SVARM 2007

Swedish Veterinary Antimicrobial Resistance Monitoring

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Preface

WELCOME to the eighth Swedish report combining results from the monitoring of antimicrobial resistance and antimicrobial usage in both veterinary and human medicine: SVARM and SWEDRES. These joint reports facilitate comparisons of resistance levels and incidence of use in the two areas.

International reports of transmission of MRSA between pigs and humans and our own experience of outbreaks affecting dogs and personnel in small animal hospitals further emphasize the zoonotic potential of antibiotic resistance and need for continuous close collaboration between human and veterinary medicine. Many questions remain to be answered such as the potential importance of transmission of some types of resistance via the food-chain or the environment.

According to the zoonosis-monitoring directive adopted in the EU in 2003, surveillance of antimicrobial resistance shall comprise zoonotic organisms such as *Salmonella* and *Campylobacter* isolated from food producing animals and from food. SVARM will therefore in the near future be extended to bacteria isolated from food of animal origin. This work will be initiated in collaboration between SVA and the National Food Administration.

The zoonosis directive also indicates that resistance in bacteria such as *E. coli* and enterococci isolated from healthy animals and food is of public health interest. Such indicator bacteria constitute a reservoir of resistance genes that may be transferred to pathogenic bacteria in animals and man and are therefore routinely monitored in SVARM.

In addition, data on resistance in animal pathogens isolated from diagnostic samples, and data on use of antimicrobials in animals is based on sales statistics from Apoteket AB (National Corporation of Pharmacies) is routinely presented. In 2005, SVARM was extended by SVARMpat, a monitoring programme run in collaboration between SVA and the Swedish Animal Health Service and financed by the Swedish Board of Agriculture. SVARMpat focuses on bacteria causing disease in pigs, cattle, sheep or poultry.

Data in this and previous reports indicate that the Swedish strategies in human and veterinary medicine have been comparatively successful in containing resistance. But some of the presented results are cause for concern. In veterinary medicine the rapid emergence and spread of multiresistant methicillin-resistant *Staphylococcus (pseud)intermedius* within and between small animal hospitals is a serious animal health problem, as the options left for treatment are scant.

To preserve the effectiveness of available antimicrobials, continuous efforts are needed in all sectors. In human medicine, such work is initiated and co-ordinated by Strama. In 2007, Strama VL, a network with a similar remit in the veterinary and food sector has been initiated. The network is supported by a secretariat founded at SVA. Strama VL will provide a platform for all stakeholders to exchange information, analyze problems, pinpoint solutions and initiate prioritized activities. Our hope is this report, produced in collaboration between the Section of Antibiotics and Strama VL, will contribute to that work and that the information, when needed, is translated into action.

Summary

THE EIGHT REPORT FROM SVARM shows that the situation regarding antimicrobial resistance in bacteria of animal origin remain favourable from an international perspective. The situation can rapidly change however, as illustrated by emergence of methicillin-resistant *Staphylococcus aureus* (MRSA) in companion animals and methicillin-resistant *Staphylococcus (pseudo)intermedius* (MRSP) in dogs. These findings are cause for concern from a zoonotic and an animal health perspective, respectively, and emphasize the need for continuous vigilance in this dynamic field.

The total amount of antimicrobials used for animals 2007 was 17 106 kg, which is similar to year 2000. The amount of antimicrobials for in-feed or in-water medication has decreased by 94% since 1984 and is today but 13% of the total sales. However, from year 2004, an increase in sales of pleuromutilins, macrolides and tetracyclines formulated for in-feed or in-water medication is noted. These products are mainly used for medication of groups of pigs, and among plausible explanations for this trend are increased problems with acute respiratory infections caused by *Actinobacillus pleuropneumoniae*. The sales of products for medication of individual animals have remained relatively unchanged over the last decade. Trends in the sales of certain classes, such as the cephalosporins, are heavily influenced by use for dogs. Until year 2007, the sales of this increased steadily. However, in 2007 a decrease by 22% compared with the previous year is noted.

In aquaculture, a prominent decrease in use of antimicrobials over time is noted. Over the last eight years, the total amounts prescribed have been around or below 40 kg and in year 2007 the estimated number of daily doses per kg was only 3% of the number in year 1995. The marked reduction correlates with an increased use of effective vaccines.

Methicillin-resistant *Staphylococcus aureus* (MRSA) was in 2007 isolated from a horse. The isolates belonged to *spa*-type t011. This is the first confirmed finding of MRSA in horses in Sweden. In 2007, five MRSA (*spa*-type t032) from dogs were confirmed and in the beginning of 2008 another isolate, with a different *spa*-type (t127), from a dog was confirmed. In total eight cases in dogs and one case from a horse have been confirmed since the first isolation of MRSA in animals in Sweden 2006.

Salmonella is rare in Swedish farm animals, most probably a result of the strategies in the Swedish *Salmonella* control programme. Few incidents involve strains resistant to antimicrobials. This year, seven of seventy-one incidents in major food producing animals involved resistant strains. Three of these strains were multiresistant *Salmonella* Typhimurium (DT104, 120 or NT). No isolate from companion animals or wildlife was multiresistant. Resistance to fluoroquinolones or third generation cephalosporins was not observed in isolates from food producing animals.

Indicator bacteria, i.e. *Escherichia coli* and *Enterococcus* spp. from the intestinal flora of healthy animals, are monitored since resistance in the normal gut flora reflects the antimicrobial selective pressure in an animal population. By using harmonised methodology, data on resistance can be compared on an international level and over time. Thereby valid conclusions on trends in resistance can be made. This year, indicator bacteria from broilers were monitored. In agreement with the limited use of antimicrobials effective against *E. coli* in this animal species, resistance was rare and few isolates were multiresistant. No isolate of *E. coli* was resistant to third generation cephalosporins by production of extended spectrum beta-lactamases (ESBL). Resistance in enterococci was more common but there are no trends towards a higher prevalence of resistance neither in *Enterococcus faecalis* nor in *E. faecium*. Instead, resistance to tetracycline or virginiamycin has declined in *E. faecium* over the period studied in SVARM.

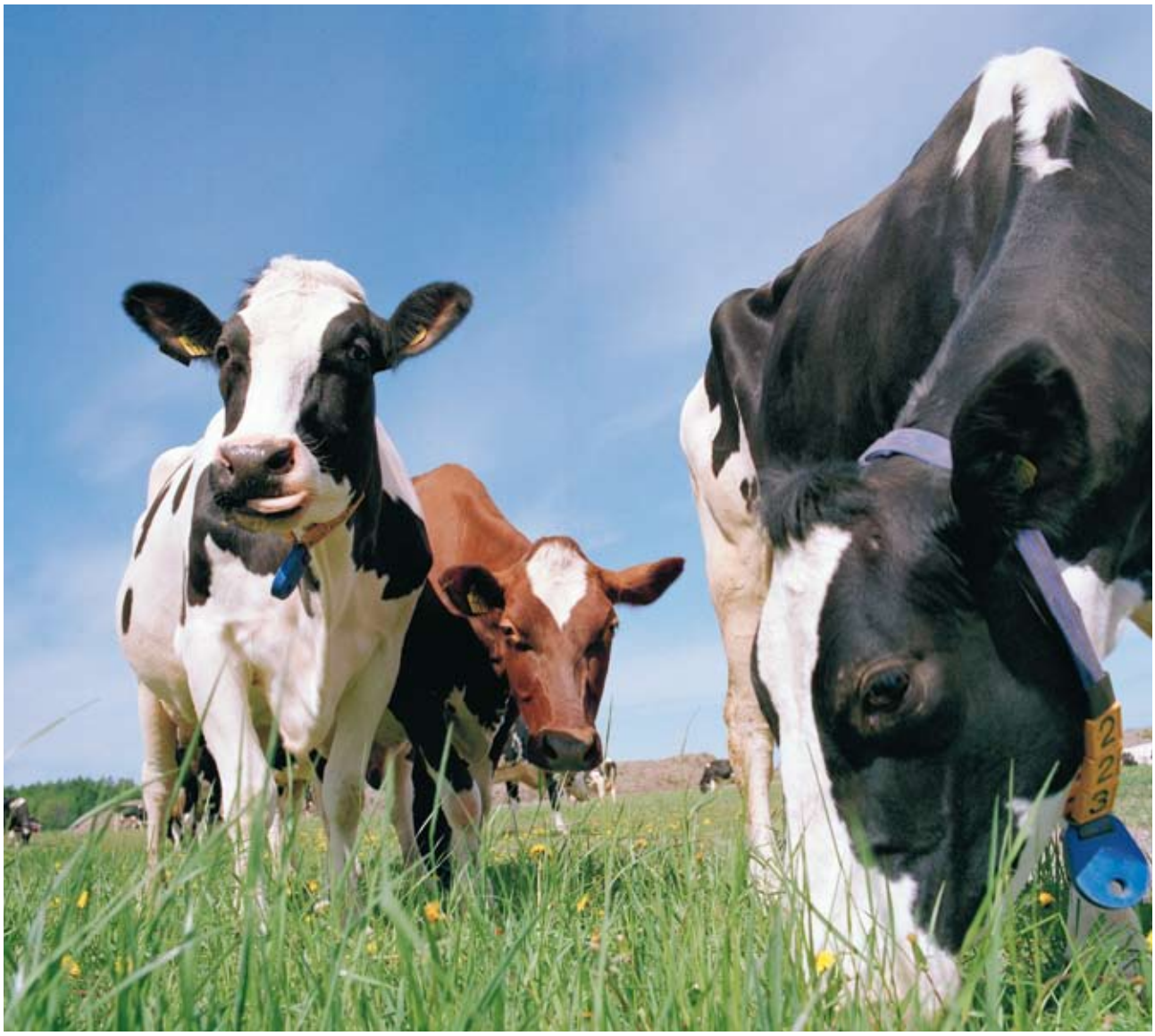
Vancomycin resistant enterococci (VRE) were isolated from 27% of 339 samples of intestinal content from broilers when cultured on media supplemented with vancomycin. The proportion of samples positive for VRE is of the same magnitude as in 2006 but lower than in 2005. This indicates that the gradual increase in prevalence of VRE observed 2000-05 has levelled off.

Escherichia coli from diagnostic submissions were often resistant to ampicillin, streptomycin, tetracycline or trimethoprim-sulphonamides, irrespective of source (pig, horse, dog, and cat). Resistance to these substances also occurred in *E. coli* from poultry, but the frequencies of resistance were lower. Multiresistance commonly involved these substances with prevalence ranging from 1% in isolates from poultry to 26% in isolates from pigs.

In ***Brachyspira*** spp. from pigs, resistance to tiamulin occurred in *B. pilosicoli* but was not observed in *B. hyodysenteriae*. The majority of both *B. pilosicoli* and *B. hyodysenteriae* were resistant to tylosin.

Resistance was rare in ***Actinobacillus pleuropneumoniae*** and in ***Pasteurella multocida*** from the respiratory tract of pigs as well as in ***Pasteurella* spp.** from the respiratory tract of calves.

Staphylococcus aureus from milk of ewes with clinical mastitis were mostly susceptible to antimicrobials. Only one isolate was resistant to penicillin through penicillinase production.



Streptococcus zooepidemicus from the respiratory tract of horses were uniformly susceptible to penicillin, but resistance to trimethoprim-sulphonamides was common.

Most ***Staphylococcus intermedius*** from dogs were resistant to penicillin. Resistance to clindamycin, erythromycin, fusidic acid, streptomycin or tetracycline was also common (between 18 and 32%). One third of *S. intermedius* were multiresistant and 6% were resistant to at least five antimicrobials.

Methicillin-resistant *Staphylococcus (pseudo)intermedius* (MRSP) in Swedish dogs were confirmed for the first time in 2006. During 2007, six times more MRSP were confirmed than in 2006. A majority of these, in total 100 isolates, have the same antibiogram and molecular typing indicate that they belong to the same clone. Most of the isolates are from dogs and spread throughout Sweden.

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Sammanfattning

DEN ÅTTONDE SVARM-RAPPORTEN visar att läget när det gäller antibiotikaresistens hos bakterier från djur är fortsatt gynnsamt ur ett internationellt perspektiv. Men påvisandet av meticillinresistent *Staphylococcus aureus* (MRSA) och meticillinresistent *Staphylococcus (pseudo)intermedius* (MRSP) hos sällskapsdjur visar att situationen snabbt kan förändras. Dessa bakterier är av betydelse från ett zoonotisk respektive ett djurhälsoperspektiv och uppträdandet bland svenska djur belyser betydelsen av vaksamhet för oönskade trender inom detta dynamiska område.

Den totala förbrukningen av antibiotika till djur var 2007 17 106 kg, vilket är i samma storleksordning som under år 2000. Volymen antibiotika för inblandning i foder eller vatten har minskat med 94 % sedan 1984 och utgör idag endast 13 % av den totala försäljningen. Men från och med 2004 har försäljningen av pleuromutiliner, makrolider och tetracykliner för inblanding i foder eller vatten ökat. Denna typ av produkter används i första hand för att behandla hela grupper av grisar, och bland tänkbara förklaringar av den ökande trenden är ökade problem med luftvägsinfektioner orsakade av *Actinobacillus pleuropneumoniae*. Försäljningen av produkter för behandling av enstaka djur har däremot varit relativt stabil under de senaste tio åren. Trender vad gäller vissa typer av antibiotika, som cefalosporiner, påverkas mycket av förskrivning för hundar. Fram till år 2007 ökade försäljningen stadigt, men har under året minskat med 22%.

Inom fiskodlingen noteras en kraftig minskning av användningen av antibiotika. Under de senaste åtta åren har den totalt förskrivna mängden årligen uppgått till kring 40 kg eller mindre. Uppskattningar visar att under 2007 var antalet dygnsdoser endast 3% av antalet 1995. Minskningen korrelerar till ökad användning av effektiva vacciner.

Meticillinresistent *Staphylococcus aureus* (MRSA) isolerades 2007 för första gången i Sverige från en häst. Isolatet var av *spa*-typ t011. Under 2007 konfirmerades dessutom fem fall av MRSA (*spa*-typ t032) hos hund och ytterligare ett fall i början av 2008 (*spa*-typ t127). Sedan MRSA för första gången påvisades hos djur i Sverige 2006 har därmed sammanlagt åtta fall konfirmerats hos hundar och ett fall hos häst.

Salmonella är ovanligt hos svenska djur vilket sannolikt är en effekt det svenska salmonellakontrollprogrammet. Antibiotikaresistenta stammar förekommer sällan. Under 2007 orsakades endast sju av de 71 utbrotten hos livsmedelsproducerande djur av resistenta salmonellabakterier. Vid tre av utbrotten isolerades multiresistent *Salmonella* Typhimurium (DT104, 120 eller NT). Inget isolat från sällskapsdjur eller vilda djur var multiresistent och inget isolat från livsmedelsproducerande djur var resistent mot kinoloner eller cefalosporiner.

Resistensläget hos indikatorbakterier (*Escherichia coli* och *Enterococcus* spp.) från tarmfloran hos friska djur anses återspegla det selektionstryck som antibiotikaanvändningen i en djurpopulation innebär. Undersökningar av indikatorbakterier med harmoniserad metodik är värdefulla eftersom resultaten kan utvärderas över tid och resistensläget i olika länder jämföras. Under 2007 undersöktes indikatorbakterier från slaktkyckling. Resistens var ovanlig bland *E. coli* och få isolat var multiresistenta. Inget isolat var resistent mot tredje generationens cefalosporiner genom produktion av beta-lakamas med utökat spektrum (ESBL). Detta är i överensstämmelse med att antibiotika verksamma mot *E. coli* används i mycket liten utsträckning till slaktkyckling. Bland enterokocker var resistens vanligare, men inga trender mot ökad förekomst kan ses, varken hos *Enterococcus faecalis* eller *E. faecium*. Däremot har resistens mot tetracyklin och virginiamycin minskat hos *E. faecium* under den period som undersökts i SVARM.

Vankomycinresistenta enterokocker (VRE) isolerades från 27 % av 339 prov av tarminnehåll från slaktkyckling. Proven odlades på odlingsmedier med tillsats av vankomycin. Andelen positiva prov är av samma storleksordning som 2006 men lägre än 2005. Detta tyder på att den ökning av VRE-förekomst hos slaktkyckling som observerats sedan år 2000 har brutits.

Escherichia coli från kliniska prov från grisar, hästar, hundar och katter var ofta resistenta mot ampicillin, streptomycin, tetracyklin eller trimetoprim-sulfa. Resistens mot dessa substanser förekom även hos E. coli från värphöns men förekomsten var låg. Frekvensen multiresistens varierade beroende på djurslag och var lägst (1 %) hos isolat från värphöns och högst (25 %) hos isolat från grisar.

Hos ***Brachyspira pilosicoli*** från grisar förekom resistens mot tiamulin men däremot inte bland ***B. hyodysenteriae***. Majoriteten av såväl *B. pilosicoli* som *B. hyodysenteriae* var resistenta mot tylosin.

Hos ***Actinobacillus pleuropneumoniae*** och ***Pasteurella multocida*** från luftvägarna hos grisar liksom hos ***Pasteurella* spp**. från kalvar med luftvägssjukdom var resistens ovanlig.

Resistens hos ***Staphylococcus aureus*** från mjölk från tackor med klinisk mastit var ovanligt. Endast ett isolat (4 %) producerade beta-laktamas och var därigenom resistent mot penicillin.

Streptococcus zooepidemicus från luftvägarna hos hästars var genomgående känsliga för penicillin men resistens mot trimetoprim-sulfa var vanlig.

Staphylococcus intermedius från hundar var i stor utsträckning resistenta mot penicillin. Resistens mot klindamycin, erytromycin, fusidinsyra, streptomycin eller tetracyklin var också vanlig (mellan 18 och 32 %). En tredjedel av *S. intermedius* var multiresistenta och 6 % var resistenta mot minst fem antibiotika.

Meticillinresistenta *Staphylococcus (pseud)intermedius* (MRSP) från svenska hundar konfirmerades för första gången 2006. Under 2007 var antalet fall av MRSP sex gånger fler än 2006. Majoriteten av de sammanlagt 100 MRSP-isolaten har samma antibiogram och molekylärbiologisk typning tyder på att de tillhör samma klon. De flesta isolaten kommer från hundar och är från i stort sett hela Sverige.

Tack

Många personer har på olika sätt varit involverade i arbetet med SVARM. Vi vill tacka alla som bidragit och särskilt:

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Use of antimicrobials

THROUGH AN INITIATIVE by SVA and Apoteket AB (the National Corporation of Swedish Pharmacies), statistics on total sales of antimicrobials 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.

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 no longer authorised.

Drug statistics are based on sales figures provided by Apoteket AB and represent the total sales of antimicrobials authorised for veterinary use, calculated to kg active substance. These figures include antimicrobial formulations for all animal species (food producing animals, pets and horses etc) for systemic, intramammary and obstetric use, and intestinal anti-infectives. Drugs authorised for human use but prescribed for animals are not included. Such antimicrobials are almost exclusively prescribed in small animal medicine. In 2005, 8% of the total number of the antimicrobials prescribed for dogs was of products for human use (ATC group J01; SVARM 2005).

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 amounts of drugs dispensed by pharmacies and a new system for retrieval of data was introduced. In both systems, data represent an approximation on the real usage of antimicrobials, assuming that the amount sold is also used during the observation period.

Details on animal numbers are found in Appendix 1, on methodology in Appendix 2 and on antimicrobial agents with general marketing authorisation in Sweden in Appendix 4.

Overall use of antimicrobials

The total yearly sales of antimicrobials over the last decade are presented in Table AC I and in Figure AC I a & b the long-term trends from year 1980 for classes that are currently used are illustrated. Figures on antimicrobials formerly used as feed additives are given for 1984 in Table AC III and for other years in SVARM 2000. In chickens, ionophoric antimicrobials 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, figures on the sales of these products, based on data from feed mills, are given under the section on group treatment (see Table AC III).

The lower total figures shown for years 2003-2005 are uncertain, as there was a change in the system for data retrieval in year 2003. It is possible that initially, part of the sales of antimicrobials sold with special licence prescription was not captured by searches in the new system. Data collection for these products was made through specified searches for individual products, which in turn depended on knowledge of what specific products to search for. This problem has been addressed, and from year 2006 all products dispensed should be captured in the searches. In year 2007, sales of products with special licence prescription amounted to 11% of the total sales, 59% of which was tetracyclines.

The potency of different antimicrobials is not equal and therefore each class should be evaluated separately. Nonetheless, the total figures may indicate trends in the material. In the five year's period from 2003 to 2007, the total amounts sold have increased slightly. Changes in the number

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

ATCvet code	Antimicrobial class	1998	1999	2000	2001	2002	2003	2004	2005	2006	2007
QJ01AA, QG01A	Tetracyclines[a]	2 897	2 251	1 754	1 453	1 415	1 307	1 329	1 562	1 516	1 853
QJ01CE, QJ01R, QJ51	Penicillin G-and V[b]	8 547	8 692	8 254	8 414	8 179	7 579	7 814	7 571	7 860	7 582
QJ01CA, QJ01CR	Aminopenicillins	824	809	852	752	767	870	875	911	920	927
QJ01D, QJ51CA	Other betalactams	133	245	315	474	676	832	928	1 009	1 217	954
QA07AA, QJ01G, QJ01R, QJ51R	Aminoglycosides and polymixins[a]	930	846	797	770	753	645	606	762	750	718
QA07AB, QJ01E	Sulphonamides	2 345	2 403	2 338	2 485	2 477	2 326	2 462	2 535	2 543	2 427
QJ01E	Trimethoprim & derivatives	390	397	390	414	414	381	406	437	450	438
QJ01F	Macrolides & lincosamides	1 846	1 467	1 352	1 510	1 412	1 124	1 095	1 080	1 254	1 520
QJ01MA	Fluoroquinolones	175	155	156	182	185	184	187	184	195	180
QJ01XX92, QJ01XX94	Pleuromutilins	1 032	847	871	841	988	744	387	338	459	506
QJ01XX91	Streptogramins[c]	150	125	-	-	-	-	-	-	-	-
Total		**19 269**	**18 237**	**17 079**	**17 295**	**17 266**	**15 992**	**16 089**	**16 389**	**17 164**	**17 106**

[a] Includes drugs marketed with special licence prescription for years 2000-2006; [b] Calculated as benzyl-penicillin; [c] From 1986 sold only on veterinary prescription at therapeutic dosages.

