use in horses were introduced on the Swedish market in the late 80s, and it is possible that the current proportions of resistance reflect an increased use of this antimicrobial combination.

For years 2001-2003, significant associations were observed for all possible dual combinations of resistance to ampicillin, streptomycin, tetracycline and trimethoprim-sulphonamides (Chi-square, P<0.0001 in all cases). The most common combination was resistance to both streptomycin and trimethoprim-sulphonamides (13% of the isolates). Ten percent of the isolates from that time period were multiresistant. Almost all multiresistant isolates were resistant to streptomycin (28/29) or trimethoprim-sulphonamides (27/29), or both (26/29). Combined resistance to ampicillin, streptomycin, tetracycline and trimethoprim-sulphonamides was observed in 3% of the total number of isolates (45% of the multiresistant isolates). Of the tested antimicrobials, the by far most commonly used drug for horses is the combination of trimethoprim-sulphonamides. It is probable that this use co-selects for resistance to other antimicrobials, considering the strong association between resistance traits and multiresistance.

Streptococcus zooepidemicus

In year 2003, more than one third (37%) of the *S. zooepidemicus* tested for susceptibility were resistant to the combination trimethoprim-sulphonamides (Table Horse II). The proportions of resistance increased markedly during the 90s, after which the figures decreased. When the yearly resistance percentages are examined, the apparent increase from 1992-2000 is significant (P<0.0001, Chi-square for trend), and so is the apparent decrease from 2000-2003 (P<0.0001). As noted under *E. coli* above, trimethoprim-sulphonamides are commonly prescribed for horses and the use has increased over the 90s. This concurs with the increase in resistance. However, the apparent decrease in resistance from year 2000 is not paralleled by a decrease in usage of these drugs. Therefore, it is probable that other factors also influence the observed trends.

S. zooepidemicus has a low inherent susceptibility to aminoglycosides, and assessment of resistance to these antimicrobials is therefore not relevant. Resistance to other antimicrobials was rare in year 2003, as in previous years.

Table Horse I. Occurrence of resistance among *Escherichia coli* from horses during different years and distribution of MICs for the isolates from 2003. Isolates are from diagnostic submissions of samples from the female genital tract.

	Years,% resistant isolates						Distribution (%) of MICs[1] (mg/L)									
Substance	1992-94 n=48	1995-97 n=216	1998-00 n=222	2001 n=103	2002 n=166	2003 n=188	≤0.12	0.25	0.5	1	2	4	8	16	32	>32
Ampicillin	15	17	10	10	10	6				5.3	54.3	33.5	0.5	6.4		
Ceftiofur	-	-	-	-	0	0		30.3	62.2	6.9	0.5					
Enrofloxacin	8	3	3	5[3]	1	2	97.3	0.5	1.1	0.5	0.5					
Florfenicol	-	-	-	-	<1	0					1.6	35.6	59.0	3.7		
Gentamicin	0	3	6	2	4	2					70.2	23.9	4.3		1.6	
Neomycin	4	5	5	3	4	2						88.3	10.1	0.5		1.1
Streptomycin	31	24	21	20	16	20						2.1	45.7	26.6	5.3	20.2
Tetracycline	6	5	9	8	7	5				28.7	54.8	9.6	2.1	4.8		
Trim/Sulph.[2]	2	15	17	18	19	17			79.8	1.6	1.1	0.5	17.0			

[1] The white fields denote range of dilutions tested for each substance. MICs above the range are given as the concentration closest to the range. MICs equal to or lower than the lowest concentration tested are given as the lowest tested concentration. Bold vertical lines indicate cut-off values defining resistance; [2] Concentration of trimethoprim given, tested in concentration ratio 1/20 (trimethoprim/sulphametoxazole); [3] 102 isolates tested.

Table Horse II. Occurrence of resistance among *Streptococcus zooepidemicus* from horses during different years and distribution of MICs for the isolates from 2003. The isolates are from diagnostic submissions of samples from the respiratory tract.

	Years,% resistant isolates						Distribution (%) of MICs[1] (mg/L)									
Substance	1992-94 n=218	1995-97 n=402	1998-00 n=409	2001 n=188	2002 n=167	2003 n=150	≤0.12	0.25	0.5	1	2	4	8	16	32	>32
Ampicillin	0	<1	0	0	0	0				100.0						
Enrofloxacin	-	-	-	-	NR	NR	0.7		0.7	63.5	33.3					
Florfenicol	-	-	-	2[4]	1[5]	1					86.7	11.3	0.7	0.7	0.7	
Gentamicin	NR[3]	NR	NR	NR	NR	NR					0.7	0.7	4.7	33.3	60.7	
Neomycin	NR	NR	NR	NR	NR	NR						0.7	0.7	4.7	26.7	67.3
Penicillin	0	<1	0	0	0	0	98.7	0.7		0.7						
Spiramycin	<1	1	0	1	2	0						96.0	4.0			
Streptomycin	NR	NR	NR	NR	NR	NR						0.7		2.0	51.3	46.0
Tetracycline	4	3	4	3	8	4				47.3	35.3	12.7	0.7	4.0		
Trim/Sulph.[2]	1	11	57	43	28	37			45.3	10.0	3.3	4.0	37.3			

[1] The white fields denote range of dilutions tested for each substance. MICs above the range are given as the concentration closest to the range. MICs equal to or lower than the lowest concentration tested are given as the lowest tested concentration.. Bold vertical lines indicate cut-off values defining resistance; [2] Concentration of trimethoprim given, tested in concentration ratio 1/20 (trimethoprim/sulphametoxazole); [3] Not relevant as the iherent susceptibility is such that the MIC range is above concentrations that can be obtained during therapy; [4] 41 isolates tested; [5] 163 isolates tested.

Dog

Isolates included

Isolates of *E. coli* are from urine samples, submitted either as urine or as dip-slide cultures. *Staphylococcus intermedius* are from skin samples and *Pseudomonas aeruginosa* are from samples from the external ear canal. Data may contain repeat isolates from the same patient.

Approximately half of the urine samples originate from the Eastern-central part of Sweden, and that region is overrepresented in the material. This is likely to be true also for the ear and skin samples.

For all data, it is probable that there is a bias towards isolates from dogs with recurrent disease or from therapeutic failures. In years 1993 and 2002, 79% and 45% of the urine samples, respectively, were referred to SVA by animal hospitals and the remainder from smaller animal clinics. It is probable that the bias is stronger among samples submitted from animal hospitals that receive more referral cases, than among animal clinics. The fact that the proportion of samples has changed over time must be borne in mind when interpreting the data.

Escherichia coli

The proportion of *E. coli* resistant to the tested antimicrobials was of similar magnitude as in previous years (Table Dog I). Resistance against ampicillin, enrofloxacin, streptomycin, tetracycline or the combination trimethoprim-sulphonamides occurred in 9-18% of the isolates.

In Sweden, aminopenicillins are commonly used for treatment of infections in dogs, including uncomplicated cystitis. Of all prescriptions of antimicrobials for dogs in 1998, 47% were beta-lactam antibiotics, mostly aminopenicillins (Odensvik *et al.*, 2001). This figure corresponds to approximately 132 prescriptions per 1 000 dogs, assuming a dog population of 800,000 individuals. Considering this strong selective pressure, the high proportion of resistance to ampicillin (18%) among isolates from urine is not surprising.

The percentages of resistance to fluoroquinolones are high throughout the study period (8-10%). The cut-off value (>0.25 mg/L) chosen for this study is low compared to breakpoints recommended by, e.g., NCCLS (2002). Nonetheless, isolates for which the MIC is >0.25 mg/L have a decreased susceptibility compared with inherently susceptible strains. In 1998, around 24 000 prescriptions of fluoroquinolones for dogs were dispensed at Swedish pharmacies, which corresponds to about 31 prescriptions per 1 000 dogs (Odensvik *et al.*, 2001). No updated figures on prescription of antimicrobials for dogs are available, but as several new fluoroquinolones have recently been introduced on the Swedish market, the occurrence of resistance should be monitored closely.

Multiresistance was observed in 12% of the isolates from years 2001-2003. Of the 73 multiresistant isolates, 72 were resistant to streptomycin, 64 to ampicillin, 58 to tetracycline and 49 to trimethoprim-sulphonamides. The association between all possible dual combinations of these antimicrobials was strong (P<0.0001 in all cases, Chi-square). Simultaneous resistance to all these four antimicrobials was observed in 5% of all isolates.

The three drug classes most commonly used for treatment of cystitis are aminopenicillins, fluoroquinolones and trimethoprim-sulphonamides. In years 2001-2003, 3% of the isolates were resistant to all these antimicrobials, but all of these were susceptible to at least one other drug that could be used for treatment. These figures emphasise the need for culture and subsequent testing for susceptibility before treatment of recurrent or non-responding urinary tract infections in dogs.

Staphylococcus intermedius

Most isolates of *S. intermedius* produce beta-lactamases and are thereby resistant to penicillin (Table Dog II). The per-

Table Dog I. Occurrence of resistance among *Escherichia coli* from dogs during different years and distribution of MICs for the isolates from 2003. The isolates are from diagnostic submissions of urinary tract samples.

	Years,% resistant isolates						Distribution (%) of MICs[1] (mg/L)									
Substance	1992-94 n= 245	1995-97 n=296	1998-00 n=418	2001 n=183	2002 n=204	2003 n=234	≤0.12	0.25	0.5	1	2	4	8	16	32	>32
Ampicillin	18	18	18	19	18	18				3.4	62.0	15.8	0.9	17.9		
Enrofloxacin	9	9	10	9[4]	8	9	90.2	0.9	2.1	2.1	4.7					
Gentamicin	2	1	2	4	<1	2					75.2	21.4	1.7	0.4	1.3	
Nitrofurantoin	3	3	1	2	1	3								94.4	3.0	2.6
Streptomycin	16	18	15[3]	16	14	16						5.1	42.3	31.6	4.7	16.2
Tetracycline	16	14	12	10[4]	11	12				44.9	37.6	4.7	0.9	12.0		
Trim/Sulph.[2]	9	8	11	11	12[5]	9			83.8	3.8	0.4	2.6	9.4			

[1] The white fields denote range of dilutions tested for each substance. MICs above the range are given as the concentration closest to the range. MICs equal to or lower than the lowest concentration tested are given as the lowest tested concentration. Bold vertical lines indicate cut-off values defining resistance; [2] Concentration of trimethoprim given, tested in concentration ratio 1/20 (trimethoprim/sulphametoxazole); [3] 417 isolates tested; [4] 181 isolates tested; [5] 203 isolates tested.

Table Dog II. Occurrence of resistance among *Staphylococcus intermedius* from dogs during different years and distribution of MICs for the isolates from 2003. The isolates are from diagnostic submissions of samples from the skin of dogs.

	Years,% resistant isolates						Distribution (%) of MICs[1] (mg/L)									
Substance	1992-94 n=304	1995-97 n=322	1998-00 n=433	2001 n=156	2002 n=124[6]	2003 n=102	≤0.12	0.25	0.5	1	2	4	8	16	32	>32
Cephalothin	<1	<1	0	0	2	2					98.0				2.0	
Clindamycin	12	20	21	18	16	19				78.4		2.9	18.6			
Enrofloxacin	-	-	-	-	2	2	64.7	31.4	2.0	1.0	1.0					
Erythromycin	21	28	27	28	19	22			77.5				22.5			
Fucidic acid	9	14	20[4]	26[5]	13	21					76.5	2.9	20.6			
Gentamicin	<1	<1	<1	0	0	0					99.0	1.0				
Nitrofurantoin	1	1	<1	1	1	0								100.0		
Oxacillin	1	2	1	<1	2	2			98.0		2.0					
Penicillin[2]	79	80	80	82	77	81										
Streptomycin	-	-	-	-	19	20						74.5	2.9	2.0	1.0	19.6
Tetracycline	24	12	28	25	25	25				72.5		1.0	1.0	25.5		
Trim/Sulph.[3]	1	2	1	3	3	2			65.7	30.4	2.0	1.0	1.0			

[1] The white fields denote range of dilutions tested for each substance. MICs above the range are given as the concentration closest to the range. MICs equal to or lower than the lowest concentration tested are given as the lowest tested concentration. Bold vertical lines indicate microbiological cut-off values defining resistance; [2] Denotes beta-lactamase production; [3] Concentration of trimethoprim given, tested in concentration ratio 1/20 (trimethoprim/sulphametoxazole); [4] 421 isolates tested; [5] 120 isolates tested; [6] 9 isolates included in SVARM 2002 excluded in this report (see text).

centages have remained around 80% since at least the late 70s (Franklin, 1978). As mentioned above, beta-lactam antibiotics are commonly prescribed for dogs and it is probable that this selective pressure contributes to the stable maintenance of resistance to penicillinase sensitive penicillins. Resistance in occasional isolates to cephalotin or oxacillin is probably due to methodological errors or to high levels of beta-lactamase production, and not to the presence of the *mecA* gene. The current routine at SVA is to retest all isolates for which the MIC of oxacillin is >2 mg/L at lower temperatures (33-34° C) and with 2% NaCl added to the broth. If a high MIC is confirmed, the genotype is examined with PCR for the *mecA* gene. Hitherto, no *mecA* carrying coagulase-positive staphylococci have been found.