Figure 1a

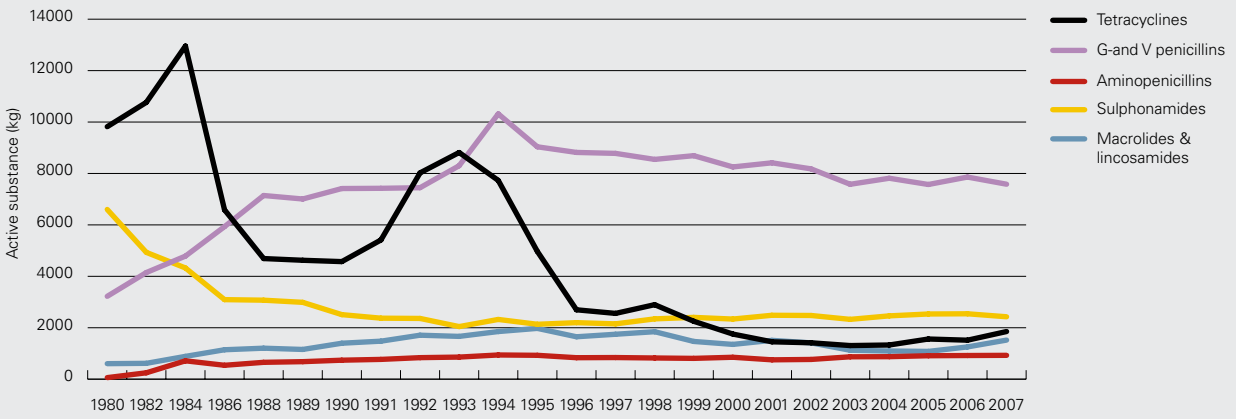

Figure 1b

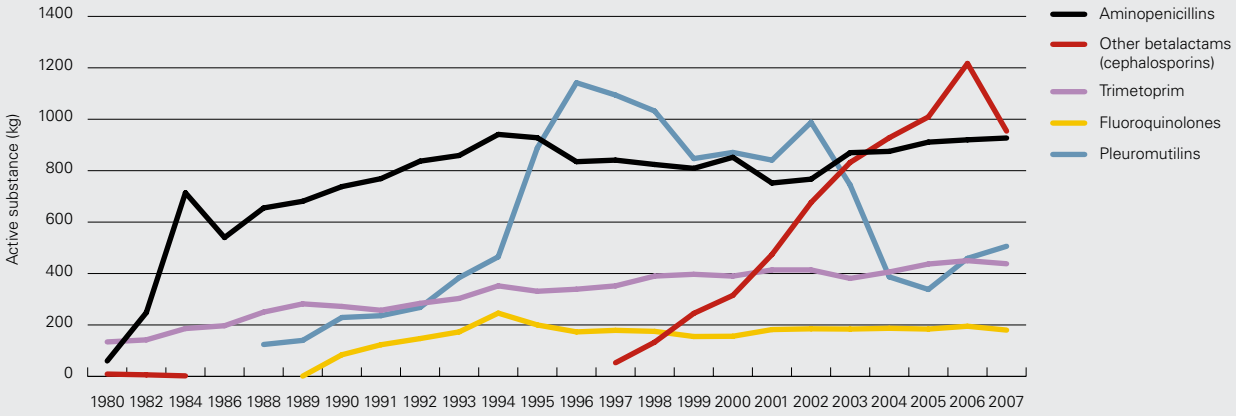

Figure AC I a & b. Sales of antimicrobials for animals from 1980-2007. Amfenicols, nitromimidazoles, streptogramins, quinoxalines and other feed additives were withdrawn from the market during the time period and are not shown. Note that the scales on the Y-axis are different in figure a and b.

of animals may affect trends in statistics on use of antimicrobials. In year 2007, the numbers of cattle and pigs slaughtered were 7 and 9% lower than in year 2003, respectively, while the number of slaughtered broilers was roughly unchanged. Thus, the overall use per animal may have increased over the last five years.

The sales of tetracyclines, 'macrolides and lincosamides' and pleuromutilins, have increased notably in the last three to four years (by 19, 41 and 50%, respectively). These antimicrobials are mainly used for pigs, and mainly in feed or in water (66-92% of the sales per class). As noted above, the pig population has decreased over the last five years and the increase therefore probably reflects a true increase in sales. This is further commented under 'Treatment of groups or flocks'.

In year 2007 about 12% of the total sales of veterinary products (2000 kg) were prescribed for use in dogs and cats in 'out-patient care'. Trends in the use of certain classes are highly influenced by this use. This is the case for the previous increase, 97% of which consisted of first generation cephalosporins in 2007.

Treatment of individual animals

In table AC II, the sales of products for use in individual animals, excluding topical, intrauterine and intramammary use are presented. In year 2007, this subset was 82% of the overall use. The total sales in this subset have been relatively unchanged over the last decade.

The sales of intestinal anti-infectives for individual have declined by 37% since year 2003. Products in this ATCvet category contain either aminoglycosides or certain formulations of sulphonamides. The decrease is explained by changes in sales of products of the latter type, which today are not generally available on the Swedish market but are sold with special licence prescriptions.

Since 1998, the sales of penicillins for individual use have decreased by 10%. The main indication for penicillins is treat-

Table AC II. Yearly sales of antimicrobial drugs authorised for individual treatment expressed in kg active substance. Only products for systemic use (QJ01) or for use as intenstinal anti-infective (QA07) are included. Based on sales statistics from Apoteket AB.

ATCvet code	Antimicrobial class	1998	1999	2000	2001	2002	2003	2004	2005	2006	2007
QA07A	Intestinal anti-infectives[a]	649	607	587	614	594	594	586	496	434	372
QJ01A	Tetracyclines	656	695	634	623	628	606	611	623	609	632
QJ01C	Penicillins[b, c]	9 287	9 424	9 037	9 095	8 894	8 406	8 644	8 404	8 686	8 403
QJ01D	Cephalosporins	133	245	315	474	676	832	928	1 009	1 212	950
QJ01E	Sulfonamides & trimethoprim	2 335	2 376	2 336	2 478	2 483	2 280	2 427	2 610	2 689	2 619
QJ01F	Macrolides & lincosamides	645	559	531	522	477	430	382	400	417	413
QJ01G	Aminoglycosides[c, d]	535	528	474	454	460	367	344	362	345	343
QJ01M	Fluoroquinolones	150	144	150	169	178	177	180	179	190	177
QJ01X	Pleuromutilins	64	52	56	48	49	77	32	29	39	36

[a] Drugs marketed with special licence prescription are included from year 2000; [b] Procaine-penicillin calculated to benzyl-penicillin; [c] The amount includes QJ01R; [d] Does not include QA07A, intestinal anti-infectives.

ment of mastitis in dairy cows. Over the same time period, the number of dairy cows has decreased by 20%. Thus, the overall use per animal may have increased, and in particular it is possible that the use of penicillins for other animals than dairy cows (eg. pigs or horses) has increased.

Up until year 2007, the use of cephalosporins for individual use has increased steadily. In 2007, however, the use of cephalosporins decreased by 22%. Changes within this group are almost entirely explained by the amounts prescribed for dogs (see SVARM 2005 for statistics on use for dogs).

The sales of sulphonamides and trimethoprim for individual use have increased steadily over time, but seem to have stabilised from year 2005. In year 2007, 75% of the sales of the combination sulphonamides and trimethoprim were products for oral use in horses (paste or powder). This type of products was introduced on the market in the late 80s, and since, most of the increasing trend in use of trimethoprim and sulphonamides (Figure ACI a & b) is derived from that type of products. In year 2007, a total number of 110 632 doses (dose applicators or powders) of this type of products was sold. The equine population was estimated to around 265 000-300 000 horses in year 2004. Using that figure, the approximate incidence of use is 369-417 doses/1000 horses. Trimethoprim-sulphonamides is the only class of antimicrobials available for oral use in adult horses, and the convenience of the route of administration probably influences the veterinarian's choice of treatment.

Treatment of groups or flocks

When considering the risk for development of resistance, the consumption of antimicrobials intended for group or flock medication, e.g. administration via feed or water, is of special interest. Figures on sales of that subset of drugs over the last decade are given in Table AC III. As a reference, figures for 1984, the last year before the ban of antimicrobials feed additives (growth promoting use), are given. More complete data sets for previous years are available in SVARM 2000. From year 2005, products of the class 'intestinal anti-infectives' that are sold with a special licence prescription are included. The active substances in products in that group are currently neomycin or colistin.

Overall, the sales of products intended for medication of groups of animals have decreased by 94% since 1984, and is today but 13% of the total sales (total sum of Table AC III divided by total sum of Table I). Products for group treatment are mainly used in pigs except those with penicillins that are used for poultry and for those with fluoroquinolones that are used for poultry but also in minor quantities for other species. The number of pigs slaughtered has varied somewhat over the years, and was 16% lower in year 2007 than in 1990, and 10% lower than in 2004.

In Figure AC II, the development of sales of veterinary medicines and antimicrobial feed additives (before 1986) is shown. Substances grouped as 'others' are the feed additives and other substances that are no longer available on the market (e.g. nitroimidazoles). The figure shows a prominent decrease over the 90s, but from year 2004, an increase year by year can be noted. Two methodological factors could partly contribute to the apparent increase. Firstly, intestinal anti-infectives for medication of groups are included in the statistics from year 2004. Secondly, as noted previously the retrieval system was changed in 2003 and it cannot be excluded that part of the sales of drugs with special licence prescription were initially not captured by the system. However, none of these factors would affect the figures on sales of macrolides or pleuromutilins. The observed increases in these two groups, and also at least partly of the tetracyclines, therefore probably reflect a true increase in use of antimicrobials for group medication.

The sales of pleuromutilins have increased from year 2004, but the figures are still considerably lower than in earlier years. Pleuromutilins (tiamulin, valnemulin) are authorised for use in pigs with swine dysentery as the main indication. It is probable that efforts to control the disease have resulted in a decreased need to treat swine dysentery, leading to overall declining sales figures since 1998. Increases in use of pleuromutilins in certain years may be related to a temporary, but extensive, use within programmes for eradication of swine dysentery.

The use of macrolides has increased by around 60% since the years 2003-2005. Trends in use of the class of tetracyclines are confounded by the fact that use of doxycycline has increased steadily over the last six years. Doxycycline has a higher bioavbailability, and the dose is lower (250 ppm when mixed in feed) compared with that for, e.g. chlortetracycline (1000 ppm when mixed in feed). Dose and population corrected figures on sales of tetracyclines indicate that use of this class has more than doubled since year 2003 (Figure AC III).

Several factors are likely to contribute to the observed

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

ATCvet code	Antimicrobial class	1984	1998	1999	2000	2001	2002	2003	2004	2005	2006	2007
QA07A	Intestinal anti-infectives[a]				-	-	-	-	-	163	170	158
QJ01A	Tetracyclines[b]	12 300	2 230	1 545	1 111	822	777	695	712	934	903	1217
QJ01C	Penicillins	-			-	-	-	-	-	-	11	28
QJ01F	Macrolides & lincosamides	607	1 201	908	821	988	935	694	713	680	837	1 107
QJ01M	Fluoroquinolones	-	25	11	7	13	7	8	7	5	5	3
QJ01M	Quinoxalines[c]	9 900			-	-	-	-		-	-	-
QJ01XX91	Streptogramins[c]	8 800	150	125	-	-	-	-		-	-	-
QJ01XX92, QJ01XX94	Pleuromutilins	-	969	795	815	793	939	667	355	309	420	471
QP51AA	Nitroimidazoles	1 440	-	-	-	-	-	-	-	-	-	-
	Feed additives[d]	700	-	-	-	-	-	-	-	-	-	-
QP51AH	Ionophoric antibiotics (coccidiostats)[e]	7 900	8 267	11 643	9 368	10 019	8 439	10 920	10 486	11 095	12 335	12 527

[a] Drugs with special licence prescription are included from year 2005; [b] Drugs marketed with special licence prescription are included from year 2000; [c] Years 1980-1984 sold as feed additives, thereafter on veterinary prescription at therapeutic dosages; [d] Feed additives other than quinoxalines and streptogramins: avoparcin, bacitracin, nitrovin, oleandomycin and spiramycin; [e] 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).

increases in use of group treatments for pigs. The average herd size has increased over time. In larger herds, the risk for spread of bacterial infections could be increased, and for practical reasons the veterinarian may be more inclined to prescribe group treatments instead of individual treatments. However, the trend towards larger herds is not recent, and the observed increase in use was preceded by a decrease over several years. Two specific diseases have probably had more impact, possibly in interaction with the increased herd size. In later years, problems with acute respiratory infections caused by *Actinobacillus pleuropneumoniae* have increased. Further, postweaning multisystemic wasting syndrome (associated with porcine circovirus type 2, PCV2) was diagnosed for the first time in Sweden in year 2003. By December 2006, the cumulated number of affected herds was 123 (Wallgren et al., 2007). Group treatment with antimicrobials was used in 73 of these herds, though not all had identified other diseases judged to have a significant impact. In herds where no significant infections other than PCV2 were diagnosed, the treatments were mostly without observable effect.

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.

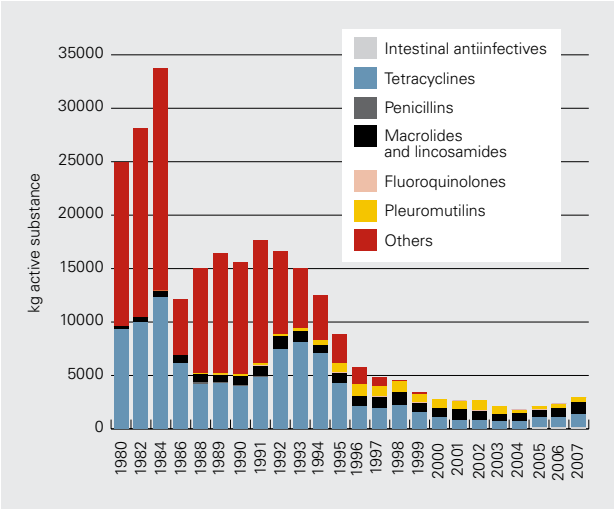

Figure AC II. Yearly sales of antimicrobial drugs authorised for group treatment measured as kg active substance (based on Table AC III and data from SVARM 2000)

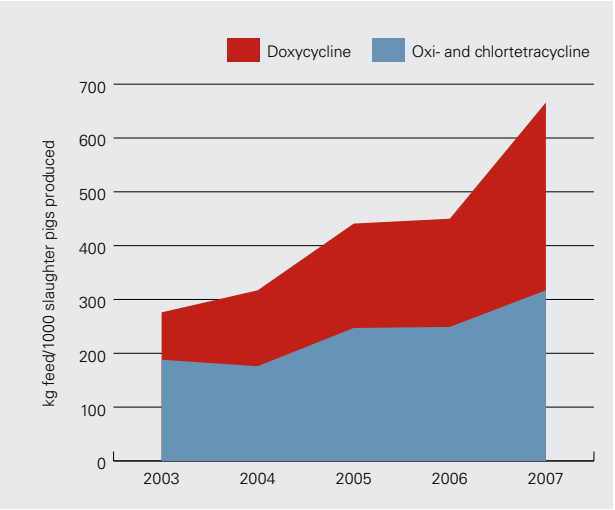

Figure AC III. Yearly sales of tetracyclines for group treatment calculated as kg feed per 1000 pigs slaughtered

Use of antimicrobials and antimicrobial resistance in aquaculture

Material included

Data on use of antimicrobials and occurrence of diseases are taken from the annual report by Fiskhälsan FH AB (Fish Health Control Program; www.fiskhalsan.se) and include prescriptions of antimicrobials for fish farmed for direct food production as well as for sports fishing (i.e. fish for stocking enhancement as well as recreation fishing). Details on methodology are given in Appendix 2.

Use of antimicrobials in aquaculture

In Table AQ I, statistics on yearly amounts of antimicrobials prescribed for use in farmed fish (fish for consumption and for sports fishing, defined as above) are shown. Table AQ II shows the amounts prescribed for in-feed medication divided per fish species. 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 licence prescription. The amounts used decreased notably in the beginning of the 90s and have during the last 8 years been around or below 40 kg active substance. Increases in individual years, such as in 2006, is usually linked to a summer season with water temperatures higher than average.

The potency of the various antimicrobials is not equal, which could confound the trends in total amounts prescribed. Figure AQ I shows an estimate of the number of daily doses per kg live weight of the amounts prescribed for in feed medication. A prominent decrease over time can be noted, and in year 2007 the number of daily doses per kg was only 3% of the number in year 1995. The amount of fish produced has been comparatively stable over the years, although the number of holdings has decreased. The marked reduction in use is correlated with an increased use of effective vaccines against two of the former main indications (see below).

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 AQ I). Treatment by immersion is used particularly for eel, a species that rapidly becomes anorectic when subject to bacterial infections.

Fiskhälsan FH AB estimates the total production of fish for consumption to 10 000 metric tons (live weight), and using that figure the total use of antibiotics in 2007 was around 1.6 g per ton fish produced. In year 2007, only 5% of the total amount prescribed was used for treatment of fish for consumption.

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 used in fish for consumption, and Fiskhälsan FH AB estimates that today, 85-90% of fish farmed in coastal areas are vaccinated. Treatment with antimicrobials for furunculosis is rarely needed. Likewise, treatments for vibriosis have declined considerably, but in the last years fishs in some holdings with unvaccinated fish have been treated. In recent years, the dominating indication for antimicrobial treatment has been flavobacteriosis in rainbow trout. In holdings where such treatments are needed, investigations aiming to optimise preventive strategies will be initiated.

Antimicrobial susceptibility of bacterial fish pathogens

To test antimicrobial susceptibility of bacteria from fish is a valuable tool to guide therapy in single incidents of disease but it is also important to compile available data and monitor susceptibility over time. Thereby trends in resistance that could

Table AQ I. 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	2002	2004	2005	2006	2007
In feed												
QJ01AA	Tetracyclines	992	108	128	47	32	2	16	2	10	13	10
QJ01BA	Amfenicols	0	0	0	0	3	5	10	7	4	12	5
QJ01EW	Trimethoprim-sulphonamides	0	130	19	87	-	-	-	-	-	-	-
QJ01MB	Quinolones	29	63	101	63	5	9	11	6	3	3	1
Intra-peritoneal												
QJ01EW	Trimethoprim-sulphonamides	-	<1	-	-	-	<1	-	<1	-	-	-
Immersion												
QJ01AA	Tetracyclines	-	20	5	3	-	<1	<1	-	-	-	-
QJ01MB	Quinolones	-	-	6	-	16	20	3	2	-	-	5
Total		**1 021**	**321**	**259**	**200**	**56**	**37**	**40**	**17**	**17**	**28**	**21**

Table AQ II. Yearly amounts (kg active substance) of antimicrobials prescribed 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	2004	2005	2006	2007
Rainbow trout	*Oncorhynchus mykiss*	36.3	28.5	7.1	15.9	22.8	9.9	7.3	11.7	20.8	11.3
Brown trout	*Salmo trutta*	2.8	5.7	2.8	4.3	6.7	5.9	5.3	3.1	3.5	2.7
Arctic char	*Salvelinus alpinus*	0.8	3.1	5.9	2.0	5.2	11.8	1.7	1.9	2.5	0.3
Other species		0.1	1.0	0.1	0.2	2.1	4.5	0.6	0.9	1.2	1.9
Total		**40.0**	**38.3**	**15.9**	**22.4**	**36.8**	**32.1**	**14.9**	**17.6**	**28**	**16.2**

be cause for re-evaluation of therapeutic recommendations or other interventions can be detected. However, until recently there have been no accepted standard reference methods for testing antimicrobial susceptibility of bacteria from fish and no accepted criteria (breakpoints/cut-off values) for interpretation of such data. Obviously published data on antimicrobial resistance in bacteria from fish is therefore scarce.

The lack of harmonized methodology was recognised in the late 90s and through an initiative within the EU a workshop on this issue was organised, eventually publishing draft protocols for antimicrobial susceptibility testing of bacteria associated with fish diseases (Alderman & Smith, 2001). The drafts were based on methods for testing bacteria from terrestrial animals issued by The Clinical and Laboratory Standards Institute (CLSI, formerly NCCLS). The drafts from the workshop were further elaborated by CLSI and recently guidelines on disc diffusion (CLSI 2006a) and broth dilution (CLSI 2006b) for susceptibility testing of bacteria from aquatic animals were issued. Interpretive criteria are still lacking, however.

In an effort to standardize susceptibility testing of bacteria from fish at SVA, a microdilution system for testing bacteria from warm-blooded animals, VetMIC™ (SVA, Uppsala, Sweden), was adapted to bacteria from fish according to the first recommendations issued by Alderman & Smith (2001). The methodology has been used since 2005 for routine testing of isolates from samples of clinical submissions. Data on minimum inhibitory concentrations (MIC) of *A. salmonicida* subsp. *achromogenes*, *Flavobacter columnare* and *Flavobacter psychrophilum* from these analyses are presented in Table AQ III. Most isolates represent a unique batch of fish but occasional isolates are duplicates within the same batch. The majority of *A. salmonicida* subsp. *achromogenes* and *F. columnare* are from brown trout, 57 and 72%, respectively, whereas the majority of *F. psychrophilum* are from rainbow trout (71%). Bacteriological culture and susceptibility testing was performed at the Department for Fish Diseases, SVA. For antimicrobials tested and range of dilutions see Table AQ III.

Interpretation of the data is hampered by the lack of accepted interpretative criteria. However, the shapes of the distributions of MICs can be evaluated for indications of the presence of isolates with deviating MICs, possibly due to acquired reduced susceptibility (resistance). In the present material, the distributions of gentamicin and streptomycin MICs for *A. salmonicida* subsp. *achromogenes* are examples of well defined unimodal distributions (Table AQ III). Such distributions indicate that none of the isolates tested have

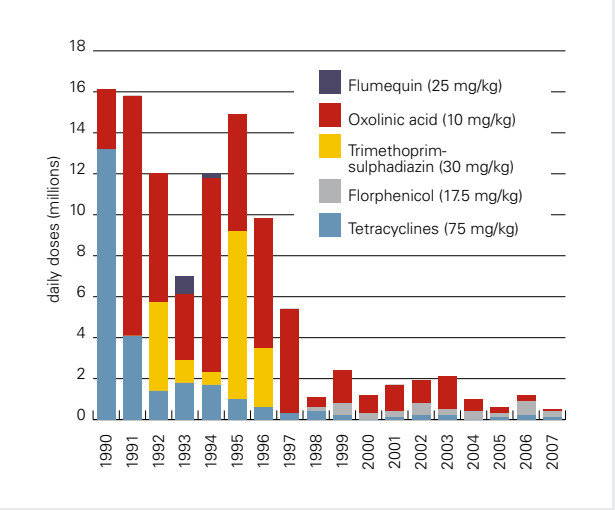

Figure AQ I. Amounts of antimicrobials prescribed for in feed medication expressed as estimated daily doses per kg liveweight. The doses used for the estimates are shown in brackets after the substance names.

acquired resistance to these antimicrobials, which is likely since the two antimicrobials are not used in fish in Sweden (Table AQ I).

In contrast, MIC distributions for the quinolones, i.e. nalidixic acid and ciprofloxacin or enrofloxacin, are bimodal in all three bacterial species. Moreover, isolates with an elevated MIC to nalidixic acid (≥16 mg/L) also had elevated MICs to ciprofloxacin or enrofloxacin (data not shown). This indicates the presence of acquired resistance to quinolones in about 15% of the isolates of all three bacterial species, probably due to the past and present use of the quinolone oxolinic acid in aquaculture (Table AQ I).

The tendency for bimodal MIC distributions for sulphonamide, trimethoprim and ampicillin in *A. salmonicida* subsp. *achromogenes* also indicate that some isolates have acquired resistance to these antimicrobials (Table AQ III). The same may apply for tetracycline in *Flavobacter* but for this antimicrobial MICs are truncated at the lower end of the range of concentrations tested. This makes interpretation difficult in the absence of accepted breakpoints for resistance. However, elevated MICs in some isolates of *Flavobacter* may indicate acquired tetracycline resistance. In Sweden infections with *Flavobacter* are often treated with tetracycline and occurrence of resistance could be a consequence of this use.

Truncation of MICs in the upper or lower part of the range of concentrations tested can be avoided by an appropriate

design of the test panel. Since the panel used was not designed for testing bacteria from fish it is not optimal for some combinations of antimicrobial and pathogen, e.g. tetracyclines in all three species. Also for florphenicol, distributions are truncated at the lower end of the range tested making interpretation difficult.

Obviously the method used at SVA needs further adaptation and evaluation to be a reliable tool for routine as well as monitoring purposes of bacteria from fish. However, using microdilution according to harmonized methodology and with panels designed for testing bacteria from fish in a wider perspective would make it possible to compile data on MIC for relevant combinations of bacteria and antimicrobials. Thereby interpretive criteria for reduced susceptibility could be determined according to the principles used by the European Committee on Antimicrobial Susceptibility Testing (EUCAST) (www.eucast.org) for bacteria from humans and warm blooded animals. This would be of great importance for routine clinical use as well as for monitoring purposes.

Table AQ III. Distribution of MICs for *Aeromonas salmonicida* subsp. *achromogenes* (ASA, n=67), *Flavobacter columnare* (FP, n=30) and *Flavobacter psychrophilum* (FC, n=42). Isolates from 2005-2007.