Resistance to macrolides (erythromycin) and lincosamides, fucidic acid, streptomycin and tetracycline was common in 2003, as in previous years. In 1978, resistance to erythromycin was still rare (<2%; Franklin, 1978), indicating a substantial increase over the last 20 years. Resistance to macrolides and lincosamides in *S. intermedius* is commonly mediated by *erm*-genes. The gene can be inducible, in which case the resistance phenotype only includes erythromycin resistance, or it can be expressed constitutively giving a phenotype with resistance to all macrolides, lincosamides and streptogramin B (MLSB-type resistance). The proportion of the erythromycin resistant isolates that also show resistance to clindamycin was 58% in years 1992-94, compared with 83% in 2003. The apparent increase of this phenotype may be associated with the increased use of clindamycin for dogs (Odensvik *et al.*, 2001).

The percentage of resistance to trimethoprim-sulphonamides from year 2002 presented in last years report (SVARM 2002) was 10%. This figure is markedly higher than in all other years. Close examination of data revealed that the dates for testing 9 of the resistant isolates were clustered closely in time. These 9 isolates are not included in this years report, as methodological errors cannot be excluded.

The associations between different resistance traits,

Table Dog III. Association between resistance traits and cross-resistance in *Staphylococcus intermedius* isolated from dogs during years 1998-2003 (n=815). For each substance the first line gives the resistance percentages for susceptible isolates (S) and the second line rates for resistant isolates (R).

			Resistance (%)[1]						
Substance		n	Cl	Em	Fu[2]	Pc	Sm[3]	Tc[4]	TS
Clindamycin	S	656	0	7.5	14.5	76.5	6.4	20.9	1.8
	R	159	100.0	99.4	42.6	95.0	82.1	50.3	1.9
Erythromycin	S	608	0.2	0	12.9	74.8	2.2	18.8	2.0
	R	207	76.3	100.0	40.9	95.7	85.1	49.8	1.4
Fucidic acid[2]	S	614	13.8	18.6	0	76.2	14.8	20.7	2.1
	R	153	41.2	51.6	100.0	94.1	43.2	47.7	1.3
Penicillin	S	162	4.9	5.6	5.8	0	0.0	3.1	3.1
	R	653	23.1	30.3	23.5	100.0	24.6	31.4	1.5
Streptomycin[3]	S	182	3.8	3.8	11.5	74.2	0	18.7	2.2
	R	44	72.7	90.9	36.4	100.0	100.0	52.3	4.5
Tetracycline[4]	S	597	13.2	17.4	14.1	74.9	12.4	0	2.0
	R	217	36.9	47.5	36.5	94.5	40.4	100.0	1.4
Trim/Sulph.	S	800	19.5	25.5	20.1	80.4	19.1	26.8	0
	R	15	20.0	20.0	13.3	66.7	33.3	20.0	100.0

[1] Cl: clindamycin; Em: erythromycin; Fu: fucidic acid; Pc: penicillin Sm: streptomycin; Tc: tetracycline; TS: trimethoprim/sulphamethoxazole ; [2] 767 isolates tested; [3] 226 isolates tested; [4] 814 isolates tested.

Table Dog IV. Distribution of MICs of *Pseudomonas aeruginosa* from years 2002 and 2003 (n=234). The isolates are from diagnostic submissions of samples from the ear canal of dogs.

	Distribution (%) of MICs[1] (mg/L)									
Substance	≤0.12	0.25	0.5	1	2	4	8	16	32	>32
Enrofloxacin	2.1	1.7	19.2	33.8	43.2					
Gentamicin					55.1	22.6	12.8	4.7	4.7	

[1]The white fields denote range of dilutions tested for each substance. MICs above the range are given as the concentration closest to the range. MICs equal to or lower than the lowest concentration tested are given as the lowest tested concentration.

or where applicable cross-resistance, in years 2001-2003 for selected antimicrobials are shown in Table Dog III. Resistance to trimethoprim-sulphonamides was not associated with resistance to any of the other included antimicrobials. Interestingly, for all other possible combinations the associations were significant (P<0.001, but mostly P<0.00001, Chi-square). It should be noted that the analysis included 20 repeated Chi-square calculations, which means that there is a risk for mass significance.

In years 2002-2003, 26% of the isolates were multiresistant, and 10% were resistant to at least five antimicrobials. Resistance to penicillin, erythromycin (mostly with cross-resistance to clindamycin), streptomycin and tetracycline occurred in 23 of 62 multiresistant isolates. A prospective study showed that the probability of multiresistance with that phenotype is higher among isolates of *S. intermedius* from recurrent cases of pyoderma, compared with first-time cases (Holm *et al.*, 2002). This indicates that previous antimicrobial exposure has a strong influence on the occurrence of multiresistance. The frequent occurrence of resistance to streptomycin and tetracycline is probably explained by co-selection due to linkage of resistance traits, as these antimicrobials are less frequently used for treatment of pyoderma in dogs.

Pseudomonas aeruginosa

During the last year, we have received a number of questions on treatment of infections in dogs with *P. aeruginosa*. The MICs of most antimicrobials for wild-type *P. aeruginosa* are high in comparison with those for e.g. *Enterobacteriaceae*, and this species is considered clinically resistant to e.g. trimethoprim-sulphonmides, tetracyclines and aminopenicillins (including combinations with clavulanic acid). For gentamicin, the clinical breakpoint for resistant is 8 mg/L (NCCLS, 2002) and using that, 10% of the isolates from years 2002-2003 were resistant (Table Dog IV). For fluoroquinolones, the range of MICs of wild-type strains is 0.5-2 (EUCAST, www.escmid.org). The range of enrofloxacin in the panels used stops at 1 mg/L, which means that among the isolates with MICs >1 there will be both such that are part of the normal, wild type, population and truly resistant strains. The maximum plasma concentration (C_{max}) of the fluoroquinolones currently authorised for use in dogs in Sweden, after oral treatment at the label dosage, ranges from 1.5-2.5 mg/L. The effect of the fluoroquinolones depends on the degree of exposure of target bacteria, i.e. the drug concentration in relation to MIC. To prevent the emergence of resistant strains during treatment the C_{max} to MIC ratio should preferably be more than 8-10. It is clear that with dosages currently authorised for systemic treatment, this ratio is not reached even for the more susceptible isolates.

Cat

Isolates included

Isolates of *E. coli* are from urine samples, submitted either as urine or as dip-slide cultures. Data may contain repeat isolates from the same patient.

It is probable that samples from cats in the Eastern-central part of Sweden are over-represented in the material. Further, it is likely that there is a bias towards isolates from cats with recurrent disease or from therapeutic failures. The number of isolates tested each year is small, but has increased during the study period. The criteria for submission may have changed, and any inferences on trends must be made with caution.