Anti-microbial	Species	Distribution (%) of MICs[a] (mg/L)																			
		≤0.004	0.008	0.016	0.03	0.06	0.12	0.25	0.5	1	2	4	8	16	32	64	128	256	512	1024	>1024
Ampicillin	ASA										32.8	6.0	7.5		53.7						
	FP						100.0														
	FC						100.0														
Chloram-phenicol	ASA								93.9	6.1											
	FP								23.8	33.3	38.1	2.4	2.4								
	FC								33.3	60.0	3.3		3.3								
Cipro-floxacin	ASA	2.5	25.0	40.0	17.5		10.0	5.0													
	FP		16.0	32.0	32.0	4.0	4.0			12.0											
	FC	23.5	58.8	5.9						11.8											
Enro-floxacin	ASA			25.9	48.1	11.1	7.4	7.4													
	FP			58.8	17.6	11.8			5.9	5.9											
	FC			92.3				7.7													
Florfenicol	ASA										97.0	3.0									
	FP										100.0										
	FC										96.7	3.3									
Genta-micin	ASA							3.0	7.5	73.1	16.4										
	FP							92.9	2.4	4.8											
	FC							26.7	60.0	10.0	3.3										
Nalidixic acid	ASA								82.1	4.5					3.0	6.0	4.5				
	FP								11.9		45.2	26.2		2.4	2.4		11.9				
	FC								76.7	6.7	3.3				3.3	3.3	6.7				
Strepto-mycin	ASA										1.5	4.5	29.9	61.2	3.0						
	FP									100.0											
	FC									100.0											
Sulphon-amide	ASA												4.5	1.5	18.2	6.1	7.6	7.6	4.5	6.1	43.9
	FP												53.7	14.6	22.0	7.3	2.4				
	FC												70.0		6.7	10.0					13.3
Tetra-cycline	ASA							89.6	10.4												
	FP							76.2	7.1	2.4	4.8	9.5									
	FC							90.0	6.7			3.3									
Trime-thoprim	ASA						3.0	4.5	28.4	16.4	1.5	3.0	20.9	13.4	9.0						
	FP											2.4		2.4	95.2						
	FC						3.3					13.3	13.3	30.0	40.0						

[a] 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 epidemiological cut-off values for resistance

Resistance in zoonotic bacteria

ZOONOSES are diseases and infections that can be naturally transmitted between animals and man. Antimicrobial resistance in zoonotic bacteria is therefore of public health concern. For that reason, antimicrobial susceptibility of *Salmonella* from reported incidents in warm-blooded animals is monitored in SVARM. Selected *Campylobacter* from animals are usually also tested but not included this year because an EU wide monitoring of prevalence and antimicrobial resistance of *Campylobacter* in broilers is scheduled for 2008. More information on infections with zoonotic bacteria in Sweden is presented in the yearly report, Zoonoses in Sweden available at www.sva.se.

Antimicrobial susceptibility of *Salmonella* from Swedish animals has been monitored regularly since 1978. Microdilution methods were used in all surveys although antimicrobials tested have varied. Data from previous years are therefore presented for comparison to data for 2007. Some cut-off values defining resistance (breakpoints) previously used have been changed, however. To facilitate comparisons when retrospect data are presented, levels of resistance have been recalculated using current cut-off values. In SVARM, isolates are classified as susceptible or resistant by epidemiological cut-off values issued by EUCAST (see Appendix 3 for details). This classifies isolates with acquired reduced susceptibility as resistant, which is relevant for monitoring purposes, but it should be understood that this not always implies clinical resistance.

Salmonella

Isolates included

Findings of *Salmonella* in animals are notifiable in Sweden and isolates from each incident are confirmed at SVA. From each notified incident in cattle, pigs, poultry, horses, dogs, wild mammals and wild birds 2007, one isolate from each involved animal species was tested for antimicrobial susceptibility. If an incident involved more than one serovar or phage type, one isolate of each serovar and phage type was tested. Due to a large number of isolates from cats and wild birds in 2007, a random sample of isolates from these animal species was selected for susceptibility testing. One isolate of *S.* enterica subspecies *enterica* (I) from a sheep was not available for testing. Antimicrobials tested and cut-off values used are given in Table Salm II further details on methodology are given in Appendix 3.

Results and comments

This year, 112 isolates were tested. About two thirds (63%) of the isolates were from major food-producing animals (cattle, pigs and poultry) and the majority (64%) were *S.* Typhimurium (Table Salm I). Occurrence of resistance and distributions of MICs and are given in Table Salm II-III.

The majority of isolates (92%) were susceptible to all antimicrobials tested but nine isolates were resistant to at least one substance. Four isolates were resistant to one antimicrobial. Of these, one isolate of *S.* Typhimurium NST from poultry and one isolate of *S.* Agona from cattle were resistant to ampicillin and streptomycin, respectively. Two isolates from dogs, *S.* Muenster and *S.* Livingstone, were resistant to ciprofloxacin and cefotaxime, respectively. The isolate resistant to cefotaxime (MIC 1 mg/L) was susceptible to ampicillin (MIC 4 mg/L) and negative for production of extended spectrum beta-lactamases (ESBL) when tested by the phenotypic confirmatory test recommended by CLSI (see Appendix 3 for details). These findings indicate that the isolate could be an outlier within the wild-type distribution of MICs for cefotaxime and not an ESBL or AmpC producer.

Two isolates of *S.* Typhimurium DT 104 from two epidemiologically linked cattle farms were resistant to ampicillin and sulphonamides. This resistance phenotype was found on one of the farms already in 2006 and the same year also on another epidemiologically linked pig farm.

Two isolates of *S.* Typhimurium from cattle and pigs, phage types NT and DT 120 respectively, were resistant to ampicillin, sulphonamides, streptomycin, and tetracycline. Already in 2006, *S.* Typhimurium phage type NT, with this resistance phenotype was isolated from four incidents involving; cattle, cattle and horses, ducks for food production, and ducks in a hobby flock. Epidemiological links between these incidents have not been documented.

Finally, one isolate of *S.* Typhimurium DT 104 from pigs had the typical penta-resistance; ampicillin, sulphonamides, streptomycin, tetracycline and chloramphenicol/florfenicol.

From a public health perspective, the prevalence of resistance in *Salmonella* from food-producing animals is more important than resistance in isolates from wild animals or pets. In SVARM, 305 isolates from incidents in food-producing animals have been tested the 2000-07. This includes the vast majority of isolates involved in notified incidents in food-producing animals in the period. Of these isolates, 137 (45%) were *S.* Typhimurium and half of these were from pigs (50%), about one fourth from cattle (22%) and poultry (27%), respectively. Two isolates (1%) were from sheep. Among *S.* Typhimurium 22 isolates (16%) were resistant to at one least antimicrobial and 12 to more than three substances (Table Salm V & IV). Among other serovars, 15 isolates (9%) were resistant to at least one antimicrobial and three of these to two substances.

Twelve of the 135 incidents of *S.* Typhimurium in food-producing animals reported 2000-07 involved multiresistant strains, i.e. resistant to at least three antimicrobials. All twelve incidents were among 83 incidents reported 2004-07, whereas none of 52 incidents in 2000-03 involved multiresistant strains. Of the incidents with multiresistant strains, six were in cattle, one in ducks for food production, one in ducks in a hobby flock and three were in pigs. Three of the incidents

in cattle were epidemiologically linked through trade of calves whereas epidemiological links between the other incidents are unknown. Resistance phenotypes of the isolates involved are given in Table Salm VI.

Multiresistance in *Salmonella* from Swedish food-producing animals occurred also before 2004. In 1997 to 1999, five of 51 incidents in food-producing animals involved multiresistant *S.* Typhimurium, either DT 104 or DT 193. The cluster of incidents with multiresistant strains in later years is therefore probably coincidental and not an indication of an overall increased occurrence.

From an international perspective, the overall situation of *Salmonella* among Swedish animals is favourable. Swedish food-producing animals are virtually free from Salmonella, most likely a result of the strategies in the Swedish *Salmonella* control programme, and few incidents involve multiresistant strains. Nevertheless, in view of the public health consequences of multiresistant *Salmonella*, vigilance towards such strains in food-producing animals is warranted.

Table Salm I. Number of *Salmonella enterica* tested year 2007 presented by serovar and source.

Serovar	Cattle	Pig	Poultry	Horse	Dog	Cat	Wildlife	Total
Agona	2		2		1			5
Bredeney					1			1
Dublin	5							5
Duesseldorf	2							2
Infantis	1	12						13
Java			1					1
Livingstone			1		1			2
London					1			1
Muenster					1			1
Newport							1	1
Reading	2	1	1	1				5
Typhimurium DT 1							1	1
Typhimurium DT 40		5	2			1	1	9
Typhimurium DT 99		1						1
Typhimurium DT 104	2	1						3
Typhimurium DT 120		1	1				1	3
Typhimurium DT NST	4	5	10					19
Typhimurium DT NT	1		1					2
Typhimurium DT U277		1	1					2
Typhimurium, not phage typed	1	1		2		9	19	32
Worthington			2					2
Subsp I		1						1
Total	**20**	**29**	**22**	**3**	**5**	**10**[a]	**23**[b]	**112**
Percent of total	18	26	20	3	4	9	21	

[a] Randomly selected from 117 isolates available; [b] Randomly selected from 29 isolates available.

Table Salm II. Distribution of MICs for all serovars of *Salmonella enterica* (n=112) from animals in 2007.

Antimicrobial	Resistance (%)	Distribution (%) of MICs[a] (mg/L)																		
		≤0.008	0.016	0.03	0.06	0.12	0.25	0.5	1	2	4	8	16	32	64	128	256	512	1024	>1024
Ampicillin	5							21.4	71.4	0.9	0.9					5.4				
Cefotaxime	<1				37.5	58.0	3.6		0.9											
Chloramphenicol	<1									21.4	73.2	1.8	2.7				0.9			
Ciprofloxacin	<1			85.7	13.4	0.9														
Florfenicol	<1									16.1	77.7	1.8	3.6	0.9						
Gentamicin	0							42.9	54.5	2.7										
Kanamycin	0									50.0	49.1	0.9								
Nalidixic acid	0									3.6	89.3	7.1								
Streptomycin	4											30.4	65.2	0.9	1.8		1.8			
Sulphonamide	4											0.9	5.4	30.4	53.6	5.4				4.5
Tetracycline	3								86.6	9.8	0.9		0.9			1.8				
Trimethoprim	0						49.1	50.0	0.9											

[a] White fields denote range of dilutions tested. Values above the range denote MICs greater than the highest concentration tested. MICs equal to or lower than the lowest concentration tested are given as the lowest tested concentration. Vertical lines indicate cut-off values for resistance.

Table Salm III. Distribution of MICs for *Salmonella* Typhimurium (n=53) from animals in 2006.

Antimicrobial	Resistance (%)	Distribution (%) of MICs[a] (mg/L)																		
		≤0.008	0.016	0.03	0.06	0.12	0.25	0.5	1	2	4	8	16	32	64	128	256	512	1024	>1024
Ampicillin	8							13.9	77.8							8.3				
Cefotaxime	0				38.9	59.7	1.4													
Chloramphenicol	1									25.0	73.6						1.4			
Ciprofloxacin	0			87.5	12.5															
Florfenicol	1									25.0	73.6			1.4						
Gentamicin	0							45.8	51.4	2.8										
Kanamycin	0									51.4	47.2	1.4								
Nalidixic acid	0									2.8	94.4	2.8								
Streptomycin	4											22.2	73.6		1.4		2.8			
Sulphonamide	7											1.4	2.8	27.8	55.6	5.6				6.9
Tetracycline	4								90.3	5.6			1.4			2.8				
Trimethoprim	0						51.4	47.2	1.4											

[a] White fields denote range of dilutions tested. Values above the range denote MICs greater than the highest concentration tested. MICs equal to or lower than the lowest concentration tested are given as the lowest tested concentration. Vertical lines indicate cut-off values for resistance.

Table Salm IV. Resistance (%) and source of isolates in *Salmonella* Typhimurium from animals 1978 to 2007.

Antimicrobial	Cut-off value (mg/L)	Resistance (%)							
		1978-88[a] (n=125)	1989-99 (n=317)	2000-02 (n=108)	2003 (n=49)	2004 (n=49)	2005 (n=85)	2006 (n=53)	2007 (n=72)
Ampicillin	>4	2[b]	6[b]	3	0	8	9	17	8
Cefotaxime	>0.5	-	-	-	-	-	0	0	0
Ceftiofur	>2	-	-	0	0	0	0	0	-
Chloramphenicol	>16	4[b]	5[b]	3	0	8	9	2	1
Ciprofloxacin	>0.06	-	-	-	-	-	-	0	0
Enrofloxacin	>0.25	-	1	0	0	0	1	-	-
Florfenicol	>16	-	-	3	0	6	8	2	1
Gentamicin	>2	-	0[b]	0[c]	2	0	0	0	0
Kanamycin	>16	-	-	-	-	-	-	0	0
Nalidixic acid	>16	-	-	4	0	0	1	0	0
Neomycin	>4	0[b]	1[b]	4	0	0	0	-	-
Streptomycin	>32	74	15	4	2	8	10	11	4
Sulphonamide	>256	-	-	3	2	8	10	15	7
Tetracycline	>8	13	6	3	0	8	9	11	4
Trimethoprim	>2	-	-	0	0	0	0	0	0
Trim/sulph.	>0.5/9.5	0	3	-	-	-	-	-	-
Percent of isolates from:									
Cattle, sheep, pigs, poultry		100	46	45	12	33	19	40	53
Horses, cats, dogs			29	36	82	61	58	36	17
Wildlife			25	19	6	6	23	24	30

[a] 1988 includes isolates to September, isolates from October-December 1988 given under 1989; [b] Cut-off value for resistance >8 mg/L; [c] Cut-off value for resistance >4 mg/L.

Table Salm V. Distribution of MICs for *Salmonella* Typhimurium (n=137) from food-producing animals 2000-2007.

Antimicrobial	Resistance (%)	Distribution (%) of MICs[a] (mg/L)																	
		≤0.008	0.016	0.03	0.06	0.12	0.25	0.5	1	2	4	8	16	32	64	128	256	512	1024	>1024
Ampicillin	12							4.4	56.9	24.8	2.2				11.7					
Cefotaxime[b]	0				26.1	59.4	14.5													
Ceftiofur[c]	0							28.7	68.3	3.0										
Chloramphenicol	5									10.2	80.3	4.4				1.5	3.6			
Ciprofloxacin[d]	0			60.7	39.3															
Enrofloxacin[e]	0				54.3	42.0	3.7													
Florfenicol	4										91.2	3.6	0.7	4.4						
Gentamicin	3							14.6	65.7	16.8	2.9									
Kanamycind	0									17.9	75.0	7.1								
Nalidixic acid	<1									1.5	69.3	19.7	8.8	0.7						
Neomycin[e]	0									84.0	16.0									
Streptomycin	10										0.7	15.3	61.3	13.1	3.6	1.5	2.9	1.5		
Sulphonamide	12														47.4	32.8	8.0			11.7
Tetracycline	9								26.3	55.5	9.5		1.5		2.9	4.4				
Trimethoprim	0						31.4	57.7	10.9											

[a] White fields denote range of dilutions tested. Values above the range denote MICs greater than the highest concentration tested. MICs equal to or lower than the lowest concentration tested are given as the lowest tested concentration. Vertical lines indicate cut-off values for resistance; [b] 69 isolates tested; [c] 101 isolates tested; [d] 56 isolates tested; [e] 81 isolates tested

Table Salm VI. Resistance phenotypes and multiresistance (%) of *Salmonella* Typhimurium (n=137) from food-producing animals years 2000-2007. All isolates tested for susceptibility to ampicillin, ceftiofur/cefotaxime, enrofloxacin/ciprofloxacin, florfenicol, gentamicin, chloramphenicol, nalidixic acid, streptomycin, sulphametoxazole, tetracycline, and trimethoprim. Breakpoints for resistance are given in Table Salm V.

Resistance pattern[a]	Animal species	Phage type																
		104	120	195	193	41	40	15A	10	12	9	1	99	U277	NST	NT	Not typed	Total
AmFfCmSmSuTc	Pig	1															1	2
AmFfCmSmSuTc	Cattle	3	1															4
AmCmSmSuTc	Cattle	1																1
AmSmSuTc	Pig		1															1
AmSmSuTc	Cattle															2		2
AmSmSuTc	Poultry															2		2
AmSu	Pig	1																1
AmSu	Cattle	2																2
SmSu	Poultry							1										1
Am	Poultry														1			1
Nal	Pig									1								1
Gm	Pig						1											1
Gm	Cattle					1												1
Gm	Poultry					1									1			2
Susceptible	Pig	2	3			7	28			2		1	1	1	10	2	5	62
Susceptible	Cattle	1	2			2		1	2						9	1	2	20
Susceptible	Sheep																2	2
Susceptible	Poultry		1	1	1	2	3			1	1	1		1	17	2		31
Number of isolates		**11**	**8**	**1**	**1**	**13**	**32**	**2**	**2**	**4**	**1**	**2**	**1**	**2**	**38**	**9**	**10**	**137**
Percent of total		8	6	<1	<1	10	23	2	2	3	<1	2	<1	2	28	7	7	
Multiresistance (%)																		
Susceptible to all antimicrobials		27	75	100	100	85	97	50	100	75	100	100	100	100	95	56	90	84
Resistant to 1 antimicrobial						15	3			25					5			4
Resistant to 2 antimicrobials		27						50										3
Resistant to 3 antimicrobials																		
Resistant to >3 antimicrobials		46	25													44	10	9

[a] Am: ampicillin; Ff : florfenicol; Cm: chloramphenicol; Sm: streptomycin; Su: sulphonamides; Tc: tetracycline; Nal: nalidixic acid; Gm: gentamicin.

MRSA – Methicillin-resistant *Staphylococcus aureus*

IN RECENT YEARS, the number of international reports about methicillin resistant *Staphylococcus aureus* (MRSA) isolated from animals has increased. In Sweden, the first MRSA in veterinary medicine were found in 2006 and they were isolated from post-operative wound infections in two dogs (See SVARM 2006). From the first of January 2008, infections with methicillin-resistant coagulase positive staphylococci in animals are notifiable in Sweden.

During the first six months of 2007, another five MRSA from dogs were confirmed. One dog was sampled at the animal hospital that had the first two cases in October 2006. The other dogs where sampled at two other animal hospitals. The three involved hospitals are in different counties. All five MRSA were isolated from post-operative wound infections. They belonged to the same spa-type (t032) and had the same antibiogram. Besides being resistant to beta-lactam antibiotics, they were resistant to fluoroquinolones. In February 2008, another MRSA from a dog, sampled at the first affected animal hospital, was confirmed. The dog was sampled at the first visit to the animal hospital and the MRSA was isolated from a skin wound due to mange. This isolate had a different antibiogram compared to the other seven MRSA and belonged to *spa*-type t127. Besides resistant to beta-lactams, it was resistant to erythromycin, tetracycline, gentamicin, kanamycin and trimethoprim.

In December 2007, the first MRSA from a horse was isolated in Sweden. It was found in a screening for MRSA in Swedish horses. In this study, four different horse clinics took nasal swabs from 75 horses each at the time of admission. The samples were sent to SVA and were cultured in TSB-broth with 2% NaCl and 75 µg/ml aztreonam. Some data about the sampled horses were collected, but the identity of the horses and their owners were not recorded. The horse positive for MRSA was a mare born 2003 that had been abroad during the last six months. It had visited a horse clinic and had been treated with antimicrobials during the last months prior to the MRSA-positive sample. The mare was kept in a stable with more then 15 horses. The MRSA was, besides resistant to beta-lactam antibiotics, also resistant to aminoglycosides, tetracycline and trimethoprim. Analysis at the Swedish Institute for Disease Control (SMI) showed that the MRSA from this horse belonged to spa-type t011. This indicates that it is part of the MLST-type ST 398 that is often associated with pigs, but also horses, and frequently is reported from several European countries.

Besides screening for MRSA-carriers with nasal swabs, an investigation of MRSA-infections in horses was initiated in 2007. Here, diagnostic samples sent to SVA are cultured on a selective agar. During 2007, about 700 samples were tested and none were positive for MRSA. This study will continue until May 2008. Both these screening studies were funded by Stiftelsen Svensk Hästforskning.

In total, eight confirmed MRSA from dogs within 18 months and a single MRSA found in horses indicate that infections with MRSA in the dogs and horses in Sweden are still rare. Nevertheless, increased awareness to hand hygiene and sanitary actions are essential.

Resistance in indicator bacteria

THE PREVALENCE of acquired antimicrobial resistance in bacteria of the normal enteric microflora indicates the magnitude of the selective pressure exerted by use of antimicrobials in a population. Monitoring of resistance in so-called indicator bacteria from the enteric microbiota from healthy animals is therefore of great value to detect trends and to follow effects of interventions. Although these bacteria are unlikely to cause disease, they may form a reservoir for resistance genes that can spread to bacteria that cause infections in animals or humans. In SVARM, *Escherichia coli* and *Enterococcus* spp. from healthy animals serve as indicator bacteria.

Of special interest is the occurrence of specific patterns of resistance in indicator bacteria. Such patterns, or phenotypes, can indicate that resistance genes are located on the same genetic element. Thereby, a single transfer event can convey resistance to several antimicrobials to a recipient bacterium (co-transfer) and use of one antimicrobial can select for resistance to other, unrelated antimicrobials (co-selection).

In 2007, antimicrobial susceptibility of indicator bacteria from broilers was monitored. In addition, occurrence of vancomycin resistant enterococci (VRE) in broilers was investigated using culture on vancomycin supplemented media.

Isolates included

Escherichia coli and *Enterococcus* spp. were isolated from caecal content from broilers sampled at slaughter. For detection of vancomycin resistant enterococci (VRE), caecal content was in addition cultured on vancomycin-supplemented media. Each isolate is from unique flock but not necessarily from a unique production site. Antimicrobials tested and concentration ranges used are given in Table EC IV and ENT IX-XI. For details on methodology and sampling strategy, see Appendix 3. Some cut-off values defining resistance (breakpoints) previously used in SVARM have been changed. To facilitate comparisons, resistance data from earlier reports have therefore been recalculated using current cut-off values. In SVARM, isolates are classified as susceptible or resistant by epidemiological cut-off values issued by EUCAST (see Appendix 3 for details). This classifies isolates with acquired reduced susceptibility as resistant, which is relevant for monitoring purposes, but it should be understood that this not always implies clinical resistance.

Escherichia coli

Escherichia coli were isolated from 87% of 339 samples cultured. The majority (85%) of the 296 isolates were sensitive to all 13 antimicrobials tested but 45 isolates (15%) were resistant to at least one substance (Table EC I). Resistance to quinolones (nalidixic acid and ciprofloxacin) was the most common trait (7%) followed by resistance to sulphonamides, ampicillin, streptomycin or tetracycline (3-6%). Resistance to other antimicrobials occurred in occasional isolates but no isolate was resistant to florfenicol. Notably, three isolates (1%) were resistant to the third generation cephalosporins cefotaxime and ceftiofur. These three isolates had MICs for ceftiofur and cefotaxime of 8 and >2 mg/L, respectively. The isolates were however negative for extended spectrum beta-lactamases (ESBLs) when tested by the phenotypic confirmatory test recommended by CLSI (see appendix for details).

Sixteen isolates (5%) were resistant to more than one antimicrobial and of these four isolates were resistant to two and 12 isolates to three or more antimicrobials (Table EC I). The phenotypes of the latter isolates are presented in Table EC II. Resistance to some antimicrobials is associated with increased occurrence of resistance to other substances (Table EC III). Among the isolates from years 2000, 2001, 2002, 2004 and 2007, the association is statistically significant for several pairs of resistance traits (Table EC III).