Escherichia coli

The levels of resistance to all tested antimicrobials except gentamicin and nitrofurantoin were above 10%. The figures are generally somewhat higher than for *E. coli* isolated from dogs. Antimicrobials are less frequently prescribed for cats, compared with dogs. In year 1998, 79190 prescriptions of antimicrobials for cats were dispensed at Swedish pharmacies. Assuming a cat population of 1 million, this means 79 prescriptions per 1 000 cats (Odensvik *et al.*, 2002). The corresponding figure for dogs was 283 prescriptions per 1 000 dogs (assumed population 800 000). Consequently, the observed higher percentages of resistance among isolates from cats are probably a reflection of a larger bias towards problematic cases among isolates from cats than from dogs, rather than of differences in use.

The figures presented for year 2002 are, with the exception of fluoroquinolones and nitrofurantoin, lower than for the other years. However, the number of isolates tested each year is small and when figures from year 2002 with 2003 are compared, none of the observed differences are statistically significant.

In years 2001-2003, 13% of the isolates were multiresistant and 7% were resistant to at least four of the antimicrobials tested all years. Four percent of the isolates were simultaneously resistant to ampicillin, streptomycin, tetracycline and trimethoprim-sulphonamides. Resistance to both ampicillin and streptomycin was common (19%), as was resistance to tetracyclines and streptomycin (12%). The two drug classes most commonly prescribed for cats are beta-lactam antibiotics (mostly aminopenicillins) and tetracyclines (Odensvik *et al.*, 2002). It is probable that the exposure to these drugs co-selects for resistance to streptomycin.

Urinary tract infections in cats are usually treated with aminopenicillins or fluoroquinolones. In years 2001-2003, 7% of the isolates were resistant to both ampicillin and enrofloxacin. The cut-off value (>0.25 mg/L) chosen for this report is low compared to the breakpoints recommended by e.g. NCCLS (2002). However, for all isolates that were resistant to both ampicillin and enrofloxacin, the MIC of the latter drug was >1 mg/L. The high level of co-resistance for the two drug classes preferred for treatment, and of multiresistance, shows that in some cases the choice of antimicrobials is severely limited and must be based on culture and susceptibility tests.

Table Cat I. Occurrence of resistance among *Escherichia coli* from cats during different years and distribution of MICs for the isolates from 2003. The isolates emanate from diagnostic submissions of urine samples.

	Years,% resistant isolates					Distribution (%) of MICs[1] (mg/L)									
Substance	1992-97 n=61	1998-00 n=74	2001 n=36	2002 n=46	2003 n=52	≤0.12	0.25	0.5	1	2	4	8	16	32	>32
Ampicillin	26	34	31[4]	22	29				5.8	63.5		1.9	28.8		
Enrofloxacin	5	8	11	15	12	80.8	7.7	5.8		5.8					
Gentamicin	0	3	8	4	2					73.1	23.1	1.9		1.9	
Nitrofurantoin	2	2	0[4]	7[5]	0								98.1	1.9	
Streptomycin	25	18	14	9	25						1.9	34.6	34.6	3.8	25.0
Tetracycline	28	16	19	9	17				46.2	32.7	3.8		17.3		
Trim-Sulph.[2]	7	10[3]	14[4]	11	12			88.5				11.5			

[1] The white fields denote range of dilutions tested for each substance. MICs above the range are given as the concentration closest to the range. MICs equal to or lower than the lowest concentration tested are given as the lowest tested concentration. Bold vertical lines indicate microbiological cut-off values defining resistance; [2] Concentration of trimethoprim given, tested in concentration ratio 1/20 (trimethoprim/sulphametoxazole); [3] 73 isolates tested; [4] 14 isolates tested; [5] 45 isolates tested.

Appendix 1: Demographic data

STATISTICS on animal numbers and agricultural holdings with animals are provided by Statistics Sweden in collaboration with the Board of Agriculture. Figures are based either on total census or on samples of the populations. The counting is made in June and/or December. Statistics is published annually as a Yearbook of Agricultural Statistics and also on the Internet via the websites for Statistics Sweden (www.scb.se) or the Board of Agriculture (www.sjv.se). Specific sources are given in footnotes to the tables below.

The number of animals and holdings counted at the time of census are given in Table AP1 I and II, and the number of animals slaughtered on an annual basis is given in Table AP1 III. In addition, the volume slaughtered (expressed in tonnes) is given in Table AP1 IV.

The total number of food producing animals in Sweden has decreased notably over the last two decades and the herd size has increased. In the last year the total number of cattle decreased by about 1.5% and is estimated at 1 611 900 in June 2003 (Table AP1 1). During the same period the number of dairy cows is estimated to have decreased by about 3%. The number of fattening pigs increased by 3% since June 2002 and also the number of sheep increased, returning to the 2001 level. The changes in total number of animals were for each species reflected in the number of animals slaughtered (Table AP1 III). The number of broiler chickens slaughtered decreased by about 3% between 2002 and 2003.

Table AP1 I. Number of livestock (in thousands) from 1980-2003[1]. The figures represent census figures from counts of all, or samples of the populations in the given years.

Animal	1980	1985	1990	1995	2000[4]	2001[4]	2002[4]	2003[4]
Cattle								
Dairy cows	656	646	576	482	428	418	417	403
Beef cows	71	59	75	157	167	166	169	168
Other cattle > 1 year	614	570	544	596	589	573	553	529
Calves < 1 year	595	563	524	542	500	494	498	511
Total, cattle	1 935	1 837	1 718	1 777	1 685	1 651	1 637	1 612
Pigs								
Boars and sows	290	260	230	245	206	216	211	207
Fattening pigs >20 kg [2]	1 254	1 127	1 025	1 300	1 146	1 090	1 096	1 128
Piglets <20kg [3]	1 170	1 113	1 009	769	566	586	574	568
Total, pigs	2 714	2 500	2 264	2 313	1 918	1 892	1 881	1 903
Sheep								
Ewes and rams	161	173	161	195	198	208	198	211
Lambs	231	252	244	266	234	244	229	240
Total, sheep	392	425	405	462	432	452	427	451
Laying hens								
Hens	5 937	6 548	6 392	6 100	5 670	5 687	4 732	NA[5]
Chickens reared for laying	2 636	2 159	2 176	1 812	1 654	1 721	1 537	NA
Total, hens	8 573	8 708	8 568	7 912	7 324	7 408	6 269	NA

[1] Source: Yearbook of Agricultural Statistics, Sweden 1981, 1986, 1991, 1996, 2001, 2002, and Statistical Messages, JO 20 SM 0202 and JO 20 SM 0301. For 1980 and 1985 only cattle and sheep at premises with more than 2 ha counted; [2] Before 1995, the figure denotes pigs above 3 months of age; [3] Before 1995, the figure denotes pigs below 3 months of age; [4] The numbers are based on counting in June 2000, 2001,2002 and 2003; [5] Not available at the time of printing.

Table AP1 II. Number of holdings with animals of different types, 1980-2002[1].