Comments

Use of antimicrobials with effect against *E. coli* for treatment of broilers is rare in Sweden (SVARM 2000). Small amounts of amoxicillin, sulphonamides and enrofloxacin are used but mostly in flocks of broiler grand-parents or parents. In agreement with the limited use, prevalence of resistance is low and seems to decline as the proportion of *E. coli* susceptible to all antimicrobials tested has increased from 77% to 85% in the period studied (Table EC I). There are also numerical trends in resistance to single antimicrobials (Fig EC I). The decline in sulphonamide resistance and increase in quinolone (nalidixic acid) resistance are statistically significant (Chi Square for trend, $P<0.01$ and $P<0.05$, respectively).

The increased prevalence of quinolone resistance is difficult to explain as an effect of a selection pressure in flocks of broilers raised for slaughter. Although poultry is the only animal species for which quinolones (enrofloxacin) are licensed for group treatment in Sweden, the use is low. In Sweden over 70 million broilers were slaughtered in 2007 but only about 3 kg active substance of enrofloxacin for flock treatment was sold in the country (see Use of antimicrobials). Of the amounts registered as prescribed for poultry, an unspecified amount was probably used for game birds or backyard-flocks. Moreover, enrofloxacin prescribed for broilers is mainly used in flocks of grand parents or parent birds according to prescribing veterinarians. Thus, use of enrofloxacin in flocks of broilers for slaughter is probably rare and accordingly the selection pressure towards quinolone resistance is probably low. Other antimicrobials are also rarely used and co-selection of quinolone resistant isolates is therefore unlikely even if quinolone resistance often occurs together with resistance to other antimicrobials in *E. coli* from poultry (Table EC II & III).

Table EC I. Occurrence of resistance (%) and multiresistance (%) among isolates of indicator *Escherichia coli* from broilers, 2007. Data for dairy cows, pigs and dogs from previous SVARM reports are given for comparison.

		Resistance (%) (95% confidence interval)															
		Broilers										**Pigs**		**Dairy cows**		**Dogs**	
Antimicrobial	**Cut-off value** (mg/L)	**2007** n=296		**2004** n=300		**2002** n=306		**2001** n=296		**2000** n=274		**2005** n=390		**2006** n=314		**2006** n=257	
Ampicillin	>8	5	(2.6-7.8)	4	(2.1-6.9)	4	(2.3-7.2)	3	(1.2-5.3)	5	(2.6-8.0)	6	(4.2-9.3)	0	(0.0-1.2)	5	(3.0-9.0)
Cefotaxime	>0.25	1	(0.2-2.9)	-		-		-		-		0	(0.0-0.9)	0	(0.0-1.2)	<1	(0.0-2.1)
Ceftiofur	>1	1	(0.2-2.9)	0	(0.0-1.2)	<1	(0.1-2.3)	0	(0.0-1.2)	0	(0.0-1.3)	0	(0.0-0.9)	0	(0.0-1.2)	<1	(0.0-2.1)
Chloramphenicol	>16	<1	(0.0-1.9)	0	(0.0-1.2)	0	(0.0-1.2)	0	(0.0-1.2)	<1	(0.1-2.6)	3	(1.8-5.6)	0	(0.0-1.2)	<1	(0.1-2.9)
Ciprofloxacin	>0.06	7	(4.5-10.7)	5[b]	(2.8-8.1)	4[b]	(2.3-7.2)	2[b]	(0.6-3.9)	4[b]	(2.3-7.5)	<1[b]	(0.1-1.4)	<1	(0.1-2.3)	2	(0.6-4.5)
Florfenicol	>16	0	(0.0-1.2)	0	(0.0-1.2)	0	(0.0-1.2)	0	(0.0-1.2)	0	(0.0-1.3)	0	(0.0-0.9)	0	(0.0-1.2)	0	(0.0-1.4)
Gentamicin	>2	<1	(0.0-1.9)	<1	(0.1-2.4)	<1[c]	(0.0-1.8)	<1[c]	(0.0-1.9)	<1[c]	(0.0-2.0)	2	(0.7-3.7)	<1	(0.2-2.8)	<1	(0.0-2.1)
Kanamycin	>8	2	(0.6-3.9)	-		-		-		-		-		<1	(0.2-2.8)	2	(0.9-5.0)
Nalidixic acid	>16	7	(4.2-10.3)	5	(2.8-8.1)	5	(2.5-7.6)	2	(0.6-3.9)	4	(2.3-7.5)	<1	(0.1-1.4)	<1	(0.1-2.3)	2	(0.6-4.5)
Streptomycin	>16	4	(1.9-6.6)	6	(3.3-8.9)	5	(3.0-8.4)	6	(3.4-9.0)	5	(2.8-8.4)	14	(10.8-18.0)	2	(0.3-3.3)	7	(4.2-10.8)
Sulphonamide	>256	6	(3.7-9.5)	9	(6.0-12.8)	10	(6.7-13.7)	12	(8.4-16.1)	12	(8.1-16.0)	11	(7.7-14.0)	2	(0.5-3.7)	7	(3.9-10.4)
Tetracycline	>8	3	(1.6-6.1)	6	(3.6-9.3)	6	(3.3-8.8)	4	(2.4-7.4)	8	(4.8-11.5)	9	(6.1-12.0)	2	(0.5-3.7)	2	(0.9-5.0)
Trimethoprim	>2	<1	(0.1-2.4)	<1	(0.1-2.4)	<1	(0.0-1.8)	1	(0.4-3.4)	<1	(0.1-2.6)	6	(4.2-9.3)	<1	(0.0-1.8)	4	(1.9-7.0)
Multiresistance[a]																	
Susceptible to all		85		84		78		78		77		76		96		86	
Resistant to 1		10		9		16		17		15		10		3		6	
Resistant to 2		1		3		4		3		5		6		<1		4	
Resistant to 3		1		2		1		1		2		4		1		2	
Resistant to >3		3		3		1		1		1		4		<1		3	

[a] Enrofloxacin/ciprofloxacin/nalidixic acid as well as cefotaxime/ceftiofur counted as one substance; [b] Enrofloxacin tested, cut-off value >0.12 mg/L; [c] Cut-off value >8 mg/L.

Table EC II. Number of *Escherichia coli* resistant to three or more antimicrobials, presented by resistance phenotype. "R" in shaded fields indicates resistance.

Year					**Resistance pattern**[a]									
2007 n=296	**2004** n=300	**2002** n=306	**2001** n=296	**2000** n=274	**Su**	**Tc**	**Sm**	**Nal**	**Ci/Ef**	**Am**	**Tm**	**Cm**	**Gm**	**Ce/Ctx**
			2		R	R	R	R	R		R			
				1	R	R	R	R	R			R		
6	5	3	1	1	R	R	R	R	R					
	1				R	R	R	R		R				
	1	1			R	R	R	R						
				1	R	R	R			R	R			
	2				R	R	R			R				
			1		R	R	R				R		R	
1	2	1		1	R	R	R							
			1	1	R	R		R	R					
	1				R	R		R						
				1	R	R							R	
1					R		R	R	R				R	
			1		R		R	R	R					
1					R		R			R	R			
				1	R		R					R		
		1		1	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						R			R	R				
		1				R				R				R
1								R	R	R		R		
	1							R	R		R		R	
12 (4.1%)	**14** (4.7%)	**7** (2.3%)	**7** (2.3%)	**10** (3.6%)	**Number of isolates** (percent of all isolates)									

[a] Su: sulphonamide; Tc: tetracycline; Sm: streptomycin; Nal: nalidixic acid; Ci: ciprofloxacin; Ef: enrofloxacin; Am: ampicillin; Tm: trimethoprim; Cm: chloramphenicol; Gm: gentamicin; Ce: ceftiofur; Ctx: cefotaxime.

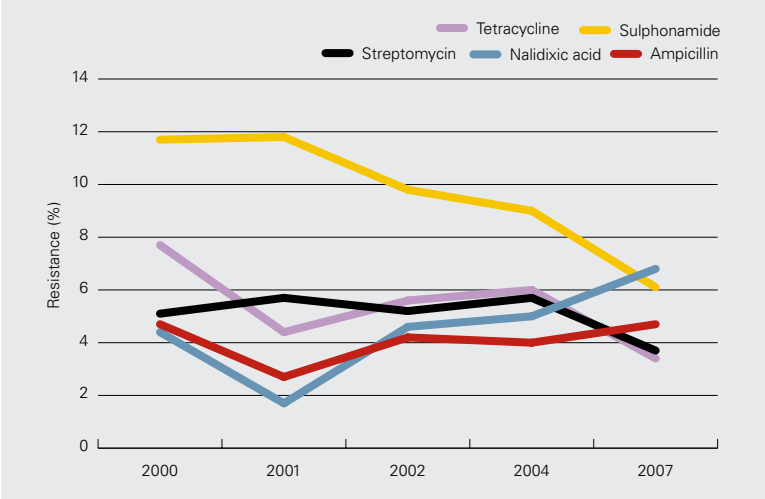

Figure EC I. Resistance (%) to selected antimicrobials in indicator *Escherichia coli* from broilers years 2000-2002, 2004 and 2007. For number of isolates see Table EC I. Data from SVARM.

Table EC III. Association between resistance traits in *Escherichia coli* isolated from broilers years 2000, 2001, 2002, 2004 and 2007. For each antimicrobial the first line gives the resistance rates for susceptible isolates (S) and the second line rates for resistant isolates (R). All antimicrobials were not tested all years, therefor all combinations of pairs of resistance traits can not be calculated. Bold and underlined figures indicate statistically significant association between pairs of resistance traits (Chi-Square or Fischer's Exact test, P<0.001).

Single substance susceptibility		n	Resistance (%)[a] Am	Ctx	Ce	Cm	Ci	Ef	Gm	Km	Nal	Nm	Sm	Su	Tc	Tm
Ampicillin	S	1412	0.0		0.0	0.1			2.1		4.5		4.8	9.1	4.8	0.6
	R	60	100.0		**8.3**	3.3			1.7		5.0		13.3	21.7	**18.3**	3.3
Cefotaxime	S	293	3.8	0.0	0.0	0.3	7.2		0.3	1.7	6.9		3.8	6.2	3.4	0.7
	R	3	**100.0**	100.0	100.0	0.0	0.0		0.0	0.0	0.0		0.0	0.0	0.0	0.0
Ceftiofur	S	1467	3.8		0.0	0.2			2.1		4.5		5.1	9.7	5.3	0.8
	R	5	**100.0**		100.0	0.0			0.0		0.0		0.0	0.0	20.0	0.0
Chloramphenicol	S	1469	4.0		0.3	0.0			2.0		4.4		5.0	9.5	5.3	0.8
	R	3	66.7		0.0	100.0			0.0		66.7		66.7	66.7	33.3	0.0
Ciprofloxacin	S	275	4.4	1.1	1.1	0.0	0.0		0.0	0.0	0.0		1.5	4.0	1.1	0.7
	R	21	9.5	0.0	0.0	4.8	100.0		4.8	**23.8**	**95.2**		**33.3**	**33.3**	**33.3**	0.0
Enrofloxacin	S	1131	4.0		0.2	0.1		0.0	2.4		0.4	0.5	4.0	9.6	4.3	0.5
	R	45	2.2		0.0	2.2		100.0	4.4		**93.3**	**28.9**	**42.2**	**35.6**	**44.4**	6.7
Florfenicol	S	1472	4.1		0.3	0.2			2.0		4.5		5.1	9.7	5.4	0.8
	R	0	0.0		0.0	0.0			0.0		0.0		0.0	0.0	0.0	0.0
Gentamicin	S	1442	4.1		0.4	0.2			0.0		4.4		4.9	9.4	5.3	0.6
	R	30	3.3		0.0	0.0			100.0		10.0		16.7	23.3	10.0	6.7
Kanamycin	S	291	4.8	1.0	1.0	0.3	5.5		0.3	0.0	5.2		2.1	4.5	1.7	0.7
	R	5	0.0	0.0	0.0	0.0	**100.0**		0.0	100.0	**100.0**		**100.0**	**100.0**	**100.0**	0.0
Nalidixic acid	S	1406	4.1		0.4	0.1			1.9		0.0		3.3	8.2	3.5	0.6
	R	66	4.6		0.0	3.0			4.6		100.0		**43.9**	**40.9**	**45.5**	4.6
Neomycin	S	1157	3.8		0.2	0.2		2.8	2.5		2.6	0.0	4.0	9.4	4.7	0.7
	R	19	10.5		0.0	0.0		**68.4**	0.0		**84.2**	100.0	**94.7**	**79.0**	**79.0**	5.3
Streptomycin	S	1397	3.7		0.4	0.1			1.8	0.0	2.7		0.0	6.9	3.2	0.4
	R	75	10.7		0.0	2.7			6.7	6.7	**38.7**		100.0	**61.3**	**46.7**	**6.7**
Sulphonamide	S	1330	3.5		0.4	0.1			1.7	0.0	2.9		2.2	0.0	2.4	0.3
	R	142	9.2		0.0	1.4			4.9	3.5	**19.0**		**32.4**	100.0	**33.1**	**4.9**
Tetracycline	S	1393	3.5		0.3	0.1			1.9	0.0	2.6		2.9	6.8	0.0	0.5
	R	79	**13.9**		1.3	1.3			3.8	6.3	**38.0**		**44.3**	**59.5**	100.0	5.1
Trimethoprim	S	1461	4.0		0.3	0.2			1.9	0.3	4.3		4.8	9.3	5.1	0.0
	R	11	18.2		0.0	0.0			18.2	0.0	27.3		**45.5**	63.6	**36.4**	100.0

[a] Am: ampicillin; Ctx: Cefotaxime; Ce: ceftiofur; Cm: chloramphenicol; Ci: ciprofloxacin; Ef: enrofloxacin; Gm: gentamicin; Km: kanamycin; Nal: nalidixic acid; Nm: neomycin; Sm: streptomycin; Su: sulphonamide; Tc: tetracycline; Tm: trimethoprim.

Table EC IV. Distribution of MICs for *Escherichia coli* from broilers 2007 (n=296). Previous data from SVARM year 2004 (n=300) and composite data for years 2000 (n=274), 2001 (n=296) and 2002 (n=306) are given for comparison.

Anti-microbial	Year	Resis-tance (%)	Distribution (%) of MICs[a] (mg/L)																			
			≤0.008	0.016	0.03	0.06	0.12	0.25	0.5	1	2	4	8	16	32	64	128	256	512	1024	2048	>2048
Ampicillin	2007	5							0.3	15.9	57.1	18.2	3.7			4.7						
	2004	4							0.3	4.0	55.0	35.7	1.0		0.3	3.7						
	2000-02	4							0.5	5.7	46.1	43.5	0.3	0.2		3.7						
Cefotaxime[b]	2007	1				52.0	37.5	9.5				1.0										
Ceftiofur	2007	1					2.0	25.0	62.8	9.1			1.0									
	2004	0					1.0	15.0	69.0	15.0												
	2000-02	<1						14.0	71.3	14.4	0.2											
Chlor-amphenicol	2007	<1								0.3	6.4	75.3	17.6					0.3				
	2004	0									8.7	72.0	19.3									
	2000-02	<1									1.1	54.7	43.8	0.1	0.2							
Ciprofloxacin	2007	7		2.4	38.2	52.4	1.0	3.4	2.7													
	2004	5[c]			19.3	62.3	13.3	2.7	1.7	0.3	0.3											
	2000-02	3[c]			24.7	69.1	2.9	0.9	1.8	0.7												
Florfenicol	2007	0										44.6	52.7	2.7								
	2004	0										53.0	46.7	0.3								
	2000-02	0									0.7	38.5	59.6	1.3								
Gentamicin	2007	<1							12.5	74.0	13.2				0.3							
	2004	<1							17.3	70.0	12.0	0.3	0.3									
	2000-02	<1							0.6	19.2	53.1	24.1	2.7	0.2	0.1							
Kanamycin[b]	2007	2									12.5	72.3	13.5		1.7							
Nalidixic acid	2007	7								2.0	40.5	49.3	1.4			1.7	3.0	2.0				
	2004	5								1.0	24.3	67.0	2.7			3.0	0.7	1.3				
	2000-02	4									9.9	49.4	34.9	2.2	0.1	0.3	1.0	2.1				
Strepto-mycin	2007	4										21.3	70.3	4.7	0.7	0.3	1.7	1.0				
	2004	6									0.3	29.3	57.3	7.3	0.7	1.3	2.0	1.3	0.3			
	2000-02	5										2.2	53.3	39.2	1.9	0.8	0.7	1.0	0.9			
Sulphon-amide	2007	6												69.3	20.9	3.4	0.3					6.1
	2004	9												54.0	25.3	8.7	3.0				0.7	8.3
	2000-02	11														54.5	33.7	0.8		11.1		
Tetracycline	2007	3							1.0	58.1	37.2		0.3			1.0	2.4					
	2004	6							1.7	41.0	50.3	1.0					6.0					
	2000-02	6							0.3	20.0	57.3	16.0	0.6	0.1	0.1	0.1	5.5					
Trimetho-prim	2007	<1						31.1	45.9	19.6	2.7					0.7						
	2004	<1						20.7	50.3	26.0	2.3	0.3			0.3							
	2000-02	<1					1.6	17.6	57.9	20.5	1.6	0.1			0.7							
			≤0.008	0.016	0.03	0.06	0.12	0.25	0.5	1	2	4	8	16	32	64	128	256	512	1024	2048	>2048

[a] 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 epidemiological cut-off values for resistance; [b] Not tested 2000-02 or 2004; [c] Enrofloxacin tested.

Enterococcus

Enterococci were isolated from 92% of the 339 samples cultured. *Enterococcus faecium* (63%) was the predominant species followed by *E. hirae* (12%), *E. faecalis* (9%) and *E. durans* (6%) (Table ENT I). Ten percent of the isolates could not be typed to species level with the simplified scheme used.

Table ENT I. Prevalence of enterococci in samples of caecal content from broilers, 2007. Species not identified as *Enterococcus faecalis, E. faecium* or *E. hirae* are given as "other species". Previous data from SVARM are given for comparison.

Year	No. of samples cultured	Positive cultures	Isolates tested for susceptibility	*Enterococcus* species isolated No. of isolates (percent of total number of isolates)			
				E. faecalis	*E. faecium*	*E. hirae*	Other species
2007	339	92%	312	28 (9%)	197 (63%)	36 (12%)	51 (16%)
2004	321	95%	306	48 (16%)	163 (53%)	34 (11%)	61 (20%)
2002	351	95%	332	57 (17%)	189 (57%)	45 (14%)	41 (12%)
2001	324	93%	302	49 (16%)	204 (68%)	27 (9%)	22 (7%)
2000	317	82%	261	47 (18%)	151 (58%)	28 (11%)	35 (13%)

In enterococci irrespective of species, resistance to narasin, was by far the most common resistance trait (83%) (Table ENT II). Resistance to erythromycin, tetracycline, bacitracin or virginiamycin were less prevalent, 5-22%. Resistance to ampicillin, kanamycin or streptomycin occurred in occasional isolates only and no isolate was resistant to chloramphenicol, gentamicin, linezolid or vancomycin.

Vancomycin resistant enterococci (VRE) were isolated from 90 (27%) of the 339 samples when cultured on vancomycin-supplemented media (16 mg/L). All 90 isolates were *E. faecium* with MIC for vancomycin >128 mg/L. In addition, all isolates were resistant to narasin (MIC 4-16 mg/L) and 87 isolates also to erythromycin (MIC 8-16 mg/L). Nineteen isolates examined by PCR all carried the *vanA*-gene.

Table ENT II. Occurrence of resistance (%) among isolates of *Enterococcus* spp. from broilers, 2007. Previous data from SVARM are given for comparison.

Antimicrobial	Cut-off value (mg/L)	Resistance (%) (95% confidence interval)									
		2007 n=312		2004 n=306		2002 n=332		2001 n=302		2000 n=261	
Ampicillin	>4	<1	(0.1-2.3)	1	(0.4-3.3)	2	(1.0-4.7)	4	(1.8-6.4)	5	(2.7-8.4)
Bacitracin[a]	>32	19	(14.4-23.4)	25	(20.4-30.4)	22	(17.9-27.2)	16	(12.3-20.9)	20	(14.9-24.9)
Chloramph.	>32	0	(0.0-1.2)	0	(0.0-1.2)	-		-		-	
Erythromycin	>4	15	(11.6-19.9)	18	(13.5-22.4)	20	(16.3-25.5)	21	(16.1-25.5)	19	(14.6-24.5)
Gentamicin	>32	0	(0.0-1.2)	0	(0.0-1.2)	<1	(0.1-2.2)	0	(0.0-1.2)	0	(0.0-1.4)
Kanamycin	>1024	<1	(0.0-1.8)	-		-		-		-	
Linezolid	>4	0	(0.0-1.2)	-		-		-		-	
Narasin	>2	83	(78.7-87.3)	81	(75.9-85.0)	72	(66.8-76.8)	75	(69.6-79.6)	72	(65.8-77-0)
Streptomycin	>512/>128[b]	<1	(0.1-2.3)	1	(0.2-2.8)	2	(0.9-4.3)	<1	(0.2-2.9)	2	(0.8-4.9)
Tetracycline	>2	22	(17.0-26.5)	22	(17.4-27.0)	29	(24.4-34.4)	33	(28.1-39.1)	38	(32.4-44.5)
Vancomycin	>4	0	(0.0-1.2)	1	(0.2-2.8)	<1	(0.1-2.2)	0	(0.0-1.2)	1[d]	(0.2-3.3)
Virginiamycin	>32/>4[c]	5	(3.2-8.6)	13	(9.5-17.4)	23	(18.2-27.5)	23	(17.6-27.3)	22	(17.3-27.8)

[a] MIC in U/mL; [b] Cut-off for *E. faecalis* >512 mg/L, for other species >128 mg/L; [c] Cut-off for *E. faecalis* >32 mg/L, for other species >4 mg/L;
[d] Isolates with MIC 8 mg.

Enterococcus faecalis

The majority of *E. faecalis* (75%) were resistant to at least one antimicrobial. Tetracycline resistance was the most frequent trait (57%) but resistance to narasin, erythromycin or bacitracin was also common (11-36%) (Table ENT III). One isolate was resistant to kanamycin (4%). No isolate was resistant to ampicillin, chloramphenicol gentamicin, linezolid, streptomycin, vancomycin or virginiamycin.

Multiresistance was rare and only a five isolates were resistant to three or more antimicrobials (Table ENT III & VI). Cross-tabulation of data from years 2000 to 2007 indicate an association between resistance to bacitracin-erythromycin, bacitracin-tetracycline and erythromycin-narasin (P<0.001) (Table ENT VII). These four antimicrobials are the most common traits in phenotypes of isolates resistant to three or more antimicrobials (Table ENT VI).

Enterococcus faecium

Almost all *E. faecium* isolates (91%) were resistant to at least one antimicrobial. Narasin was the most common trait (89%) followed by bacitracin (23%), tetracycline (16%) and virginiamycin (4%) (Table ENT IV). Resistance to ampicillin, streptomycin and virginiamycin was less common (1-4%) and no isolate was resistant to chloramphenicol, kanamycin, linezolid or vancomycin.

Multiresistance was rare and only 16 isolates (8%) were resistant to three or more antimicrobials (Table ENT IV & VI). Cross-tabulation of data from years 2000 to 2007 indicate an association between the resistance traits bacitracin-narasin, narasin-virginiamycin, virginiamycin-tetracycline and erythromycin-vancomycin (P<0.001) (Table ENT VII). Apart from vancomycin, these five antimicrobials are common in multiresistant isolates of *E. faecium* (Table ENT VI).

Enterococcus hirae

Only two isolates (6%) of *E. hirae* were susceptible to all antimicrobials tested. Narasin (94%), erythromycin (19%), tetracycline (14%) and bacitracin (8%) were the most common traits in (Table ENT V). One isolate (3%) was resistant to virginiamycin and resistance to the other antimicrobials tested was not observed. Multiresistance was rare and only two isolates were resistant to three or more antimicrobials.

Comments

In the three species *E. faecalis*, *E. faecium* and *E. hirae*, resistance to narasin, bacitracin, erythromycin or tetracycline are the most common traits (Table ENT III-V). These resistance traits are also the most prevalent in multiresistant isolates (Table ENT VI).