Animal Species	1980	1985	1990	1995	2000	2001	2002
Cattle							
Dairy cows	44 100	30 100	25 900	17 700	12 700	11 800	11 300
Beef cows	12 400	10 300	10 900	17 100	13 900	13 600	13 100
Other cattle >1 year	63 200	52 700	42 700	39 200	30 500	29 100	27 800
Calves <1 year	62 300	52 000	42 000	36 500	27 700	26 300	25 200
Sheep, excluding lambs	10 100	10 500	9 700	10 000	8 000	8 100	7 400
Pigs	26 100	19 900	14 300	10 800	4 800	4 500	2 700
Laying hens	23 600	17 500	12 900	9 600	5 700	5 800	5 300
Chickens reared for laying	5 100	2 700	1 900	1 400	700	1 000	800

[1] Source: Yearbooks of Agricultural Statistics, Sweden 1981, 1986, 1991, 1996, 2002 and Statistical Messages, JO 20 SM.

Table AP1 III. Number of animals slaughtered (in thousands) at slaughterhouses, 1980-2003[1].

Animal Species	1980	1985	1990	1995	2000	2001	2002	2003
Cattle								
Cattle >1 year	574	584	523	502	490	463	472	454
Calves <1 year	130	138	70	46	39	34	34	32
Total, cattle	704	722	593	548	529	497	506	486
Pigs	4 153	4 283	3 659	3 763	3 251	3 198	3 282	3 304
Sheep	302	328	280	145	202	197	197	192
Chickens (broiler)	40 466	36 410	38 577	60 300	68 617	73 350	77 383	74 742

[1] Sources: For 1980-1995: Yearbooks of Agricultural Statistics, Sweden 1981, 1986, 1991 and 1996 except for chickens where figures were supplied by the National Food Administration, and for 2000-2003 Statistical messages JO 48 SM 0302 and 0402 (all animal species).

Table AP1 IV. Quantity of livestock slaughtered (in tonnes) at slaughterhouses, 1990-2003[1].

Animal Species	1990	1995	2000	2001	2002	2003
Cattle						
Cattle >1 year	138.4	140.1	145.4	139.1	142.3	136.3
Calves <1 year	5.4	3.2	4.4	4.1	4.2	4.1
Total, cattle	143.8	143.3	149.8	143.2	146.5	140.4
Pigs	289.2	308.8	277.0	275.9	283.8	287.5
Sheep	4.9	3.5	3.9	3.8	3.9	3.7
Chickens (broiler)	44.0	74.2	89.9	96.1	101.4	97.9

[1] Sources: For years 1990 and 1995 Yearbooks of Agricultural Statistics, Sweden 1991 and 1996 except for chickens where figures were supplied by the National Food administration, and for 2000-2003 Statistical messages JO 48 SM 0302 and 0402 (all animal species).

Appendix 2: Materials and methods, use of antimicrobials

Source for the statistics

Antimicrobial drugs used in veterinary medicine in Sweden are only available on veterinary prescription. Furthermore, antimicrobial drugs have to be dispensed through pharmacies, which in turn are supplied solely by two drug wholesalers. Sales statistics are available from Apoteket AB (The National Corporation of Swedish Pharmacies).

From year 2003, statistics on drug sales is based on electronic records of amount of drugs dispensed (prescription based statistics). Data for previous years are the amount of antimicrobial products sold from the wholesalers to the pharmacies. Wholesalers' data have a very high degree of completeness. This is explained by the fact that the wholesalers represent the entire drug distribution network, i.e., there are no other sources of antimicrobials for use or prescription by veterinarians. As the pharmacies stock a limited amount of drugs, the current prescription based statistics is judged to be comparable with previous, wholesaler based statistics.

Sweden has a long tradition in drug consumption statistics. Apoteket AB, former Apoteksbolaget AB, has since 1976 monitored the consumption of drugs for use in humans mainly by using wholesalers' statistics. In the case of drugs for animal use, SVA and Apoteket AB have collaborated over the years and data on the total use of antimicrobials for animals in Sweden are available since 1980. For a review of the figures from 1980-2000 as well as references to publications on which that review is based, see SVARM 2000. From 2003, Apoteket AB has the formal responsibility to gather such data. Further, the Board of Agriculture has been appointed competent governmental authority and will, from 2006, report statistics per animal species (food producing animals).

Classification of drugs

Veterinary medicinal drugs are classified according to the Anatomical Therapeutic Chemical veterinary classification system (ATCvet) (WHO, Guidelines for ATCvet classification). The system is based on the same main principles as the ATC classification system for substances used in human medicine. In both the ATC and ATCvet systems, drugs are divided into groups according to their therapeutic use. First, they are divided into 15 anatomical groups, classified as QA-QV in the ATCvet system (without Q in the system for human drugs), on basis of their main therapeutic use. Thereafter subdivision is made according to therapeutic main groups, which is followed by a further division in chemical/therapeutic subgroups.

Antimicrobials are classified in the QJ group – general anti-infectives for systemic use. However, antimicrobials can also be found in other groups such as QA (alimentary tract and metabolism), QD (dermatologicals), QG (genito-urinary system) and QS (sensory organs) depending on the therapeutic use.

Inclusion criteria

All veterinary antibacterial drugs authorised for use in animals except dermatologicals, ophtalmologicals and otologicals were included (i.e., ATCvet codes QA, QG and QJ). Veterinary drugs are preparations authorised for use in animals. Human drugs may be authorised not only for humans, but for animals as well. This latter category is not included in the statistics. However, no such drugs are authorised for use in the major food producing animal species, and the volume sold is very limited.

Drugs with antibacterial activity can also be found in other groups, notably among the antiprotozoals (QP51). Of these, the nitroimidazoles were included earlier but no such substances are presently authorised for use in animals. Sulfaclozine is licensed for treament of coccidiosis only and has therefore not been included. The ionophoric antibiotics are presently regulated as feed additives and not sold though pharmacies and are therefore not included in the wholesalers' statistics. However, the Board of agriculture collects figures on sales of ionophores from the feed mills as a part of the feed control system. As the source differs, data on ionophores are given only in Table AC III.

Use of antimicrobials with mastitis as one indication

In an earlier publication, the sale of antimicrobials drugs with mastitis as one of the indications in Norway and Sweden from 1990-1997 has been described (Grave *et al.*, 1999). Updated figures have previously been published in SVARM 2001.

Figures on sales of antimicrobial drugs with mastitis as one of the approved indications were selected from the wholesalers' statistics. Most of these drugs are authorised for other indications, and for other animal species. However, as mastitis is by far the single most common indication for their use, the data can be used to evaluate trends.

To facilitate temporal analysis and comparisons, a defined daily dose for cows (DDDcow) was introduced as a unit of measurement.

For injectable drugs, doses were, with some exceptions, defined on basis of dosage recommendations given in Norwegian and Swedish pocket formularies listing pharmaceutical specialities with marketing authorisation. In the study, 500 kg cow weight was chosen to establish the total daily dose. The weight of 500 kg was chosen because it is technically easy to handle although not identical to the average weight of dairy cows in Norway and Sweden. Figures on numbers of dairy cows were obtained from Official Statistics Sweden. Finally, the number of DDDcow/1 000 cows at risk/day was calculated using the formula:

$$\frac{\text{Amount of drug sold in one year (mg)}}{\text{DDDcow (mg) * 365 * no. of cows at risk}} * 1\,000 \text{ cows at risk} = \text{DDD/1 000 cows at risk/day}$$

For intramammary drugs, one single-dose applicator was chosen as the defined dose. The number of single-dose applicators sold each year was divided by the number of cows at risk (in thousands) and days at risk (365) that year.

Aquaculture

Statistics specifically on use of antimicrobials in aquaculture is published annually by Fiskhälsan FH AB (Fish Health Control Program). Data included in SVARM 2003 have been taken from the report for year 2003 and are based on prescriptions of antimicrobials for fish farmed both for direct food production and for sports fishing (i.e. fish for stocking enhancement as well as recreation fishing).

Distribution of veterinary medicines in Sweden

Marketing of drugs in Sweden is regulated by the Medicinal Products Act, which applies both to human and veterinary drugs. According to the Act, a medicinal product may not be sold until it has been granted marketing authorisation by the Medical Products Agency (MPA). The MPA has issued provisions concerning authorisation, distribution and prescription of veterinary medicinal products.

The state-owned Apoteket AB has exclusive rights regarding retail sales of medicines in Sweden. Apoteket AB operates according to guidelines set out in an agreement with the State. According to the Act only pharmacies run by Apoteket AB are permitted to sell drugs. This implies that veterinarians in Sweden are not permitted to sell drugs, although they may for practical reasons hand over medicines for emergency use. Veterinarians are, however, under no conditions permitted to make a profit from dispensing medicines.

Appendix 3: Materials and methods, resistance monitoring

Sampling strategy

Zoonotic bacteria

Salmonella

Isolates of *Salmonella* from warm-blooded animals (wild and domesticated) are included. Salmonellosis in animals is a notifiable disease in Sweden. It is mandatory that at least one isolate from each notified incident, including incidents detected in the Swedish *Salmonella* control programme, is confirmed at SVA. The first isolate from each food animal species in each notified incident is included in the material presented in SVARM. The same inclusion criteria are also used for isolates from other warm blooded animal species, unless the epidemiological situation in a particular year is judged unusual. In year 2003, *Salmonella* was isolated from an unusually large number of cats (116 positive cases) and only selected isolates from these cases were investigated. The principle for selection was the first 20 consecutive isolates from cats, and thereafter every fifth isolate (total number of isolates 39).

Campylobacter

Samples for culture of *Campylobacter* spp. were selected from the total number of samples of colon content from healthy pigs collected at abattoirs with the purpose of isolating indicator bacteria (see below). The selection was made taking the annual volume slaughtered at each abattoir into account, with the aim to isolate approximately equal numbers of isolates of *Campylobacter* from each quartile of the year.

Indicator bacteria

Indicator bacteria, *Escherichia coli* and *Enterococcus* spp., were isolated from colon content from healthy pigs sampled at slaughter.

Seven abattoirs participated in the collection of samples. These abattoirs are geographically separated and accounted for 75% of the total volume of pigs slaughtered in Sweden during 2001. The total number of samples collected was calculated with the aim of isolating approximately 300 of *E. coli* and *Enterococcus* spp. The number of samples collected at each abattoir was proportional to the respective annual slaughter volume.

Sampling was performed weekly, with exceptions for holidays and summer vacations, by meat inspection staff or abattoir personnel. Each sample represents a unique herd. By these measures, bacterial isolates included are from randomly selected healthy individuals of Swedish slaughter pig herds.

Animal pathogens

Isolates of animal pathogens included, except mastitis pathogens from dairy cows, emanate from routine bacteriological examinations of clinical submissions or post-mortem examinations at SVA. Mastitis pathogens included were collected in a project years 2002-03 where milk samples from cases of acute mastitis were collected by practicing veterinarians. The number of samples collected in each region of the country was proportional to the number of dairy cows in the region.

Isolates included from pigs are *E. coli* from the gastro-intestinal tract (gut content, faecal samples or mesenteric lymph nodes), and *Brachyspira hyodysenteriae* and *Bracyspira pilosicoli* isolated from faecal samples. From cattle, *E. coli* and *Klebsiella* spp. isolated from milk from dairy cows with acute mastitis are included. From horses, *E. coli* from the genital tract of mares and *Streptococcus zooepidemicus* from the respiratory tract are included. From dogs and cats *E. coli* isolated from samples of urine are included and from dogs also *Staphylococcus intermedius* isolated from skin samples and *Pseudomonas aeruginosa* from samples from the ear canal.

Isolation and identification of bacteria

Zoonotic bacteria

Salmonella

Salmonella were isolated and identified at the Dept. of Bacteriology, SVA or at regional laboratories in accordance with standard procedures. All samples within official control programmes are cultured according to the procedures detailed by the Nordic Committee on Food Analysis (NMKL Nr 71 5th ed., 1999). Confirmatory identification and serotyping of isolates was performed at the Department of Bacteriology, SVA following to standard procedures according to Kaufmann and White. The Dept. of Bacteriology, SVA is accredited for isolation, identification and serotyping of *Salmonella*.

Phagetyping of *S. Typhimurium* and *S. Enteritidis* was performed by Swedish Institute for Infectious Disease Control (SMI), Stockholm using the Colindale scheme.

Campylobacter

Samples were cultured for thermophilic *Campylobacter* spp. on Preston selective agar and incubated at 42°C. Identification was based on colony morphology, microscopic appearance including motility and the following phenotypic characteristics: production of oxidase, catalase, hippurate-hydrolysis and indoxyl-actetate reaction (Nachamkin, 1999). With these tests, hippurate-positive *C. jejuni* can be identified whereas other isolates are described as hippurate-negative thermophilic *Campylobacter* spp. When such strains are isolated from pigs, the probability that they are *C. coli* is very high.

Indicator bacteria

Escherichia coli

Approximately 0.5 g of intestinal content from ceacal or colon content was diluted in 4.5 mL phosphate buffered saline (PBS, pH 7.2). After thorough mixing, 0.1 mL of this suspension was spread on MacConkey agar. After incubation overnight at 37°C, one lactose positive colony with morphology typical for *E. coli* was sub-cultured on horse-blood agar (5% v/v), after which the isolate was tested for production of tryptofanase (indole) and b-glucuronidase (p-nitrophenyl-b-D- glucopyranosiduronic acid, PGUA). Only lactose-positive isolates with typical morphology and positive reactions in both tests were selected for susceptibility tests.