In the period studied in SVARM the ionophore narasin has been used as a coccidiostat in the majority of broiler flocks. It is therefore not surprising that virtually all isolates of *E. faecium* and *E. hirae* and a large proportion of *E. faecalis* are resistant to narasin and that there appears to be no trend over time in the period studied (Fig ENT I). The impact of this selection pressure on the prevalence of resistance is evident when data on narasin resistance in enterococci from broilers, cattle, pigs and dogs are compared. In the three latter animal species narasin was never used and resistance to this antimicrobial is therefore very rare (Table ENT III-V).

Bacitracin was previously used as a growth promoter in broilers but this use was discontinued over thirty years ago (see Use of antimicrobials). Currently there is no direct selection pressure towards bacitracin resistance but it is still common and without statistically significant trends (Chi Square for trend, P>0.05) (Fig ENT I). Possibly prevalence of bacitracin resistance in *E. faecium* is upheld through co-selection by use of narasin since there is a statistically significant association between resistance to narasin and bacitracin in this species (Table ENT VIII).

Both macrolides (tylosin) and tetracyclines are used in broiler production although use is scarce (see Use of antimicrobials). Erythromycin resistance is common in all three species but without obvious trends over the years studied. (Fig ENT I). Likewise tetracycline resistance is common, especially in *E. faecalis*. Tetracycline resistance in *E. faecium* has declined since 2000 (Chi Square for trend, P<0.001).

In both *E. faecium* and *E. hirae* prevalence of resistance to virginiamycin has decreased from around 25% in year 2000 to 3-4% in 2007 (Fig ENT I). The decline is statistically significant for both species (Chi Square for trend, P<0.001) and probably due to the discontinued use of virginiamycin in broiler production year 1999 (see Use of antimicrobials).

The prevalence of VRE among broilers, studied by culture on vancomycin supplemented media, has gradually increased from less than one percent in 2000 to a peak of 41% of 99 samples cultured in 2005 (SVARM 2005). This year VRE were isolated from 27% of 339 samples which is similar to the prevalence in 2006 (28%). This indicates that the increase in prevalence observed in the first half of the 2000s has abated.

In previous years, phenotyping of VRE by the PhenePlate™ system has indicated clonality of isolates from Swedish broilers (SVARM 2005). The last two years, isolated VRE were not typed that way, but the resistance phenotype of the isolates, including vancomycin, narasin, and erythromycin, is the same as in previous years, which suggests that the dominant clone still prevails.

Table ENT III. Occurrence of resistance (%) and multiresistance (%) among *Enterococcus faecalis* from broilers, 2007. Previous data from SVARM are given for comparison. Cut-off values for resistance are given in Table ENT II.

	Resistance (%) (95% confidence interval)																	
	Broilers										**Dairy cows**		**Dogs**		**Pigs**	
Antimicrobial	**2007** n=28		**2004** n=48		**2002** n=57		**2001** n=49		**2000** n=47		**2006** n=13		**2006** n=135		**2005** n=55	
Ampicillin	0	(0.0-12.3)	0	(0.0-7.4)	0	(0.0-6.3)	0	(0.0-7.3)	0	(0.0-7.5)	0	(0.0-24.7)	<1	(0.0-4.1)	0	(0.0-6.5)
Bacitracin	11	(2.3-28.2)	29	(17.0-44.1)	35	(22.9-48.9)	31	(18.3-45.4)	23	(12.3-38.0)	0	(0.0-24.7)	1	(0.2-5.2)	2	(0.0-9.7)
Chloramph.	0	(0.0-12.3)	0	(0.0-7.4)	-		-		-		0	(0.0-24.7)	7	(3.1-12.3)	5	(1.1-15.1)
Erythromycin	29	(13.2-48.7)	25	(13.6-39.6)	26	(15.5-39.7)	41	(27.0-55.8)	30	(17.3-44.9)	0	(0.0-24.7)	14	(8.7-21.1)	33	(45.9-73.0)
Gentamicin	0	(0.0-12.3)	0	(0.0-7.4)	2	(0.0-9.4)	0	(0.0-7.3)	0	(0.0-7.5)	0	(0.0-24.7)	<1	(0.0-4.1)	5[a]	(1.1-15.1)
Kanamycin	4	(0.1-18.3)	-		-		-		-		0	(0.0-24.7)	4	(1.6-9.4)	-	
Linezolid	0	(0.0-12.3)	-		-		-		-		0	(0.0-24.7)	0	(0.0-2.7)	-	
Narasin	36	(18.6-55.9)	35	(22.2-50.5)	39	(26.0-52.4)	45	(30.7-59.8)	43	(28.3-57.8)	8	(0.2-36.0)	1	(0.2-5.2)	0	(0.0-6.5)
Streptomycin	0	(0.0-12.3)	4	(0.5-14.3)	11	(4.0-21.5)	6	(1.3-16.9)	9	(2.4-20.4)	0	(0.0-24.7)	9	(4.7-15.0)	16	(7.8-28.8)
Tetracycline	57	(37.2-75.5)	48	(31.4-60.8)	63	(49.3-75.6)	69	(54.6-81.7)	60	(44.3-73.6)	15	(1.9-45.4)	32	(24.1-40.4)	64	(49.6-76.2)
Vancomycin	0	(0.0-12.3)	0	(0.0-7.4)	0	(0.0-6.3)	0	(0.0-7.3)	0	(0.0-7.5)	0	(0.0-24.7)	0	(0.0-2.7)	0	(0.0-6.5)
Virginiamycin	0	(0.0-12.3)	0	(0.0-7.4)	0	(0.0-6.3)	0	(0.0-7.3)	0	(0.0-7.5)	0	(0.0-24.7)	0	(0.0-2.7)	0	(0.0-6.5)
Multiresistance																
Susceptible to all	25		23		18		8		15		77		59		25	
Resistant to 1	36		29		26		35		47		23		24		38	
Resistant to 2	21		35		37		29		13				11		27	
Resistant to 3	14		8		7		14		15				2		2	
Resistant to >3	4		4		12		14		11				4		7	

[a] Cut-off value >512 mg/L.

Table ENT IV. Occurrence of resistance (%) and multiresistance (%) among *Enterococcus faecium* from broilers, 2007. Previous data from SVARM are given for comparison. Cut-off values for resistance are given in Table ENT II.

	Resistance (%) (95% confidence interval)																	
	Broilers										**Dairy cows**		**Dogs**		**Pigs**	
Antimicrobial	**2007** n=197		**2004** n=163		**2002** n=189		**2001** n=204		**2000** n=151		**2006** n=98		**2006** n=29		**2005** n=47	
Ampicillin	1	(0.1-3.6)	2	(0.7-6.2)	4	(1.8-8.2)	5	(2.4-8.8)	8	(4.2-13.5)	0	(0.0-3.7)	0	(0.0-11.9)	0	(0.0-7.5)
Bacitracin	23	(17.2-29.3	32	(24.8-39.6)	24	(18.4-31.1)	15	(10.1-20.3)	20	(13.8-27.1)	1	(0.1-5.6)	3	(0.1.17.8)	2	(0.1-11.3)
Chloramph.	0	(0.0-1.9)	0	(0.0-2.2)	-		-		-		0	(0.0-3.7)	0	(0.0-11.9)	2	(0.1-11.3)
Erythromycin	11	(7.1-16.4)	10	(5.7-15.5)	11	(7.0-16.5)	15	(10.1-20.3)	12	(7.2-18.2)	7	(2.9-14.2)	28	(12.7-47.2)	21	(10.7-35.7)
Gentamicin	0	(0.0-1.9)	0	(0.0-2.2)	0	(0.0-1.9)	0	(0.0-1.8)	0	(0.0-2.4)	0	(0.0-3.7)	0	(0.0-11.9)	2[a]	(0.1-11.3)
Kanamycin	0	(0.0-1.9)	-		-		-		-		0	(0.0-3.7)	0	(0.0-11.9)	-	
Linezolid	0	(0.0-1.9)	-		-		-		-		0	(0.0-3.7)	0	(0.0-11.9)	-	
Narasin	89	(83.6-92.9)	93	(88.2-96.6)	78	(71.2-83.5)	80	(73.7-85.2)	79	(72.1-85.6)	0	(0.0-3.7)	7	(0.8-22.8)	0	(0.0-7.5)
Streptomycin	1	(0.1-3.6)	<1	(0.0-3.4)	0	(0.0-1.9)	0	(0.0-1.8)	<1	(0.0-3.6)	0	(0.0-3.7)	0	(0.0-11.9)	0b	(0.0-7.5)
Tetracycline	16	(10.9-21.6)	18	(12.8-25.2)	27	(20.8-33.9)	29	(23.3-36.2)	40	(32.5-48.7)	3	(0.6-8.7)	17	(5.8-35.8)	13	(4.8-25.7)
Vancomycin	0	(0.0-1.9)	2	(0.4-5.3)	1	(0.1-3.8)	0	(0.0-1.8)	1c	(0.2-4.7)	0	(0.0-3.7)	0	(0.0-11.9)	0	(0.0-7.5)
Virginiamycin	4	(1.8-7.8)	9	(5.2-14.7)	24	(18.4-31.1)	22	(16.6-28.4)	24	(17.9-32.2)	1	(0.1-5.6)	0	(0.0-11.9)	13	(4.8-25.7)
Multiresistance																
Susceptible to all	9		3		11		10		11		89		55		62	
Resistant to 1	47		41		31		35		28		10		35		30	
Resistant to 2	36		44		38		37		34		1		10		6	
Resistant to 3	7		10		17		15		19							
Resistant to >3	1		3		3		3		7						2	

[a] Cut-off value >512 mg/L; [b] Cut-off value >256 mg/L; [c] Isolates with MIC 8 mg.

Table ENT V. Occurrence of resistance (%) and multiresistance (%) among *Enterococcus hirae* from broilers, 2007. Previous data from SVARM are given for comparison. Cut-off values for resistance are given in Table ENT II.

	Resistance (%) (95% confidence interval)															
	Broilers										**Dairy cows**		**Dogs**		**Pigs**	
Antimicrobial	**2007** n=36		**2004** n=34		**2002** n=45		**2001** n=27		**2000** n=28		**2006** n=147		**2006** n=22		**2005** n=112	
Ampicillin	0	(0.0-9.7)	0	(0.0-10.3)	0	(0.0-7.9)	4	(0.1-19.0)	0	(0.0-12.3)	0	(0.0-2.5)	0	(0.0-15.4)	0	(0.0-3.2)
Bacitracin	8	(1.8-22.5)	0	(0.0-10.3)	2	(0.1-11.8)	4	(0.1-19.0)	7	(0.9-23.5)	0	(0.0-2.5)	0	(0.0-15.4)	0	(0.0-3.2)
Chloramph.	0	(0.0-9.7)	0	(0.0-10.3)	-		-		-		0	(0.0-2.5)	0	(0.0-15.4)	0	(0.0-3.2)
Erythromycin	19	(8.2-36.0)	26	(12.9-44.4)	40	(25.7-55.7)	22	(8.6-42.3)	25	(10.7-44.9)	<1	(0.0-3.7)	14	(2.9-34.9)	0	(0.0-3.2)
Gentamicin	0	(0.0-9.7)	0	(0.0-10.3)	0	(0.0-7.9)	0	(0.0-12.8)	0	(0.0-12.3)	0	(0.0-2.5)	0	(0.0-15.4)	0[a]	(0.0-3.2)
Kanamycin	0	(0.0-9.7)	-		-		-		-		0	(0.0-2.5)	5	(0.1-22.8)	-	
Linezolid	0	(0.0-9.7)	-		-		-		-		0	(0.0-2.5)	0	(0.0-15.4)	-	
Narasin	94	(81.3-99.3)	91	(76.3-98.1)	87	(73.2-95.0)	89	(70.8-97.6)	89	(71.8-97.7)	2	((0.4.5.8)	5	(0.1-22.8)	5	(2.0-11.3)
Streptomycin	0	(0.0-9.7)	0	(0.0-10.3)	0	(0.0-7.9)	0	(0.0-12.8)	4	(0.1-18.3)	0	(0.0-2.5)	5	(0.1-22.8)	0[b]	(0.0-3.2)
Tetracycline	14	(4.7-29.5)	3	(0.1-15.3)	7	(1.4-18.3)	4	(0.1-19.0)	7	(0.9-23.5)	0	(0.0-2.5)	14	(2.9-34.9)	11	(5.7-18.0)
Vancomycin	0	(0.0-9.7)	0	(0.0-10.3)	0	(0.0-7.9)	0	(0.0-12.8)	0	(0.0-12.3)	0	(0.0-2.5)	0	(0.0-15.4)	0	(0.0-3.2)
Virginiamycin	3	(0.1-14.9)	26	(12.9-44.4)	33	(20.0-49.0)	59	(38.8-77.6)	29	(13.2-48.7)	0	(0.0-2.5)	5	(0.1-22.8)	2	(0.2-6.3)
Multiresistance																
Susceptible to all	6		3		7		7		4		97		77		82	
Resistant to 1	58		50		27		22		36		3		14		18	
Resistant to 2	31		44		58		56		57				5			
Resistant to 3	3		3		9		11		4							
Resistant to >3	3						4						5			

[a] Cut-off value >512 mg/L, [b]Cut-off value >256 mg/L.

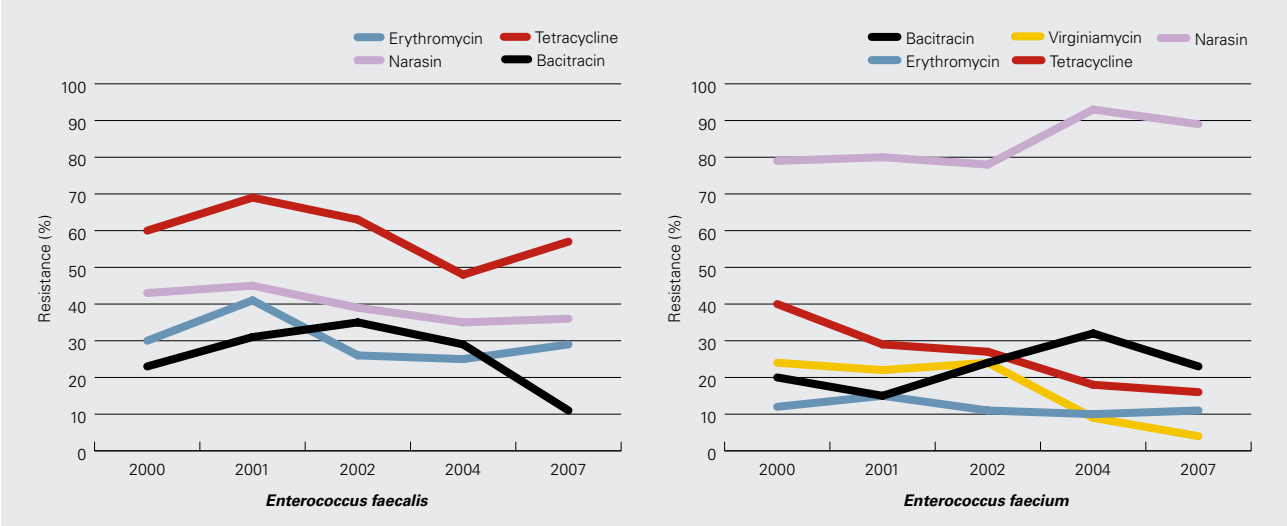

Figure ENT I. Resistance (%) to selected antimicrobials in indicator *Enterococcus faecalis* and *E. faecium* from broilers years 2000-2002, 2004 and 2007. For number of isolates see Table ENT III and IV. Data from SVARM.

Table ENT VI. Resistance phenotypes of *Enterococcus faecalis* resistant to three or more antimicrobials and *E. faecium*, resistant to four or more antimicrobials, broilers 2007. "R" in shaded fields indicates resistance. Previous data from SVARM are given for comparison.

E. faecalis											
Year					Resistance pattern[a]						
2007 n=28	**2004** n=48	**2002** n=57	**2001** n=49	**2002** n=47	**Em**	**Na**	**Ba**	**Tc**	**Sm**	**Km**[b]
	1	2		2	R	R	R	R	R	
1		4	7	2	R	R	R	R		
	1		1	1	R	R	R			
		1			R	R	R		R	
				1	R	R		R	R	
3	1	1	4	1	R	R		R		
			1		R	R			R	
	2			5	R		R	R		
1					R			R		R
	1				R			R	R	
		2	1			R	R	R		
		1				R	R		R	
5 (18%)	**6** (13%)	**11** (19%)	**14** (29%)	**12** (25%)	Number of isolates					

E. faecium												
Year					Resistance pattern[a]							
2007 n=197	**2004** n=163	**2002** n=189	**2001** n=204	**2000** n=151	**Na**	**Tc**	**Ba**	**Vi**	**Em**	**Am**	**Sm**	**Va**
				2	R	R	R	R	R			
				1	R	R	R	R		R		
				1	R	R	R	R				R
1		2	2	1	R	R	R	R				
		1		1	R	R	R		R			
				2	R	R	R			R		
1	1				R	R	R				R	
			1		R			R	R	R		
	2	2		1	R	R		R	R			
			1	1	R	R		R		R		
			1	1	R	R			R	R		
		1			R		R	R				R
	1				R			R	R	R		
2 (1%)	**4** (3%)	**6** (3%)	**5** (3%)	**11** (7%)	Number of isolates							

[a] Em: erythromycin; Na: narasin; Ba: bacitracin; Tc: tetracycline; Sm: streptomycin; Km: kanamycin; Vi: virginiamycin; Am: ampicillin; Va: vancomycin; [b] Not included years 2000-2004.

Table ENT VII. Association between resistance traits in *Enterococcus faecalis* isolated from broilers years 2000, 2001, 2002, 2004 and 2007. For each antimicrobial the first line gives the resistance rates for susceptible isolates (S) and the second line rates for resistant isolates (R). All antimicrobials were not tested all years, therefor all combinations of pairs of resistance traits can not be calculated. Bold and underlined figures indicate statistically significant association between pairs of resistance traits (Chi-Square or Fischer's Exact test, P<0.001).

Single substance susceptibility		**n**	**Resistance** (%)[a]								
			Am	**Ba**	**Em**	**Gm**	**Na**	**Sm**	**Tc**	**Va**	**Vi**
Ampicillin	S	229	0.0	27.5	30.1	0.0	39.7	6.6	59.8	0.0	0.0
	R	0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Bacitracin	S	166	0.0	0.0	23.5	0.0	38.0	4.8	50.6	0.0	0.0
	R	63	0.0	100.0	**47.6**	0.0	44.4	11.1	**84.1**	0.0	0.0
Chloramphenicol	S	76	0.0	22.4	26.3	0.0	35.5	2.6	51.3	0.0	0.0
	R	0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Erythromycin	S	160	0.0	20.6	0.0	0.0	27.5	3.8	56.3	0.0	0.0
	R	69	0.0	**43.5**	100.0	0.0	**68.1**	13.0	68.1	0.0	0.0
Gentamicin	S	229	0.0	27.5	30.1	0.0	39.7	6.6	59.8	0.0	0.0
	R	0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Kanamycin	S	27	0.0	11.1	25.9	0.0	37.0	0.0	55.6	0.0	0.0
	R	1	0.0	0.0	100.0	0.0	0.0	0.0	100.0	0.0	0.0
Linezolid	S	28	0.0	10.7	28.6	0.0	35.7	0.0	57.1	0.0	0.0
	R	0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Narasin	S	138	0.0	25.4	15.9	0.0	0.0	4.3	63.0	0.0	0.0
	R	91	0.0	30.8	**51.6**	0.0	100.0	9.9	54.9	0.0	0.0
Streptomycin	S	214	0.0	26.2	28.0	0.0	38.3	0.0	59.8	0.0	0.0
	R	15	0.0	46.7	60.0	0.0	60.0	100.0	60.0	0.0	0.0
Tetracycline	S	92	0.0	10.9	23.9	0.0	44.6	6.5	0.0	0.0	0.0
	R	137	0.0	**38.7**	34.3	0.0	36.5	6.6	100.0	0.0	0.0
Vancomycin	S	229	0.0	27.5	30.1	0.0	39.7	6.6	59.8	0.0	0.0
	R	0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Virginiamycin	S	229	0.0	27.5	30.1	0.0	39.7	6.6	59.8	0.0	0.0
	R	0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0

[a] Am: ampicillin; Ba: bacitracin; Em: erythromycin; Gm: gentamicin; Na: narasin; Sm: streptomycin; Tc: tetracycline; Va: vancomycin.

Table ENT VIII. Association between resistance traits in *Enterococcus faecium* isolated from broilers years 2000, 2001, 2002, 2004 and 2007. For each antimicrobial the first line gives the resistance rates for susceptible isolates (S) and the second line rates for resistant isolates (R). All antimicrobials were not tested all years, therefor all combinations of pairs of resistance traits can not be calculated. Bold and underlined figures indicate statistically significant association between pairs of resistance traits (Chi-Square or Fischer's Exact test, P<0.001).

Single substance susceptibility		n	Resistance (%)[a]								
			Am	Ba	Em	Gm	Na	Sm	Tc	Va	Vi
Ampicillin	S	868	0.0	22.2	11.8	0.0	84.2	0.5	25.1	0.8	16.7
	R	36	100.0	27.8	13.9	0.0	72.2	0.0	41.7	0.0	16.7
Bacitracin	S	701	3.7	0.0	13.4	0.0	81.3	0.3	27.8	0.7	18.7
	R	203	4.9	100.0	6.4	0.0	**92.1**	1.0	18.7	1.0	9.9
Chloramphenicol	S	360	1.7	26.9	10.6	0.0	90.8	0.8	16.9	0.8	6.4
	R	0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Erythromycin	S	797	3.9	23.8	0.0	0.0	83.4	0.4	24.7	0.4	17.2
	R	107	4.7	12.1	100.0	0.0	86.0	0.9	33.6	**3.7**	13.1
Gentamicin	S	904	4.0	22.5	11.8	0.0	83.7	0.4	25.8	0.8	16.7
	R	0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Kanamycin	S	197	1.0	22.8	11.2	0.0	88.8	1.0	15.7	0.0	4.1
	R	0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Linezolid	S	197	1.0	22.8	11.2	0.0	88.8	1.0	15.7	0.0	4.1
	R	0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Narasin	S	147	6.8	10.9	10.2	0.0	0.0	1.4	23.8	0.0	6.8
	R	757	3.4	**24.7**	12.2	0.0	100.0	0.3	26.2	0.9	**18.6**
Streptomycin	S	900	4.0	22.3	11.8	0.0	83.9	0.0	25.7	0.8	16.7
	R	4	0.0	50.0	25.0	0.0	50.0	100.0	50.0	0.0	25.0
Tetracycline	S	671	3.1	24.6	10.6	0.0	83.3	0.3	0.0	0.7	12.2
	R	233	6.4	16.3	15.5	0.0	85.0	0.9	100.0	0.9	**29.6**
Vancomycin	S	897	4.0	22.4	11.5	0.0	83.6	0.4	25.8	0.0	16.6
	R	7	0.0	28.6	**57.1**	0.0	100.0	0.0	28.6	100.0	28.6
Virginiamycin	S	753	4.0	24.3	12.4	0.0	81.8	0.4	21.8	0.7	0.0
	R	151	4.0	13.2	9.3	0.0	**93.4**	0.7	**45.7**	1.3	100.0

[a] Am: ampicillin; Ba: bacitracin; Em: erythromycin; Gm: gentamicin; Na: narasin; Sm: streptomycin; Tc: tetracycline; Va: vancomycin; Vi: virginiamycin.

Table ENT IX. Distribution of MICs for Enterococcus faecalis from broilers (n=28) year 2007. Data from SVARM year 2004 (n=48) and composite data for years 2000 (n=47), 2001 (n=49) and 2002 (n=57) are given for comparison.