Enterococci

Ceacal or colon content was diluted as described for *E. coli* and cultured both on solid media without selective antibiotics, in enrichment broth supplemented with vancomycin (8 mg/L) and on selective plates with ampicillin (16 mg/L; only fall 2003).

Culture without selective antibiotics: Of the diluted intestinal content, 0.1 mL was spread onto Slanetz-Bartley (SlaBa) agar and incubated for 48 h at 37°C. One colony, randomly chosen, was sub-cultured on bile-esculin agar and blood agar (37°C, 24 h). Colonies with morphology consistent with enterococci, and with a positive reaction on bile-esculin agar were tested for antimicrobial susceptibility and identified to species level according to Devriese *et al.* (1993) by use of the following biochemical tests: mannitol, sorbitol, arabinose, saccharose, ribose and methyl-a-D-glucopyranoside.

Enrichment for vancomycin resistant enterococci: Approximately 0.5 g of colon content was added to 4.5 mL enrichment broth (Enterococcosel) supplemented with 8 mg/L vancomycin and incubated in 37°C for 24 hours. After incubation in 37°C for 24 h, 0.1 mL of the enriched culture was spread on SlaBa agar supplemented with 8 mg/L vancomycin and incubated in 37°C for 48 hours. From plates showing growth of colonies typical for enterococci, at least one colony of each morphological type was sub-cultivated on bile-esculin agar and blood agar (37°C, for 24 h). Identification of presumptive enterococci was performed as above.

Selective culture for ampicillin resistant enterococci: During the fall 2003, samples were cultured on SlaBa with ampicillin (16 mg/L). Identification of presumptive enterococci was performed as above.

Animal pathogens

Animal pathogens, except udder pathogens, were isolated and identified at the Dept. of Bacteriology, SVA with accredited methodology, following standard procedures.

Udder pathogens were isolated by the practising veterinarians who collected the milk samples. Subsequently, the original culture plates were sent to the Dept. of Mastitis, SVA for final bacteriological diagnosis by use of accredited methodology, following standard procedures.

Susceptibility testing

All antimicrobial susceptibility tests were performed using dilution methods. For bacteria other than *Campylobacter* spp. and *Brachyspira* spp., the tests were performed following the standards for microdilution of the National Committee of Clinical Laboratory Standards (NCCLS, 2002) in cation adjusted Mueller-Hinton broth (CAMBH). The microdilution panels used, VetMIC™, are produced at the Dept. of Antibiotics, SVA. Different panels were used depending on the bacterial species tested and the original purpose of the investigation (monitoring or clinical diagnostics).

For *Campylobacter* spp. and *Brachyspira* spp., there are currently no accepted standards for broth dilution susceptibility tests. The microdilution method described by NCCLS was adapted for *Campylobacter* spp. Each well in the microdilution panels was inoculated with 100 µl CAMBH with an inoculum density of approximately 10^6 CFU/ml. The panels were incubated in 37°C for 48 hours in a microaerophilic atmosphere.

For susceptibility testing of *Brachyspira hyodysenteriae*, a broth dilution method was used (Karlsson *et al.*, 2003). The antimicrobials were dried in serial twofold dilutions in the tissue culture trays with 48 wells per plate. The wells were filled with 0.5 mL of a suspension of bacteria in brain heart infusion broth with 10% fetal calf serum ($1x10^6$-$5x10^6$ CFU/ml). The trays were incubated in an anaerobic atmosphere for four days on a shaker.

Minimum inhibitory concentration (MIC) was recorded as the lowest concentration of the antimicrobial that inhibits bacterial growth. An isolate was regarded as resistant to a specific antimicrobial when its MIC was distinctly higher than those of inherently susceptible strains of the bacterial species in question. In other words, microbiological cut-off values were used to define resistance. Where appropriate, the breakpoints suggested by NCCLS (2002) for animal pathogens were also taken into consideration. The cut-off values used for defining resistance are shown in Table AP3 I.

Bacitracin values in this report are given in units/mL. In an attempt to convert unit/mL to mg/L we discovered that there appears to be some confusion in the matter. The bacitracin compound used in SVARM is obtained from Sigma and meets the standards set by the United States Pharmacopoeia (USP), stating that one unit is equivalent to 26 µg of the US standard. However, according to the International Standard Preparations, one international unit is equivalent to 13.51 µg. On the other hand, if the bacitracin is of a very high degree of purity, though unstable, it correspond to 66 (-70) units/mg, that is, one unit is equivalent to approximately 15 µg. Feedingstuff grade of bacitracin correspond to 42-50 units/mg (one unit=20-24 µg) (Otten *et al.*, 1975).

Quality assurance system

The Dept. of Antibiotics and Dept. of Bacteriology are accredited according to SS-EN ISO/IEC 17025 by the Swedish Board for Accreditation and Conformity Assessment (SWEDAC) to perform antimicrobial susceptibility tests with microdilution methods. Likewise, the laboratories responsible for isolation and identification of animal pathogens and *Salmonella* (Dept. of Bacteriology and Dept. of Mastitis) are accredited for these procedures according to the same standard.

For susceptibility tests of zoonotic and indicator bacteria, *Escherichia coli* ATCC 25922, *Enterococcus faecalis* ATCC 29212 and *Campylobacter jejuni* CCUG 11284 (analogue to *Campylobacter jejuni* ATCC 33560) were included as quality controls. Relevant control strains were also included and evaluated at least once weekly for animal pathogens. For *Brachyspira* spp., there are yet no internationally recognised quality control strains. The *B. hyodysenteriae* type strain B78^T ATCC 27164^T and *B. hyodysenteriae* CCUG 47386 were used for internal performance control.

The Dept. of Antibiotics participates in several proficiency tests for antimicrobial susceptibility testing. These are arranged either as national or international studies. Likewise, the Dept of Bacteriology and the Dept. of Mastitis participate in proficiency tests concerning isolation and identification of *Salmonella* spp. and general clinical veterinary bacteriology and susceptibility tests.

Data handling

Records on *Salmonella* and animal pathogens such as source of cultured sample, identification results, antimicrobial susceptibility etc. are routinely registered in an Oracle database at SVA. From this, relevant data were extracted to an Access database.

Data on animal species, date of sampling, abattoir and herd of origin were recorded in an Access database on arrival of samples for samples for cultivation of indicator bacteria and *Campylobacter*.

Calculations and analysis of data were performed in the computer programs Access, Excel, Minitab or the module Statcalc in EpiInfo.

Concerning confidence limits

When the prevalence of antimicrobial resistance is close to zero, e.g. when one out of 120 isolates is resistant, the question arises how to calculate the prevalence of resistance and its confidence intervals. In the example, the prevalence could be estimated to 0.83% while the 95% confidence interval is trickier. The normal approximation to the binomial distribution would give a lower confidence of -0.8% and an upper confidence limit of 2.5%. The lower limit is nonsensical and indicates the unsuitability of the normal approximation in this case.

There are several ways out of the dilemma; one is to calculate the exact binomial confidence limits, which would be possible in some cases (small number of isolates). Another alternative is to run Monte-Carlo simulations based on the beta-distribution which is possible but quite laborious for a huge set of data since each prevalence estimate has to be simulated 10 000 times. Finally the relationship between the F-distribution, the beta-distribution and the binomial distribution can be used. This gives the formulae that enable calculations of the confidence interval (Rao, 1965). Using this approach, the confidence intervals in the example would be 0.021% and 4.6%.

In conclusion, the normal approximation to the binomial distribution might be unsuitable when the prevalence is close to 0% or close to 100% since the approximation might lead to confidence intervals lower than 0% or higher than 100%. Moreover, when the prevalence of resistance is less than 5% using the link between the F-distribution and the binomial distribution yield different confidence intervals compared to those obtained from the normal approximation and should accordingly be preferred.

Table AP3 I. Cut-off values (mg/L) defining resistance used for antimicrobial susceptibility testing of bacteria. Isolates with MIC higher than the given values are considered resistant.

Substance	*Salmonella enterica*	*E. coli (indicator)*	*E. coli (pathogen; pig)*	*E. coli and Klebsiella (pathogen; cattle, horse)*	*E. coli (pathogen; dog, cat)*	*Enterococci (indicator)*	*Streptococcus zooepidemicus*	*Streptococcus dysgalactiae Streptococcus uberis*	*Staphylococcus intermedius*	*Staphylococcus aureus*	*Brachyspira*	*Campylobacter*
Amoxicillin/clavulanic acid[1]	>8	>16										
Ampicillin	>8	>8	>8	>8	>8	>8	>8					>16
Apramycin	>32	>32										
Avilamycin						>16		>16		>16		
Bacitracin[2]						>32						
Ceftiofur	>2	>2	>2	>2			>2					
Cephalothin	>16							>1	>2	>1		
Chloramphenicol	>16	>16	>16	>16	>16		>8	>8	>16	>16		
Clindamycin							>4	>4	>4	>4		
Enrofloxacin	>0.25	>0.25	>0.25	>0.25	>0.25				>0.5			>1
Erythromycin						>4	>4	>2	>4	>2		>16
Flavomycin						>32						
Florfenicol	>16	>16	>16	>16			>16					
Gentamicin	>8	>8	>8	>8	>8	>512			>4	>4		>8
Nalidixic acid	>16	>16										>16
Narasin						>2						
Neomycin	>8	>8	>16	>8	>8	>1024			>32	>32		
Nitrofurantoin			>32	>32	>32				>32			
Oxacillin									>1	>2		
Penicillin							>1	>0.25	[4]	[4]		
Spiramycin							>16	>16	>16	>32		
Streptomycin	>32	>32	>32	>32	>32	>1024				>32		
Sulphamethoxazole	>256	>256										
Tetracycline	>8	>8	>8	>8	>8	>8	>8	>8	>8	>8		>8
Tiamulin											>2	
Trimethoprim	>8	>8										
Trimethoprim/sulfamethoxazole[3]	>0.5		>4	>4	>4		>4	>4	>2	>2		
Tylosin											>16	
Vancomycin						>16		>16		>16		
Virginiamycin						>8		>4		>4		

[1] Concentration of amoxicillin given, tested with clavulanic acid in concentration ratio 2/1; [2] MIC in U/mL; [3] Concentration of trimethoprim given, tested with sulfamethoxazole in concentration ration 1/20; [4] β-lactamase production.

Appendix 4: Antimicrobial agents licensed

ANTIMICROBIAL AGENTS licensed for therapy in veterinary medicine in Sweden year 2003 are listed in Table AP4 I.

Only substances licensed for systemic, oral, intrauterine or intramammary use are included (ATCvet codes QJ, QG, QA and QP). Data from FASS VET. 2003. For explanation of ATCvet code, see Appendix 2.

Table AP4 I. Antimicrobial agents authorised for therapeutic use in cattle, pigs, poultry, horses, dogs and cats in Sweden, 2003. Routes of administration are indicated[1].

		Animal species					
Antimicrobial agent	ATCvet code	Cattle	Pigs	Poultry	Horses	Dogs	Cats
Tetracyclines							
Doxycycline	QJ01A A02		O			O	O
Oxytetracycline	QJ01A A06, QG51A A01	I O U	I O U	O		O	O
ß-lactams, penicillins							
Ampicillin	QJ01C A01	O	O		O	O	O
Amoxicillin	QJ01C A04		I			I O	O
Penicillin G, potassium/sodium	QJ01C E01	I	I		I		
Penicillin G, procaine	QJ01C E09	I	I		I	I	I
Penicillin G, penethamathydroiodide	QJ01C E90	I					
Amoxicillin/Clavulanic acid	QJ01C R02		I			I O	I O
ß-lactams, cephalosporins							
Cephalexin	QJ01D A01					O	
Cefadroxil	QJ01D A09					O	O
Ceftiofur	QJ01D A90	I					
Sulphonamides /Trimethoprim							
Sulphadiazine/Trimethoprim	QJ01E W10	I	I		I O	O	O
Sulphadoxine/Trimethoprim	QJ01E W13	I	I		I		
Sulphonamides							
Formosulphatiazole	QA07A B90	O	O		O	O	O
Sulphaclozin	QP51A G04			O			
Macrolides							
Spiramycin	QJ01F A02	I					
Tylosin	QJ01F A90	I	I O	O		I	I
Lincosamides							
Clindamycin	QJ01F F01					O	O
Pirlimycin	QJ51F F90	M					
Aminoglycosides							
Gentamicin	QJ01G B03				I U	I	I
Dihydrostreptomycin (DHS)	QA07A A90	O U	O U		O U	O	O
Fluoroquinolones							
Enrofloxacin	QJ01M A90	I	I	O		I O	I O
Danofloxacin	QJ01M A92	I	I				
Marbofloxacin	QJ01M A93					O	O
Orbifloxacin	QJ01M A95					O	
Pleuromutilins							
Tiamulin	QJ01X X92		I O				
Combinations							
Penicillin G, procaine/DHS	QJ01R A01, QJ51R C23	I M	I		I	I	I
Penicillin G, benzatin/DHS	QJ51R C24	M					
Penicillin G, ester/Framycetin	QJ51R C25	M					
Penicillin G, ester/DHS	QJ51R C25	M					

[1] O = oral; I = injection; U = intrauterine; M = intramammary.

Appendix 5: References

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