Antimicrobial	Year	Resistance (%)	Distribution (%) of MICs[a] (mg/L)															
			≤0.12	**0.25**	**0.5**	**1**	**2**	**4**	**8**	**16**	**32**	**64**	**128**	**256**	**512**	**1024**	**2048**	**>2048**
Ampicillin	2007	0			17.9	82.1												
	2004	0		2.1	20.8	72.9	4.2											
	2000-02	0		2.0	7.2	80.4	9.8	0.7										
Bacitracin[b]	2007	11						14.3	53.6	17.9	3.6		3.6	7.1				
	2004	29				2.1		12.5	31.3	22.9	2.1	2.1	27.1					
	2000-02	30				3.9	1.3	4.6	20.9	32.0	7.2	30.1						
Chloramph.[c]	2007	0						25.0	75.0									
	2004	0						41.7	54.2	4.2								
Erythromycin	2007	29			25.0	28.6	14.3	3.6		17.9			10.7					
	2004	25			33.3	25.0	16.7		8.3	8.3	2.1		6.3					
	2000-02	32		2.6	21.6	11.8	26.1	5.9	7.8	3.3	2.0	19.0						
Gentamicin	2007	0						3.6	21.4	75.0								
	2004	0			2.1			6.3	66.7	18.8	6.3							
	2000-02	<1				1.3	2.0	6.5	38.6	41.8	9.2				0.7			
Kanamycin[d]	2007	4									32.1	60.7	3.6					3.6
Linezolid[d]	2007	0			3.6	3.6	85.7	7.1										
Narasin	2007	36		35.7	28.6			25.0	10.7									
	2004	35		25.0	33.3		6.3	16.7	16.7	2.1								
	2000-02	42	6.5	21.6	18.3	3.3	8.5	24.8	13.7	2.6	0.7							
Streptomycin	2007	0								3.6	3.6	50.0	42.9					
	2004	4									6.3	64.6	25.0				4.2	
	2000-02	8						0.7		2.0	11.8	49.7	27.5			2.0	6.5	
Tetracycline	2007	57			25.0	17.9				3.6	17.9	35.7						
	2004	48			22.9	29.2			2.1	12.5	10.4	14.6	8.3					
	2000-02	64		0.7	2.0	24.2	9.2	1.3	1.3	18.3	22.2	20.9						
Vancomycin	2007	0				25.0	67.9	7.1										
	2004	0				6.3	75.0	18.8										
	2000-02	0				13.7	71.2	15.0										
Virginiamycin	2007	0					3.6		21.4	64.3	10.7							
	2004	0			2.1		2.1	12.5	33.3	47.9	2.1							
	2000-02	0			2.0	2.0	5.2	10.5	23.5	50.3	6.5							
			≤0.12	**0.25**	**0.5**	**1**	**2**	**4**	**8**	**16**	**32**	**64**	**128**	**256**	**512**	**1024**	**2048**	**>2048**

[a]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 for resistance; [b]MIC in U/mL, see Appendix 3 for details; [c]Not tested 2000-02; [d]Not tested 2000-02 and 2004.

Table ENT X. Distribution of MICs for *Enterococcus faecium* from broilers (n=197) year 2007. Data from SVARM year 2004 (n=163) and composite data for years 2000 (n=151), 2001 (n=204) and 2002 (n=189) are given for comparison.

		Resis-	Distribution (%) of MICs[a] (mg/L)															
Antimicrobial	**Year**	tance (%)	**≤0.12**	**0.25**	**0.5**	**1**	**2**	**4**	**8**	**16**	**32**	**64**	**128**	**256**	**512**	**1024**	**2048**	**>2048**
	2007	1		14.7	15.7	29.9	27.4	11.2	1.0									
Ampicillin	2004	2		10.4	18.4	19.0	38.0	11.7	2.5									
	2000-02	6		9.0	20.2	24.6	25.6	15.1	5.3	0.2								
	2007	23				28.4	6.6	4.1	13.7	19.3	5.1	19.3	1.5	2.0				
Bacitracin[b]	2004	32				21.5	3.7	3.7	9.8	19.6	9.8	18.4	13.5					
	2000-02	19			1.8	17.8	3.7	4.2	18.9	21.7	12.3	19.5						
Chloramph.[c]	2007	0					2.0	65.0	31.0	1.5	0.5							
	2004	0					1.8	65.6	31.3	1.2								
	2007	11			26.9	49.2	11.2	1.5	1.5	2.0	1.5	0.5	5.6					
Erythromycin	2004	10			37.4	43.6	6.7	2.5	3.1	4.3			2.5					
	2000-02	13		4.4	19.1	22.2	31.3	10.3	2.6	1.1	0.4	8.6						
	2007	0					2.5	35.5	52.3	9.1	0.5							
Gentamicin	2004	0				1.2	3.7	32.5	54.0	8.6								
	2000-02	0			0.2	0.6	4.4	24.4	50.6	18.2	1.7							
Kanamycin[d]	2007	0									1.0	28.9	49.2	17.3	3.0	0.5		
Linezolid[d]	2007	0				5.1	80.7	14.2										
	2007	89			8.6	1.5	1.0	53.8	35.0									
Narasin	2004	93			3.1	1.8	1.8	35.0	55.2	3.1								
	2000-02	79	0.4	1.3	4.2	6.3	8.8	28.9	46.9	3.3								
	2007	1								1.0	47.2	48.7	2.0		0.5		0.5	
Streptomycin	2004	<1									50.3	48.5	0.6			0.6		
	2000-02	<1					0.2	0.2	0.4	12.9	48.9	35.1	2.2				0.2	
	2007	16			82.2	1.5	0.5	1.5	1.0	0.5	3.6	7.6	1.5					
Tetracycline	2004	18			60.1	20.9	0.6		2.5	2.5	4.9	6.7	1.8					
	2000-02	32		1.5	9.4	50.2	7.4	1.3	1.3	5.9	8.6	14.5						
	2007	0				98.0	1.5	0.5										
Vancomycin	2004	2				89.0	7.4	1.8						1.8				
	2000-02	<1				78.1	15.3	5.9	0.6					0.2				
	2007	4			19.8	43.7	25.4	7.1	3.0	1.0								
Virginiamycin	2004	9			16.6	41.7	28.2	4.3	7.4	1.8								
	2000-02	24			13.8	29.6	28.7	4.4	13.4	9.2	0.9							
			≤0.12	**0.25**	**0.5**	**1**	**2**	**4**	**8**	**16**	**32**	**64**	**128**	**256**	**512**	**1024**	**2048**	**>2048**

[a]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 for resistance; [b]MIC in U/mL, see Appendix 3 for details; [c]Not tested 2000-02; [d]Not tested 2000-02 and 2004.

Table ENT XI. Distribution of MICs for *Enterococcus hirae* from broilers (n=36) year 2007. Data from SVARM year 2004 (n=34) and composite data for years 2000 (n=28), 2001 (n=27) and 2002 (n=45) are given for comparison.

		Resis-	Distribution (%) of MICs[a] (mg/L)															
Antimicrobial	**Year**	tance (%)	**≤0.12**	**0.25**	**0.5**	**1**	**2**	**4**	**8**	**16**	**32**	**64**	**128**	**256**	**512**	**1024**	**2048**	**>2048**
Ampicillin	2007	0		47.2	27.8	19.4	5.6											
	2004	0		70.6	17.6	11.8												
	2000-02	1		45.0	24.0	13.0	16.0	1.0	1.0									
Bacitracin[b]	2007	9				55.6	11.1	5.6	13.9	2.8	2.8	5.6	2.8					
	2004	0				11.8	20.6	14.7	11.8	11.8	29.4							
	2000-02	4				13.0	18.0	12.0	14.0	14.0	25.0	4.0						
Chloramph.[c]	2007	0					5.6	72.2	22.2									
	2004	0						55.9	44.1									
Erythromycin	2007	20			72.2	2.8	2.8	2.8		2.8			16.7					
	2004	26			70.6		2.9						26.5					
	2000-02	31		12.0	48.0	6.0	1.0	2.0	2.0			29.0						
Gentamicin	2007	0					47.2	13.9	13.9	25.0								
	2004	0				8.8	47.1	35.3	2.9	5.9								
	2000-02	0				1.0	27.0	42.0	12.0	13.0	5.0							
Kanamycin[d]	2007	0								47.2	11.1	30.6	8.3	2.8				
Linezolid[d]	2007	0			2.8	8.3	88.9											
Narasin	2007	97		2.8			2.8	61.1	33.3									
	2004	91		5.9			2.9	32.4	52.9	5.9								
	2000-02	88		2.0	7.0	1.0	2.0	34.0	50.0	4.0								
Streptomycin	2007	0								5.6	55.6	22.2	16.7					
	2004	0									64.7	32.4	2.9					
	2000-02	1						1.0		12.0	59.0	15.0	12.0				1.0	
Tetracycline	2007	14			77.8	8.3		2.8			2.8	8.3						
	2004	3			35.3	61.8						2.9						
	2000-02	6		1.0	5.0	63.0	25.0			2.0	1.0	3.0						
Vancomycin	2007	0				91.7	8.3											
	2004	0				97.1	2.9											
	2000-02	0				92.0	8.0											
Virginiamycin	2007	3			19.4	8.3	58.3	11.1		2.8								
	2004	26				8.8	52.9	11.8	23.5		2.9							
	2000-02	39				3.0	56.0	2.0	19.0	15.0	5.0							
			≤0.12	**0.25**	**0.5**	**1**	**2**	**4**	**8**	**16**	**32**	**64**	**128**	**256**	**512**	**1024**	**2048**	**>2048**

[a]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 for resistance; [b]MIC in U/mL, see Appendix 3 for details; [c]Not tested 2000-02; [d]Not tested 2000-02 and 2004.

Resistance in animal pathogens

ISOLATES TESTED are from clinical submission of samples to SVA if not stated otherwise. For these samples, information on the indications for sampling is not available but the vast majority of clinical submissions are likely from diseased animals. Therefore, data are probably biased towards samples from treated animals or from herds where antimicrobial treatments are common. Any assessment of trends is based on the assumption that this bias is inherent throughout the observation period.

In SVARM, isolates are, when possible, classified as susceptible or resistant by epidemiological cut-off values issued by EUCAST (see Appendix 3 for details). This classifies isolates with acquired reduced susceptibility as resistant, which is relevant for monitoring purposes, but it should be understood that this not always implies clinical resistance. Some cut-off values defining resistance (breakpoints) previously used in SVARM have been changed. To facilitate comparisons, resistance data from earlier reports have therefore been recalculated using current cut-off values when possible.

Pig

Isolates included

Isolates of *Escherichia coli* from years 1992-2007 are from diagnostic submissions of samples from the gastro-intestinal tract (intestinal content, faecal samples or mesenteric lymph nodes), while data from 1989-1991 include all *E. coli* isolated from pigs, irrespective of material type. On the first of October, 2007, the criteria for an isolate to be susceptibility tested were changed. At that time new diagnostics for *E. coli* using a PCR for genes coding virulence factors were introduced (see Highlight SVARMpat). Therefore, resistance data for *E. coli* is comprised of those isolated until the 30th of September. Isolates of *Brachyspira hyodysenteriae* are from clinical submissions of faecal samples from pigs. *Actinobacillus pleuropneumoniae* from years 1992-2000 were isolated from the respiratory tract (nasal swabs and lung, including regional lymph nodes) but from years 2005-2007 all isolates are from lungs sampled post mortem. *Pasteurella multocida* are from nasal swabs collected within a control programme for atrophic rhinitis in nucleus and multiplying herds.

Escherichia coli

As in previous years, resistance to ampicillin, streptomycin, tetracycline or trimethoprim-sulphonamides in *E. coli* was common in 2007 (Table Pig I). In the 70s and 80s, prevalence of *E. coli* resistant to ampicillin was only around seven percent (Franklin, 1976; Franklin, 1984). From the early 90s to year 2004, prevalence of ampicillin resistance rose gradually to 22% and remained at this level until 2007, when the figure rose further to 30% (Chi-square for trend, $P<0.01$).

Resistance to ampicillin alone was rare, 78% of the ampicillin resistant isolates were resistant to at least one other antimicrobial. Resistance to ampicillin and trimethoprim-sulphonamides was the most common combination of traits. Of the ampicillin resistant isolates, 64% were also resistant to trimethoprim-sulphonamides and 75% of isolates resistant to trimethoprim-sulphonamides, were also resistant to ampicillin. This indicates that the genes coding for resistance to ampicillin and trimethoprim-sulphonamides are linked.

Multiresistance (i.e. resistance to three or more antimicrobials) occurred in 25% of the isolates, one of these was resistant to six antimicrobials. The most frequent combination, found in 71% of the multiresistant isolates, was resistance to ampicillin, trimethoprim-sulphonamides, and streptomycin.

The extent of use of aminopenicillins or trimethoprim-sulphonamides for Swedish pigs during the last years is not known. Therefore, it is not possible to draw any inferences on the association between resistance and use. However, although the amount of tetracycline used in feed or water to pigs has doubled since year 2003 (see Use of antimicrobials), the prevalence of resistance to tetracycline has been stable during the last five years. The *E. coli* isolates presented here are probably from younger animals than those that receive tetracycline treatment in feed or water. This could be one explanation to why resistance to tetracycline has not increased in *E. coli*.

Brachyspira hyodysenteriae

All isolates of *B. hyodysenteriae* were susceptible to tiamulin (Table Pig II). Sweden has a programme for controlling swine dysentery by three strategies; nucleus and multiplying herds are tested for *B. hyodysenteriae* twice a year, eradication of the bacteria in infected herds and tracing the source of infection. Nevertheless, it is imperative that all herds where treatment failure is suspected are thoroughly investigated.

In the late 80s, susceptibility of *B. hyodysenteriae* was tested with an agar dilution technique, and 20% of the isolates were resistant to tylosin (Gunnarsson et al., 1991). In year 2001, the figure had increased dramatically to around 80% (Table Pig II). This year's figure is numerically lower but a small number of isolates precludes valid conclusions on trends. It is important to continue to monitor the resistance development in *B. hyodysenteriae* since only tylosin and tiamulin are licensed for treatment of spirochetal diarrhoea in pigs and in addition, use of macrolides (e.g. tylosin) and pleuromutilins (e.g. tiamulin) in pigs has increased during the last five years (see Use of Antimicrobials).

Brachyspira pilosicoli

In 2001, the first isolates of *B. pilosicoli* resistant to tiamulin were confirmed in Sweden. These isolates were associated with treatment failure in a Swedish pig herd with spirochaetal diarrhoea (see SVARM 2003). Since then, tiamulin resistant strains have been isolated every year but there is no apparent increasing trend in prevalence of resistance (Table Pig III). The frequency of resistance to tylosin has during the last two

Table Pig I. Resistance (%) in *Escherichia coli* from pigs 1989-2007 and distribution of MICs for isolates from 2007. Isolates are from diagnostic submissions of faecal samples or samples taken post mortem from the gastro-intestinal tract.

	Resistance (%)								Distribution (%) of MICs[a] (mg/L)									
Antimicrobial	1989-91 n=248	1992-94 n=431	1995-97 n=1244	1998-00 n=1074	2001-03 n=935	2004-05 n=711	2006 n=298	2007 n=93	≤0.12	0.25	0.5	1	2	4	8	16	32	>32
Ampicillin	6	10	9	11	17	22	21	30				10.8	48.4	10.8		30.1		
Ceftiofur	-	-	-	-	<1[h]	<1	<1	0		49.5	43.0	7.5						
Enrofloxacin	1[c,g]	7[c]	5[c]	6[c]	8[c]	9	8	4	95.7	2.2			2.2					
Florfenicol	-	-	-	-	<1[h]	0	<1	0					6.5	36.6	48.4	8.6		
Gentamicin	1[d]	1[d]	<1[d]	1[d]	4[d]	1	1	2					94.6	3.2	1.1		1.1	
Neomycin	17	14	9	6	5[i]	4	3	3						95.7	1.1			3.3
Streptomycin	44[e]	44[e]	32[e]	30[e]	36	37	32	40						14.0	33.3	12.8	11.8	28.0
Tetracycline	28	35	31	33	30	26	26	27				31.5	40.2		1.1	27.2		
Trim/Sulph.[b]	17[f]	15[f]	13[f]	14[f]	19	26	21	27			71.0	2.2		1.1	25.8			

[a] 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; [b] Concentration of trimethoprim given, tested in concentration ratio 1/20 (trimethoprim/sulphametoxazole); [c] Cut-off value was >0.25 mg/L until year 2001; [d] Cut-off value was >8 mg/L until year 2002; [e] Cut-off value was >32 mg/L until year 2001; [f] Cut-off value was >4 mg/L until year 2001; [g] 227 isolates tested; [h] 688 isolates tested; [i] 926 isolates tested.

Table Pig II. Resistance (%) in *Brachyspira hyodysenteriae* from pigs 2001-07 and distribution of MICs for isolates from 2007. Isolates are from diagnostic submissions of faecal samples.

	Resistance (%)						Distribution (%) of MICs[a] (mg/L)											
Antimicrobial	2001 n=75	2002 n=109	2003 n=100	2005 n=31	2006 n=26	2007 n=23	≤0.06	0.125	0.25	0.5	1	2	4	8	16	32	64	128	>128
Tiamulin	0	0	0	0	0	0	47.8	26.1	13.0	13.0									
Tylosin	83	73	89	81	85	65							26.1	8.7				4.3	60.9

[a] 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.

Table Pig III. Resistance (%) in *Brachyspira pilosicoli* from pigs 2002-07 and distribution of MICs for isolates from 2007. Isolates are from diagnostic submissions of faecal samples.

	Resistance (%)				Distribution (%) of MICs[a] (mg/L)												
Antimicrobial	2002-03 n=93	2005 n=57	2006 n=72	2007 n=44	≤0.06	0.125	0.25	0.5	1	2	4	8	16	32	64	128	>128
Tiamulin	14	16	12	9	40.9	25.0	15.9	2.3	4.5	2.3		2.3	6.8				
Tylosin	50[b]	63	67	61						11.3	15.9	11.3		2.3		4.5	54.5

[a] 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; [b] 86 isolates tested.

years been stable, around 60% of the isolates being resistant to this antimicrobial (Table Pig III).

In 2007, resistance to both antimicrobials occurred in three isolates, i.e. 7% of all isolates, and 11% of *B. pilosicoli* resistant to tylosin were resistant also to tiamulin. Although such isolates may be susceptible to other antimicrobials, only tiamulin and tylosin are currently licensed for treatment of spirochaetal diarrhoea in pigs in Sweden. The findings stress the need for susceptibility testing of *B. pilosicoli* from herds where tiamulin is to be used.

Actinobacillus pleuropneumoniae

Antimicrobial resistance was rare in isolates of *A. pleuropneumoniae* from the last three years (Table Pig IV). The high prevalence of tetracycline resistance observed in the 90s did not appear in this data.

In years 2005 to 2007 around 30 strains of *A. pleuropneumoniae* were isolated and susceptibility tested each year. This is a considerable increase compared to the situation in the 90s when only 18 isolates were tested for antimicrobial susceptibility. Nonetheless, the number of isolates tested is low and a higher frequency of sampling and susceptibility testing is desirable if emerging resistance is to be detected early. Especially, since pneumonia caused by *A. pleuropneumoniae* is an increasing problem in Swedish pig production.

Pasteurella multocida

Antimicrobial resistance was rare in isolates of *P. multocida* as it was in the beginning of the current decade (Table Pig V). *Pasteurella multocida* are from nasal swabs collected within a control programme for atrophic rhinitis in nucleus and multiplying herds. The disease, caused by toxin produc-

Table Pig IV. Resistance (%) in *Actinobacillus pleuropneumoniae* from pigs the years 1992-2000 and 2005-07. Distribution of MICs for isolates from 2005-07. Isolates are from diagnostic submissions of samples from the respiratory tract or from post mortem investigations of lungs.

	Resistance (%)		**Distribution** (%) **of MICs**[a] (mg/L)																
Antimicrobial	**1992-00** n=18	**2005-07** n=84	**≤0.016**	**0.03**	**0.06**	**0.12**	**0.25**	**0.5**	**1**	**2**	**4**	**8**	**16**	**32**	**64**	**128**	**256**	**512**	**>512**
Ampicillin	6	0				71.4	29.6												
Cefotaxime	-	0		100.0															
Ceftiofur	-	0			100.0														
Chloramphenicol	11	0						100.0											
Ciprofloxacin	6[b]	0	2.4	97.6															
Florfenicol	-	0								100.0									
Gentamicin	-	0								10.7	86.9	2.4							
Nalidixic acid	-	0								47.6	52.4								
Penicillin	6	0				3.6	94.0	2.4											
Streptomycin	-	0								1.2		6.0	83.3	9.5					
Sulphonamide	-	0												2.4	27.4	66.7	3.6		
Tetracycline	11[c]	0					16.7	76.2	6.0	1.2									
Trimethoprim	-	0				28.6	69.0	2.4											

[a] 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; [b] tested as enrofloxacin, cut-off value 2 mg/l.; [c] cut-off value >8 mg/l.

Table Pig V. Resistance (%) in *Pasteurella multocida* from pigs 2000-01 and 2005-07. Distribution of MICs for isolates from 2005-07. Isolates are from the respiratory tract, isolated from nasal swabs.

	Resistance (%)		**Distribution** (%) **of MICs**[a] (mg/L)																
Antimicrobial	**2000-01** n=75	**2005-07** n=38	**≤0.016**	**0.03**	**0.06**	**0.12**	**0.25**	**0.5**	**1**	**2**	**4**	**8**	**16**	**32**	**64**	**128**	**256**	**512**	**>512**
Ampicillin	0	0					100.0												
Cefotaxime	-	0			100.0														
Ceftiofur	-	0				100.0													
Chloramphenicol	1	0							92.1	7.9									
Ciprofloxacin	1[b]	0	92.1	7.9															
Florfenicol	-	0									92.1	7.9							
Gentamicin	4	0							13.2	78.9	7.9								
Nalidixic acid	-	0							65.8	31.6	2.6								
Penicillin	0	0				13.2	84.2	2.6											
Streptomycin	4	0										57.9	36.8	5.3					
Sulphonamide	-	0											18.4	7.9	26.3	5.3	42.1		
Tetracycline	1	0						97.2	2.6										
Trimethoprim	-	0					65.8	21.1	5.3	7.9									

[a] 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; [b] enrofloxacin tested, cut-off value 2 mg/l.

ing *P. multocida*, is demonstrated in very few herds affiliated to the programme and it is therefore unlikely that the material is biased towards herds with respiratory problems. Thus, the situation regarding antimicrobial resistance might be different in *P. multocida* from production herds with respiratory problems.

Antimicrobial resistance in *Escherichia coli* from pigs in relation to frequency of post-weaning diarrhoea and antimicrobial use

POST-WEANING DIARRHOEA in pigs (PWD) is a multifactorial disease comprising husbandry factors and where overgrowth of *Escherichia coli* in the intestinal tract plays an important role. The objectives of this study were to investigate antimicrobial resistance in *E. coli* from clinically healthy pigs in relation to frequency of PWD on a herd level.

From all Swedish herds with more than 100 sows, in total 400 herds, every second was selected, i.e. 200 herds. From each herd, one healthy suckling piglet and one healthy weaned piglet were sampled by the herd veterinarian using rectal swabs. The piglets were younger than 12 weeks. The herd veterinarian also recorded information on frequency of PWD among pigs up to two weeks after weaning (0%, ≤25% or >25%). i.e. how many of the animals in that age group that were affected with the disease within a batch. For each herd, the antimicrobials used to treat PWD were recorded. Isolation, identification and susceptibility testing of *E. coli* are presented in Appendix 3 under Indicator bacteria and cut-off values for interpretation of antimicrobial susceptibility are shown in Appendix 3, Table AP3.

Rectal swabs from 180 herds were sent in to SVA. The herds were distributed according to incidence of PWD as follows: 0%: 42 herds (23%), ≤25%: 116 herds (64%) and >25%: 22 herds (12%). In herds that treated PWD with antimicrobials (46%), the most frequently used substances were trimethoprim-sulphonamides (in 50% of these herds), tylosin (33%), fluoroquinolones (18%) and colistin (16%). In total, 342 *E. coli* were isolated and distributed according to Table I.

Occurrence of resistance and distribution of MICs for antimicrobials tested are shown in Table II. Resistance to streptomycin, sulphonamides, tetracycline, ampicillin or trimethoprim were the most common traits. None of the isolates was resistant to gentamicin, florfenicol, ceftiofur or cefotaxime with exception of one isolate that had a MIC of 1 mg/l to cefotaxime. However, the isolate was negative for extended spectrum beta-lactamases (ESBLs) when tested by the phenotypic confirmatory test recommended by CLSI (see appendix for details). Multiresistance, i.e. resistance to three or more substances, occurred in 68 isolates (20%) and half of these were resistant to ampicillin, sulphonamides and trimethoprim, the most common resistance phenotype. Twenty-seven isolates were resistant to more than four substances (8%). These figures, both for individual substances as for multiresistance, are considerably higher than data from slaughtered pigs in SVARM 2005. One explanation could be that in SVARM older pigs are sampled and intestinal bacteria in younger animals usually display a higher prevalence of antimicrobial resistance (Mathew et al., 1999; Khachatryan et al., 2004).

The relation between resistance, age and herd frequency of PWD is shown in Figure I. The percentage of *E. coli* resistant to ampicillin or trimethoprim was higher in herds with >25% frequency of PWD compared to herds with ≤25% and 0% PWD (Chi-square, $P<0.05$). There was also a larger proportion of *E. coli* resistant to sulphonamides in herds with >25% frequency of PWD compared to those with 0% (Chi-square, $P<0.05$). For the other antimicrobials there was no significant difference between herds with different frequency of PWD and for all tested substances no significant differences between the two different age groups were recorded. One explanation to these results is that there probably is a more extensive use of antimicrobials in herds with higher frequency of PWD. In this study, PWD was most often treated with trimethoprim-sulphonamides. The higher selective pressure exerted on the enteric microflora could be indirectly measured by the occurrence of resistant *E. coli*.

Table I. Number of *Escherichia coli* isolated from suckling and weaned piglets from herds with different frequencies of post-weaning diarrhoea (PWD) up to two weeks after weaning (0%, ≤25% or >25%).

	Frequency of PWD			
	0%	≤25%	>25%	Total
Suckling piglets	42	110	20	172
Weaned piglets	37	111	22	170

Table II. Occurrence of resistance and distribution among *Escherichia coli* from healthy suckling and weaned piglets, in year 2006, isolated from rectal samples.

Antimicrobial	Resistance (%) n=342	Distribution (%) of MICs[a] (mg/L)																
		≤0.03	0.06	0.12	0.25	0.5	1	2	4	8	16	32	64	128	256	512	1024	>1024
Ampicillin	14					0.6	14.4	44.8	24.6	2.0		1.4	12.1					
Chloramphenicol	8							2.9	67.6	20.8	0.3	5.2	2.3	0.3	0.6			
Ciprofloxacin	5	56.6	38.4	0.9	1.7	0.3	0.3	1.4										
Nalidixic acid	5						0.3	28.6	61.8	4.3		0.3	0.6	1.1	2.6			
Streptomycin	22							0.6	11.0	41.9	16.2	7.8	4.3	6.6	8.4	3.2		
Sulphonamides	31										38.7	15.6	10.7	3.2				30.9
Tetracycline	16						31.2	49.7	1.4	0.6		1.2	6.4	9.0				
Trimethoprim	18				23.7	47.1	10.7	0.3	0.9	0.3		1.2	15.7					

[a] 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;

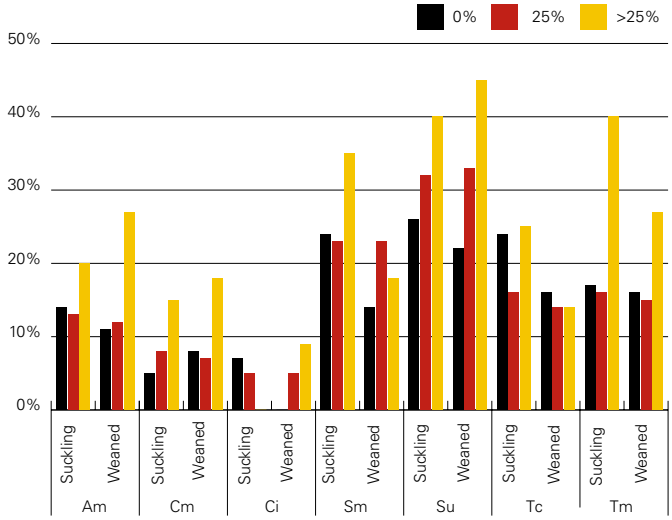

Figure 1. Resistance (%) in *Escherichia coli* in relation to age of piglets (suckling or weaned) and herd frequency of post-weaning diarrhoea up to two weeks after weaning (0%, ≤25% or >25%).

Am: ampicillin; Cm: chloramphenicol; Ci: ciprofloxacin; Sm: streptomycin; Su: sulphonamides; Tc: tetracycline; Tm: trimethoprim.

Cattle

Isolates included

The *Pasteurella* spp. from 2005 to 2007 were isolated from diagnostic submissions of samples from calves with respiratory disease or from post-mortem investigations of lungs. The isolates from years 1997-2000 are from a field study on respiratory pathogens in calves presented in SVARM 2000.

Pasteurella spp.

Antimicrobial resistance among isolates of *Pasteurella* spp. is rare (Table Cattle I). In year 2003, the first Swedish isolates of beta-lactamase producing *Pasteurella* spp. were confirmed. Resistance to penicillin and tetracycline, the substances commonly used for therapy of respiratory disease in calves, was not detected in this year's material. The number of isolates is low and more frequent sampling of calves with respiratory disorders and subsequent susceptibility testing is desirable if emerging resistance is to be detected early.

Table Cattle I. Resistance (%) in *Pasteurella* spp. from calves 1997-2000 and 2005-07. Distribution of MICs for isolates from 2005-07. Isolates are from the respiratory tract of calves.

	Resistance (%)		Distribution (%) of MICs [a] (mg/L)									
Antimicrobial	1997-00 n=254	2005-07 n=27	≤0.12	0.25	0.5	1	2	4	8	16	32	>32
Ampicillin	<1	0				100.0						
Ceftiofur	-	0		100								
Enrofloxacin	2	0	92.9	7.1								
Florfenicol	-	0					100					
Penicillin	0	0	55.6	37.0	7.4							
Tetracycline	3	0				92.9	7.1					
Trim/Sulph.[b]	2	0			85.7	7.1	3.6	3.6				

[a] 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; [b] Concentration of trimethoprim given, tested in concentration ratio 1/20 (trimethoprim/sulphametoxazole).

Sheep

Isolates included

Isolates of *S. aureus* are from a field study where farmers collected milk samples from ewes with clinical mastitis. Each isolate represents a unique herd. (see Appendix 3 for details on sampling).

Staphylococcus aureus

Antimicrobial resistance among *Staphylococcus aureus* was rare. Only one isolate had decreased susceptibly to clindamycin (Table Sheep I). In addition, a single isolate was positive for beta-lactamase production.

Table Sheep I. Resistance (%) and distribution of MICs among *Staphylococcus aureus* from ewes, 2007. Isolates are from milk samples from ewes with clinical mastitis.

	Resistance (%)	Distribution (%) of MICs [a] (mg/L)										
Antimicrobial	2007 n=25	≤0.06	0.12	0.25	0.5	1	2	4	8	16	32	64	>64
Cephalothin	0			76.0	24.0								
Chloramphenicol	0							16.0	84.0				
Ciprofloxacin	0		40.0	52.0	8.0								
Clindamycin	4			96.0	4.0								
Erythromycin	0				80.0	20.0							
Fusidic acid	0	8.0	12.0	36.0	44.0								
Gentamicin	0				76.0	20.0	4.0						
Kanamycin	0					4.0	72.0	24.0					
Oxacillin[b]	0			12.0	52.0	36.0							
Penicillin	4[c]	28.0	56.0	12.0		4.0							
Tetracycline	0				88.0	12.0	4.0						
Trimethoprim	0						44.0	56.0					

[a] 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; [b] tested with 2% NaCl; [c] denotes β-lactamase production.

SVARMpat – results are coming up

THE PURPOSE of SVARMpat is to increase the knowledge on resistance in animal pathogens from Swedish farm animals (for more information See SVARM 2005) and the programme has been running since 2005. SVARMpat is a co-operation between the National Veterinary Institute (SVA) and the Swedish Animal Health Service and is financed by the Swedish Board of Agriculture. Results are reported yearly in the SVARM report, and in addition three times yearly in newsletters directly to veterinary practitioners. The purpose of the newsletters is to continuously inform practitioners on activities and results but also to deepen their knowledge on antimicrobials, antimicrobial treatment and resistance.

An important activity in SVARMpat has been to encourage practitioners and pathologists to submit samples for microbiological culture and susceptibility testing. In this year's SVARM report some results from this work are presented, e.g. susceptibility data on *Actinobacillus pleuropneumoniae* from pigs and on *Pastuerella* spp from both cattle and pigs. Also the data on *Staphylococcus aureus* isolated from milk from ewes with mastitis were collected in the SVARMpat programme. Moreover, a study on antimicrobial resistance and post-weaning diarrhoea was also enabled by SVARMpat and is presented in a highlight. In addition, specific studies have been initiated and are running within the framework of SVARMpat:

- Investigation of antimicrobial resistance in indicator bacteria (*E. coli* and *Enterococcus* spp.) from different age groups of healthy sheep.
- Investigation of prevalence of udder pathogens, including antimicrobial susceptibility, from dairy cows with subclinical mastitis.

Achievements in SVARMpat

In October 2007 routine diagnostics of *Escherichia coli* from pigs was improved at SVA by PCR analysis for genes coding virulence factors (toxin production and adhesion factors). Previoulsy, *E. coli* isolated from clinical submissions were only serotyped and tested for antimicrobial susceptibility. With this new diagnostics, the practitioners will get useful knowledge whether the isolated *E. coli* produce toxins and have adhesions factors. Hopefully, antimicrobial treatment will only be initiated when "true" pathogens are present.

In SVARMpat a PCR to subtype *Fusobacterium necrophorum* was developed according to Narongwanichgarn et al., (2003). The test is able to differentiate between the two subtypes *F. necrophorum* subsp. *necrophorum* and subsp. *funduliforme*, where the first is considered to be the pathogenic subtype. Of 32 samples from interdigital dermatitis in cattle, 20 *F. necrophorum* were isolated and 18 isolates were tested by PCR. Results from the PCR showed that 14 isolates belonged to subsp. necrophorum and the remaining four were of subsp. funduliforme. A broth dilution method for susceptibility testing of *F. necrophorum* in microtitreplates was successfully developed during 2007. Five isolates were examined and they were susceptible to most substances including penicillin and tetracycline, but resistance occurred to macrolides and trimethoprim.

SVARMpat is financing a full-time PhD-student working on genotyping of resistance genes in *Escherichia coli* from faecal samples from diseased pigs, where a major part of the research will be based on a microarray technique. However, the first study was on the prevalence of plasmid-mediated quinolone resistance genes in porcine *E. coli* from 2000–2006 (Thyselius et al., 2007). Here, 57 enrofloxacin resistant *E. coli* (MIC≥ 0.25 mg/L) were analysed for *qnrA*, *qnrB*, *qnrS*, *aac(6')-Ib-cr* and quinolone resistance determining region (QRDR) gyrA by PCR and sequencing. Two isolates (3.5%) harboured the *qnrB* gene. The isolates were resistant to fluoroquinolones but susceptible to nalidixic acid. The other 55 isolates had a single- or double mutation in gyrA and were resistant to both fluoroquinolones and nalidixic acid.

Another PhD project – Vancomycin resistant enterococci in Swedish broilers –is partly financed by SVARMpat. In the project, started 2007, the apparent spread of vancomycin resistant enterococci (VRE) in Swedish broilers since 2000 is investigated. The aim of the project is to elucidate the epidemiology of VRE in broilers and, if possible, mitigate further spread and reduce the prevalence on farms where VRE already occur.

Investigations in the first year of the project confirmed, by multilocus sequence typing (MLST), that the majority of VRE from Swedish broilers belong to one clone (Nilsson et al., 2008a). Further studies show that commercial feed, home produced whole wheat or day old chickens are unlikely to be continuous sources of VRE to broiler farms (Nilsson et al., 2008b)

Poultry

Isolates included

Isolates of *E. coli* are from laying hens sent for post mortem investigation to SVA 2003-2006. Each of the 70 isolates represents a unique flock but not always a unique production site. Most isolates (57%) are from birds where the main finding on post-mortem examination was salphingitis and related infections whereas 37% were isolated from birds with colibacillosis/sepsis. The remaining isolates (6%) are from birds with peritonitis or respiratory infections.

Escherichia coli

The majority of isolates (90%) were susceptible to all antimicrobials tested. Resistance to ampicillin was the most common trait (7%) followed by tetracycline, sulphonamides and streptomycin (4-6%). One isolate was resistant to quinolones. This isolate was in addition resistant to ampicillin, streptomycin and tetracycline and the only isolate resistant to more than three antimicrobials.

Resistance traits found in these *E. coli* from diseased hens are the same that predominate in *E. coli* from the intestinal flora of healthy broilers (see Indicator bacteria). Also the prevalence of resistance is of the same magnitude except for quinolone resistance which is more common in *E. coli* from broilers than in isolates from laying hens.

The rare occurrence of resistance is probably a reflection of the limited use of antimicrobials in poultry production (SVARM 2000). Resistance to ampicillin, tetracycline and, occasionally, to quinolones in isolates from diseased birds however indicate that testing for antimicrobial susceptibility sometimes is necessary for selection of appropriate therapy for treatment of poultry.

Table Poultry I. Resistance (%) and distribution of MICs among *Escherichia coli* from laying hens, 2003-2006. Isolates are from diagnostic submissions of diseased birds for post mortem examination.

	Resistance (%)	Distribution (%) of MICs[a] (mg/L)																			
Antimicrobial	2003-06 n=70	≤0.008	0.016	0.03	0.06	0.12	0.25	0.5	1	2	4	8	16	32	64	128	256	512	1024	2048	>2048
Ampicillin	7								10.0	81.4	1.4				7.1						
Cefotaxime	0				90.0	10.0															
Ceftiofur	0						80.0	20.0													
Chloramphenicol	0										85.7	14.3									
Ciprofloxacin	1			84.3	14.3		1.4														
Florfenicol	0										84.3	14.3	1.4								
Gentamicin	0							12.9	74.3	12.9											
Kanamycin	0									4.3	71.4	24.3									
Nalidixic acid	1								1.4	72.9	24.3					1.4					
Streptomycin	4										10.0	85.7			2.9	1.4					
Sulphonamide	4												7.1	70.0	17.1	1.4					4.3
Tetracycline	6								71.4	22.9					1.4	4.3					
Trimethoprim	0						1.4	58.6	37.1	2.9											

[a] 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.

Horse

Isolates included

Escherichia coli are from the genital tract of mares, while isolates of *Streptococcus zooepidemicus* are from the respiratory tract.

Escherichia coli

As in previous years, resistance to trimethoprim-sulphonamides or streptomycin were the most common resistance traits in *E. coli* from horses (Table Horse I). Trimethoprim-sulphonamides resistance is probably a consequence of the frequent use of this antimicrobial combination in horses (see Use of antimicrobials). Moreover, this usage probably co-selects for streptomycin resistance, since 15% of all isolates were resistant to both streptomycin and trimethoprim-sulphonamides. Since the introduction of trimethoprim-sulphonamides on the Swedish market as an oral formulation for horses in the late 80s, the prevalence of resistance in *E. coli* quickly increased from only 2% in years 1992-1994 to the current level of about 15% in the mid-90s.

The prevalence of gentamicin resistance is still low (3%) despite the use of gentamicin in extenders for semen and in solutions for uterine douching in equine stud practice (Table Horse I).

Multiresistance (i.e. resistance to three or more antimicrobials) occurred in 7% of the isolates. Of the 20 multiresistant isolates, 19 were resistant to ampicillin, streptomycin and trimethoprim-sulphonamides. Resistance to gentamicin did not occur alone, seven out of eight gentamicin resistant isolates were resistant to three or more antimicrobials, and it

Table Horse I. Resistance (%) in *Escherichia coli* from horses 1992-2007 and distribution of MICs for isolates from 2007. Isolates are from diagnostic submissions of samples from the female genital tract.

	Resistance (%)								Distribution (%) of MICs[a] (mg/L)									
Antimicrobial	1992-94 n=48	1995-97 n=216	1998-00 n=222	2001-03 n=457	2004 n=188	2005 n=161	2006 n=124	2007 n=273	≤0.12	0.25	0.5	1	2	4	8	16	32	>32
Ampicillin	15	17	10	9	10	4	7	8				4.0	36.3	48.7	2.6	8.4		
Ceftiofur	-	-	-	<1[g]	1	0	0	<1		21.6	67.4	10.3	0.7					
Enrofloxacin	8[c]	3[c]	3[c]	2[c]	3	4	5	1	98.9	0.4	0.7							
Florfenicol	-	-	-	0[e]	0	0	0	<1					4.4	26.4	64.8	4.0	0.4	
Gentamicin	0[d]	3[d]	6[d]	6[d]	2	2	4	3					91.9	5.1	0.7		0.7	
Neomycin	4	5	5	3	5	2	5	1						96.0	2.6	0.7		2.9
Streptomycin	31[e]	24[e]	21[e]	23	24	22	16	19						3.7	54.6	23.1	1.5	17.2
Tetracycline	6	5	9	6	10	6	6	7				36.9	49.5	4.4		6.6		
Trim/Sulph.[b]	2[f]	15[f]	17	18	21	16	14	17			81.7	1.5	0.4		16.5			

[a] 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; [b] Concentration of trimethoprim given, tested in concentration ratio 1/20 (trimethoprim/sulphametoxazole); [c] Cut-off value >0.25 mg/L until 2002; [d] Cut-off value >8 mg/L until 2002; [e] Cut-off value >16 mg/L until 2001. [f] Cut-off value >4 mg/L until 2001; [g] 353 isolates tested.

Table Horse II. Resistance (%) among *Streptococcus zooepidemicus* from horses 1992-2007 and distribution of MICs for isolates from 2007. Isolates are from diagnostic submissions of samples from the respiratory tract.

	Resistance (%)								Distribution (%) of MICs[a] (mg/L)									
Antimicrobial	1992-94 n=218	1995-97 n=402	1998-00 n=409	2001-03 n=505	2004 n=185	2005 n=175	2006 n=174	2007 n=180	≤0.12	0.25	0.5	1	2	4	8	16	32	>32
Ampicillin	0	<1	0	0	0	0	0	0				100.0						
Enrofloxacin	-	-	-	-	-	-	-	NR[c]			3.9	73.3	22.8					
Florfenicol	-	-	-	1[d]	2	0	0	0					97.8	2.2				
Gentamicin	-	-	-	-	-	-	-	NR[c]					0.6	0.6	16.1	75.0	7.8	
Neomycin	-	-	-	-	-	-	-	NR[c]						0.6		2.8	41.7	55.0
Penicillin	0	<1	0	0	0	0	0	0	100.0									
Spiramycin	<1	1	0	1	1	0	1	0						100.0				
Streptomycin	-	-	-	-	-	-	-	NR[c]								2.2	71.1	26.7
Tetracycline	4	3	4	5	3	3	2	3				71.1	23.3	2.2	0.6	2.8		
Trim/Sulph.[b]	1	11	57	36	49	41	36	17			70.6	8.9	3.3	0.6	16.7			

[a] 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; [b] Concentration of trimethoprim given, tested in concentration ratio 1/20 (trimethoprim/sulphametoxazole); [c] NR= Not relevant as the inherent susceptibility is such that the MIC range is above concentrations that can be obtained during therapy; [d] 370 isolates tested.

is possible that gynaecological use of gentamicin selects for multiresistant *E. coli*.

Streptococcus zooepidemicus

As in previous years, *Streptococcus zooepidemicus* were uniformly susceptible to penicillin (Table Horse II). Occurrence of resistance to trimethoprim-sulphonamides has been high during the last years. About one third to half of the isolates have been resistant to this antimicrobial combination. This is probably due to a concurrent increase in use of trimethoprim-sulphonamides in horses. However, in 2007 the prevalence of isolates resistant to trimethoprim-sulphonamides was numerically lower compared to the last three years. Resistance to antimicrobials other than trimethoprim-sulphonamides is rare. *Streptococcus zooepidemicus* has a low inherent susceptibility to aminoglycosides (i.e. gentamicin, neomycin and streptomycin) and it can be observed that MIC ranges are above the concentrations that can be obtained during systemic therapy with these antimicrobials.

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.

Escherichia coli

The proportions of resistant *E. coli* have remained stable during the years studied (Table Dog I). Resistance to ampicillin is around 20% and the prevalence of resistance to enrofloxacin, streptomycin, tetracycline, and trimethoprim-sulphonamides are all above or around 10%. However, resistance to nitrofurantoin is rare.

The high proportion of *E. coli* resistant to enrofloxacin throughout the study period is partly explained by the use of a low cut-off value for resistance (>0.12 mg/L), compared to the clinical break-point recommended by CLSI (2004), which is >1 mg/L. Nevertheless, isolates with MIC >0.12 mg/L have decreased susceptibility. Such phenotypes are likely to be explained by at least one mutation in one of the genes encoding the target enzymes of this class of drugs. If an infection caused by such a strain is treated with any fluoroquinolone, there is a risk of further mutations resulting in decreased susceptibility (Drlica, 2003).

Multiresistance occurred in 12% of the isolates and the prevalence of resistance to five or more antimicrobials was 2% in 2007. Of the multiresistant isolates, 66% were resistant to ampicillin, streptomycin and trimethoprim-sulphonamides, and 36% were resistant to these antimicrobials and to tetracycline.

Uncomplicated cystitis in dogs is frequently treated with aminopenicillins, which are by far the most commonly prescribed antimicrobials for dogs (Pettersson, 2007). This could explain the proportion of *E. coli* resistant to ampicillin. However, streptomycin is rarely prescribed for outpatient use for dogs (unpublished data 2006) and only 2% of all antimicrobial prescriptions for systemic treatment of dogs are for trimethoprim-sulphonamides (Pettersson, 2007). Yet, resistance to these substances has been above 10% most years.

Table Dog I. Resistance (%) in *Escherichia coli* from dogs 1992-2007 and distribution of MICs for isolates from 2007. Isolates are from diagnostic submissions of urinary tract samples.

	Resistance (%)								Distribution (%) of MICs[a] (mg/L)									
Antimicrobial	1992-94 n=245	1995-97 n=296	1998-00 n=418	2001-03 n=621	2004 n=247	2005 n=304	2006 n=366	2007 n=425	≤0.12	0.25	0.5	1	2	4	8	16	32	>32
Ampicillin	18	18	18	18	19	17	20	18				4.9	56.9	18.8	0.9	18.4		
Enrofloxacin	9[c]	9[c]	10[c]	9[c]	12	9	10	7	93.4	0.5	2.6	0.5	3.1					
Gentamicin	2[d]	1[d]	2[d]	2[d]	1	1	2	<1					90.4	8.9	0.5	0.2		
Nitrofurantoin	3	3	1	2	1	2	2	<1								97.9	1.9	0.2
Streptomycin	16[e]	18[e]	15[e]	19	15	16	16	17						9.2	51.5	22.6	2.4	14.4
Tetracycline	16	14	12	11	13	7	10	9				40.0	48.7	2.4		8.9		
Trim/Sulph[b].	9f	8f	11[f]	13	20	14	13	12			88.2		1.4		10.4			

[a] 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; [b] Concentration of trimethoprim given, tested in concentration ratio 1/20 (trimethoprim/sulphametoxazole); [c] Cut-off value >0.25 mg/L until 2002; [d] Cut-off value >8 mg/L until 2001; [e] Cut-off value >32 mg/L until 2001; [f] Cut-off value >4 mg/L until 2001.

Table Dog II. Resistance (%) in *Staphylococcus intermedius* from dogs 1992-2007 and distribution of MICs for isolates from 2007. Isolates are from diagnostic submissions of samples from skin.

	Resistance (%)								Distribution (%) of MICs[a] (mg/L)									
Antimicrobial	1992-94 n=304	1995-97 n=322	1998-00 n=433	2001-03 n=382	2004 n=159	2005 n=126	2006 n=89	2007 n=220	≤0.12	0.25	0.5	1	2	4	8	16	32	>32
Cephalothin	<1	<1	0	1	2	1	0	2					98.2	0.5			1.4	
Clindamycin	12	20	21	18	21	18	16	18				78.2		3.6	18.2			
Enrofloxacin	-	-	-	2[e]	3	3	1	4[h]	79.7	13.2	3.3	0.9	2.8					
Erythromycin	21	28	27	24	30	22	25	25			74.9	0.5			24.7			
Fusidic acid	9	14	20[d]	20[f]	27	25	23	24					68.2	7.3	24.5			
Gentamicin	<1	<1	<1	0	1	1	0	2					97.7	0.5			1.8	
Nitrofurantoin	1	1	<1	1	0	1	0	<1								99.5		0.5
Oxacillin	1	2	1	2	2	1	0	1			98.6		1.4					
Penicillin[b]	79	80	80	80	80	84	91	84										
Streptomycin	-	-	-	22[e]	31	28	29	29						67.5	3.3		0.5	28.8
Tetracycline	24	12	28	25[g]	29	31	37	32				67.5	0.5		0.5	31.6		
Trim/Sulph[c]	1	2	1	3	10	6	1	5			76.4	17.5	0.9	0.9	4.2			

[a] 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; [b] Denotes β-lactamase production; [c] Concentration of trimethoprim given, tested in concentration ratio 1/20 (trimethoprim/sulphamethoxazole); [d] 421 isolates tested; [e] 273 isolates tested; [f] 346 isolates tested; [g] 381 isolates tested; [h] 212 isolates tested.

This could probably be explained by co-resistance between ampicillin, streptomycin and trimethoprim-sulphonamides. Of those isolates resistant to streptomycin, 74% were also resistant to ampicillin, and for isolates resistant to trimethoprim-sulphonamides, 91% were resistant to ampicillin. The excessive use of aminopenicillins therefore probably selects for resistance to the other two substances.

Besides aminopenicillins, urinary tract infections are often treated with fluoroquinolones, and occasionally with trimethoprim-sulphonamides. Three percent of all isolates were resistant to these three antimicrobial groups and of the multiresistant isolates, 27% were resistant to ampicillin, enrofloxacin and trimethoprim-sulphonamides.

Staphylococcus intermedius

As in previous years, the prevalence of resistance to penicillin due to production of β-lactamases (penicillinase) in *S. intermedius* was high, 84% (Table Dog II). Already in the late 70s, 70% of *S. intermedius* were resistant to penicillin (Franklin, 1978) and during the last decade, the resistance rate has been around 80%. Besides penicillin, resistance to clindamycin, erythromycin, fusidic acid, streptomycin or tetracycline was common in 2007. Noteworthy, resistance to trimethoprim-sulphonamides was low, possibly because this combination was seldom prescribed to dogs (Pettersson, 2007) and consequently the selective pressure has been low. The prescription of tetracycline to dogs was also low (Pettersson, 2007) but resistance to tetracycline has increased from 2001 to 2006 ($P<0.03$, Chi-square for trend), and in 2007 about one third of *S. intermedius* was resistant to tetracycline. This probably can be explained by co-selection through clindamycin use (see discussion below).

Multiresistance occurred in 32% of the isolates. Resistance to penicillin, clindamycin and erythromycin was the most common phenotype, occurring in 55% of multiresistant isolates. Of the multiresistant isolates, 44% were resistant to more than four antimicrobials, i.e. 6% of all isolates in this year's material. Of these, 16 isolates (7% of the total) were resistant to clindamycin, erythromycin, penicillin, streptomycin and tetracycline. Macrolide resistance in *S. intermedius* is commonly mediated by erm-genes, and if these genes are constitutively expressed, the bacteria will be resistant also to lincosamides (clindamycin) and streptogramin B. In this material, 74% of isolates resistant to erythromycin were also resistant to clindamycin.

Since the tested isolates are from diagnostic submissions of samples from skin, there is a high probability of bias towards dogs with recurrent skin infections, previously treated with antimicrobials. A prospective study by Holm et al., (2002) showed higher levels of multiresistance among isolates from recurrent compared to those from first-time pyoderma. This probably explains the high levels of resistance in this material. Clindamycin and cephalosporins are commonly used to treat pyoderma in dogs. With the high proportion of multiresistant isolates, treatment with e.g. clindamycin will co-select for resistance to erythromycin, streptomycin, and tetracycline, despite the fact the two latter substances are rarely used in treatment of pyoderma. Interestingly, resistance to enrofloxacin occurred only in multiresistant phenotypes. In year 2005, 13% of the antimicrobial prescriptions to dogs were fluoroquinolones, and the figure has increased since the 90s. (Pettersson, 2007).

At SVA, all isolates of *S. intermedius* with high MIC of oxacillin (>0.5 mg/L) are retested at a lower temperature (33-34 °C) and with 2% NaCl added to the broth, as recomended by CLSI (2007). If the MIC of oxacillin is still high, the isolates are examined for mecA gene with PCR (see Appendix 3 for details). The three isolates from year 2007 that were resistant to oxacillin harboured the *mecA*-gene and had the same antibiogram as other methicillin resistant *S. intermedius* from dogs presented in "Highlight on MRSI/P". Most likely they belong to the most frequently found MRSI/P-clone in Sweden (see "Highlight on MRSI/P").

MRSI/P – Methicillin-resistant *Staphylococcus (pseud)intermedius*

THERE HAS BEEN a dramatic increase in the number of confirmed methicillin resistant *Staphylococcous (pseudo)intermedius* from companion animals in Sweden during 2007. When laboratories have suspected methicillin resistance in staphylococci they have sent them to SVA for confirmation of *mecA*-gene by PCR. During 2007, 77 of 99 isolates submitted were confirmed methicillin resistant. This figure should be compared with 13 isolates in 2006. Before 2006, methicillin resistance was a rarely confirmed finding in Sweden. Since 2000, the prevalence of resistance in *S. intermedius* from dogs has been monitored in SVARM with data back to 1992. Resistance to cephalothin or oxacillin has been observed occasionally, but before 2006 no isolate has been confirmed to harbour the *mecA* gene. From the first of January 2008, infections with methicillin resistant coagulase positive staphylococci in animals are notifiable in Sweden.

Fifty of the 90 MRSI from 2006 and 2007 have been further analysed for clonality and species classification. Preliminary results indicate that they all are *S. pseudointermedius*, that a majority originate from post-operative wound infections and that 48 of 50 isolates belong to same clone. The antibiogram of this dominating clone is shown in Table I. Since *S. intermedius* recently have been further divided into *S. intermedius* and *S. pseudintermedius* (Devriese et al., 2005 and Sasaki et al., 2007) the acronym MRSP will be used for methicillin-resistent *Staphylococcous (pseudo)intermedius*.

Whether the increase in the number of confirmed MRSP is due to increased awareness among veterinarians and laboratories or if it stands for a true augment in the number of MRSP-infected dogs can not be determined. During the past years, there has been a quite extensive use of antimicrobials in dogs (see SVARM 2005 "Antimicrobials prescribed for dogs"; Pettersson, 2007) and spread of this multiresistant pathogen is probably favoured by this. All of the 49 MRSP-infected dogs were treated with antimicrobials on one or several occasions before isolation of MRSP.

In 2006, MRSP were only obtained from dogs that had been hospitalised at two large animal hospitals, but during 2007, these bacteria have been isolated from animals at several different hospitals and clinics, at different geographical locations. To be able to prevent spread of MRSP, the veterinarians should change their "prescription habits" and only prescribe antimicrobials when they really are needed. In addition, the animal hospitals and clinics need to set up and implement hygiene guidelines and last but not least, the practitioners have to take more bacteriological samples to confirm the cause of infection.

Table I. Antibiogram of the dominating Swedish clone of methicillin resistant *Staphylococcus (pseud)intermedius*.

Antimicrobial	MIC (mg/L)	S/R[a]
Penicillin	>4	R
Cephalothin	>8	R
Cefoxitin	8	R
Oxacillin (+ 2% NaCl)	>16	R
Erythromycin	>32	R
Chloramphenicol	64	R
Clindamycin	>32	R
Tetracycline	<=0.5	S
Fusidic acid	0.25	S
Gentamicin	32	R
Kanamycin	>32	R
Ciprofloxacin	>4	R
Trimethoprim	>32	R

[a] Susceptible (S) or resistant (R) for cut-off values see Appendix 3.

Cat

Isolates included

Isolates of *E. coli* are from urine samples, submitted either as urine or as dip-slide cultures.

Escherichia coli

As in previous years, resistance to ampicillin, streptomycin, or tetracycline were the most common resistance traits (Table Cat I). However, the figures for these substances were numerically lower compared to last year. Only one isolate was resistant to nitrofurantoin.

As for dogs, the high proportion of *E. coli* resistant to enrofloxacin throughout the study period is partly explained by the low cut-off value for resistance (>0.12 mg/L), chosen for fluoroquinolones in SVARM, compared to the break-point recommended by e.g. CLSI (2004), which is >1 mg/L. As mentioned above, strains with MIC >0.12 mg/L are less susceptible and there is a risk for further mutations during fluoroquinolone treatment.

In 2007, only 6% of the isolates were multiresistant (i.e. resistant to three or more substances), a lower figure compared to last year (16%). Of the eight multiresistant isolates, five (62%) were resistant to ampicillin, streptomycin and tetracycline and three of these were also resistant to trimethoprim-sulphonamides. One isolate was resistant to ampicillin, enrofloxacin, gentamicin, streptomycin, tetracycline and trimethoprim-sulphonamides. Urinary tract infections in cats are often treated with aminopenicillins or fluoroquinolones. This year, two isolates were resistant to both these antimicrobials.

Table Cat I. Resistance (%) in *Escherichia coli* from cats 1992-2007 and distribution of MICs for isolates from 2007. Isolates are from diagnostic submissions of urine samples.

	Resistance (%)							**Distribution** (%) **of MICs**[a] (mg/L)								
Antimicrobial	**1992-97** n=61	**1998-00** n=74	**2001-03** n=135	**2004** n=55	**2005** n=74	**2006** n=95	**2007** n=131	**≤0.12**	**0.25**	**0.5**	**1**	**2**	**4**	**8**	**16**	**32**	**>32**
Ampicillin	26	34	27	18	20	26	16				8.4	61.1	14.5		16.0		
Enrofloxacin	5[c]	8[c]	13[c]	5	11	5	4	96.2	2.3	0.8	0.8						
Gentamicin	0[d]	3[d]	5[d]	0	0	1	<1					93.9	5.3	0.8			
Nitrofurantoin	2	2	1	2	4	2	<1									99.2	0.8
Streptomycin	25[e]	18[e]	21[e]	14	18	19	12						6.9	58.0	22.9	3.0	9.2
Tetracycline	28	16	16	13	12	15	8				44.3	46.6	1.5		7.6		
Trim-Sulph.[b]	7[f]	10[f]	15	13	3	6	5			93.1	1.5			5.3			

[a] White fields denote the 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; [b] Concentration of trimethoprim given, tested in concentration ratio 1/20 (trimethoprim/sulphamethoxazole); [c] Cut-off value >0.25 (mg/L) until 2002; [d] Cut-off value >8 mg/L until 2001; [e] Cut-off value was >32 mg/L until 2001; [f] Cut-off value >4 mg/L until 2001.

Appendix 1: Demographic data

AGRICULTURAL STATISTICS are provided by Statistics Sweden in collaboration with the Board of Agriculture and published annually as a Yearbook of Agricultural Statistics and continuously as Statistical Messages (SM). The Yearbook and Statistical Messages are is available on the Internet via the websites for Statistics Sweden (www.scb.se) or the Board of Agriculture (www.sjv.se).

Annual figures on number of animals and holdings are given in Table AP1 I & II, and on numbers and volumes of animals slaughtered in Table AP1 III & IV. For details on methodology, see the respective sources of the statistics.

Over the last two decades, the total number of dairy cows, pigs, and laying hens has decreased notably concomitantly with an increase in herd size. In the same period, the number of beef cows and sheep as well as the number of broilers slaughtered has increased.

Table AP1 I. Number of livestock and horses (in thousands) 1980-2007 (Yearbook of Agricultural Statistics, Sweden 2007 and Statistical Message JO 20 SM 0801).

Animal Species	1980[a]	1985[a]	1990	1995	2000	2004	2005	2006	2007
Cattle									
Dairy cows	656	646	576	482	428	404	393	388	367
Beef cows	71	59	75	157	167	172	177	178	186
Other cattle >1 year	614	570	544	596	589	539	527	530	516
Calves <1 year	595	563	524	542	500	514	508	496	489
Total, cattle	**1 935**	**1 837**	**1 718**	**1 777**	**1 684**	**1 629**	**1 605**	**1 590**	**1560**
Pigs									
Boars & sows	290	260	230	245	206	195	188	187	181
Fattening pigs >20 kg [b]	1 254	1 127	1 025	1 300	1 146	1 094	1 085	1 002	1 015
Piglets <20kg [c]	1 170	1 113	1 009	769	566	528	539	492	480
Total, swine	**2 714**	**2 500**	**2 264**	**2 313**	**1 918**	**1 818**	**1 811**	**1 680**	**1 676**
Sheep									
Ewes and rams	161	173	162	195	198	220	222	244	242
Lambs	231	252	244	266	234	246	249	262	267
Total, sheep	**392**	**425**	**406**	**462**	**432**	**466**	**471**	**505**	**521**
Laying hens									
Hens	5 937	6 548	6 392	6 100	5 670	4 995	5 065	4 524	5 328
Chickens reared for laying	2 636	2 159	2 176	1 812	1 654	1 625	1 697	1 646	1 753
Total, hens	**8 573**	**8 708**	**8 568**	**7 912**	**7 324**	**6 620**	**6 762**	**6 170**	**7 080**
Turkeys									
Total, turkeys	-[d]	-	-	-	-	-	**122**	-	**101**
Horses									
Total, horses	-	-	-	-	-	**283**	-	-	-

[a] For 1980 and 1985 only cattle and sheep at premises with more than 2 ha counted; [b] Before 1995, the figure denotes pigs above 3 months of age; [c] Before 1995, the figure denotes pigs below 3 months of age; [d] Data not available.

Table AP1 II. Number of holdings with animals of different types, 1980-2007 (Yearbook of Agricultural Statistics, Sweden 2007 and Statistical Message JO 20 SM 0801).

Animal Species	1980	1985	1990	1995	2000	2004	2005	2006	2007
Cattle									
Dairy cows	44 143	35 063	25 921	17 743	12 676	9 147	8 548	8 027	7 100
Beef cows	12 436	10 310	10 883	17 069	13 861	13 013	12 821	12 447	12 500
Other cattle >1 year	63 179	52 652	42 696	39 160	30 457	26 291	24 808	23 700	22 500
Calves <1 year	62 314	52 001	41 986	36 542	27 733	24 116	22 888	21 752	20 800
Total holdings with cattle	**70 503**	**58 872**	**47 292**	**41 990**	**32 063**	**27 626**	**26 179**	**25 054**	**23 878**
Sheep	10 238	10 595	9 749	10 037	8 089	8 239	7 653	9 152	8 014
Pigs	26 122	19 937	14 301	10 753	4 809	3 194	2 794	2 414	2 277
Laying hens	23 603	17 531	12 900	9 593	5 678	5 376	4 916	4 877	4 245
Chickens reared for laying	5 093	2 714	1 875	1 405	715	803	634	528	496
Broilers	-[a]	-	-	-	-	237	234	192	212
Turkeys	-	-	-	-	-	-	383	-	130
Horses	-	-	-	-	-	56 000	-	-	-

[a] Data not available.

Table AP1 III. Number of animals slaughtered (in thousands) at slaughterhouses, 1980-2007. (Yearbook of Agricultural Statistics, Sweden 1981, 1986, 1991 & 2007 and Statistical Message JO 48 SM 0803).

Animal Species	1980	1985	1990	1995	2000	2004	2005	2006	2007
Cattle									
Cattle >1 year	574	584	523	502	490	458	433	434	420
Calves < 1 year	130	152	70	30	39	34	33	32	30
Total, cattle	**704**	**736**	**593**	**532**	**529**	**492**	**466**	**466**	
Pigs	4 153	4 283	3 653	3 743	3 251	3 365	3 160	3 022	3 004
Sheep	302	328	280	189	202	193	206	213	231
Broilers	40 466[a]	36 410[a]	38 577[a]	61 313	68 617	69 628	73 458	72 906	74 666

[a] Data supplied by the National Food Administration.

Table AP1 IV. Quantity of livestock slaughtered (in 1000 tonnes) at slaughterhouses, 1990-2006 (Yearbook of Agricultural Statistics, Sweden 1991 & 2007 and Statistical Message JO 48 SM 0702).

Animal Species	1990	1995	2000	2004	2005	2006	2007
Cattle							
Cattle >1 year	139.5	140.1	145.4	137.8	131.4	132.9	129.6
Calves < 1 year	6.8	3.2	4.4	4.6	4.5	4.5	4.3
Total, cattle	**146.3**	**143.3**	**149.8**	**142.4**	**135.9**	**137.4**	133.9
Pigs	293.1	308.8	277.0	294.5	275.1	265.6	264.9
Sheep	5.0	3.5	3.9	3.8	4.1	4.2	4.6
Broilers	44.0[a]	73.6[a]	89.9	91.2	96.2	95.5	97.8

[a] Data supplied by the National Food Administration.

Appendix 2: Materials and methods, use of antimicrobials

Source for the statistics

The antimicrobial drugs used in veterinary medicine in Sweden are only available on veterinary prescription. Furthermore, antimicrobial drugs are dispensed through pharmacies only. 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 at or from pharmacies, i.e. sales statistics. Data for previous years are the amount of antimicrobial products sold from the wholesalers to the pharmacies.

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.

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 (i.e., ATCvet codes QA, QG and QJ) were included. 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 treatment of coccidiosis only and has therefore not been included. The ionophoric antibiotics are presently regulated as feed additives and not sold through 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.

Aquaculture

Statistics specifically on use of antimicrobials in aquaculture is published annually by Fiskhälsan FH AB (Fish Health Control Program; www.fiskhalsan.se). Data included in SVARM 2007 have been taken from the report for year 2007 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. In case there are no authorised veterinary medicinal products for a certain condition, the MPA can also permit special license prescription for a drug.

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. Data presented in SVARM include one isolate of each serovar, and when appropriate phage-type, from each food animal species in each notified incident 2007. 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 2007, *Salmonella* was isolated from a total of 177 cats and from 29 wild birds. Of these 10 isolates from cats and 10 isolates from wild birds were randomly selected for testing.

Indicator bacteria

Indicator bacteria, *Escherichia coli* and *Enterococcus* spp., were isolated from caecal content from broilers. Samples cultured were from the Swedish *Campylobacter* programme in which whole caeca are collected from each batch of broilers slaughtered. From these samples, 172 were selected by convenience in February-May and 166 in September-November for culture in SVARM. Each sample is from a unique flock but not always from a unique production site. Samples cultured were collected at seven abattoirs that in 2007 accounted for 99.4% of the total volume of broilers slaughtered. The number of samples from each abattoir is roughly proportional to the annual slaughter volume of the abattoir.

Animal pathogens

Isolates of animal pathogens included are from routine bacteriological examinations of clinical submissions or post-mortem examinations at SVA. Actinobacillus *pleuropneumoniae* from pigs and *Staphylococcus aureus* from sheep were however isolated from samples collected in surveys initiated within SVARMpat.

Escherichia coli from pigs and cattle are from the gastrointestinal tract (gut content, faecal samples or mesenteric lymph nodes) and *E. coli* from laying hens are from post mortem examinations of diseased birds. *Escherichia coli* from horses are from the genital tract of mares and *E. coli* from dogs and cats from samples of urine. *Brachyspira* spp. from pigs are from faecal samples. *Pasteurella* spp. from cattle are from the respiratory tract and *Pasteurella multocida* from pigs from nasal swabs collected within a control programme for atrophic rhinitis in nucleus and multiplying herds. *Streptococcus zooepidemicus* from horses and *Actinobacillus pleuropneumoniae* from pigs are from the respiratory tract. *Staphylococcus intermedius* from dogs were isolated from skin samples. *Staphylococcus aureus* from sheep were isolated from milk samples from ewes with mastitis.

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 Dept. of Bacteriology, SVA according to the standard procedures of Kaufmann and White. The Dept. of Bacteriology, SVA is accredited for isolation, identification and serotyping of *Salmonella*.

Isolates of *Salmonella* Typhimurium and *S.* Enteritidis were phage-typed by the Swedish Institute for Infectious Disease Control (SMI), Stockholm using the Colindale scheme.

Indicator bacteria

Escherichia coli

Approximately 0.5 g of colon content was diluted in 4.5 mL saline. 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 tryptophanase (indole) and β-glucuronidase (p-nitrophenyl-β-D- glucopyranosiduronic acid, PGUA). Only lactose-positive isolates with typical morphology and positive reactions in both tests were selected for susceptibility tests.

Enterococci

Colon content was diluted as described for *E. coli* and cultured on solid media without antibiotics and on selective plates with vancomycin (16 mg/L).

Culture without selective antibiotics: Diluted colon content (0.1 mL) was spread onto Slanetz-Bartley (SlaBa) agar. The plates were 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, raffinose and methyl-α-D-glucopyranoside.

Selective culture for vancomycin resistant enterococci: Diluted colon content (0.1 mL) was also cultured on SlaBa with vancomycin (16 mg/L). 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.

Animal pathogens

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

Susceptibility testing

The Dept. of Antibiotics or the Dept. of Bacteriology performed antimicrobial susceptibility tests, with accredited methodology, using dilution methods in cation adjusted Mueller-Hinton broth (CAMBH). Tests were performed following the standards for microdilution of the Clinical and Laboratory Standards Institute (CLSI, 2007). 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). Minimum inhibitory concentration (MIC) was recorded as the lowest concentration of the antimicrobial that inhibits bacterial growth.

For susceptibility testing of *Brachyspira hyodysenteriae*, a broth dilution method was used (Karlsson et al., 2001). 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% foetal calf serum ($1x10^6$-$5x10^6$ CFU/ml). The trays were incubated in an anaerobic atmosphere at 37°C for four days on a shaker.

Screening for methicillin resistance was performed with microdilution according to CLSI (2007), testing oxacillin with 2% NaCl added to the broth, and in addition oxacillin without added NaCl and cefoxitin. Presence of the mecA gene in *Staphylococcus aureus* and *S. intermedius* was tested by polymerase chain reaction (PCR) modified from Smyth et al. (2001) in isolates with a phenotype indicating methicillin resistance.

Phenotypic confirmatory test for production of extended spectrum beta-lactamases (ESBLs) in *Escherichia coli* was performed by the standard disc diffusion test recommended by CLSI (2007).

For every fifth consecutive enterococcal isolate with MICs of vancomycin >128 mg/L, the resistance genotype was confirmed with PCR for the *vanA* gene according to Dutka-Malen et al. (1995).

Epidemiological cut-off values issued by the European Committee on Antimicrobial Susceptibility Testing (EUCAST) (http://www.escmid.org) were used for interpretation of results of susceptibility testing of zoonotic bacteria (*Salmonella*) and indicator bacteria (*E. coli* and *enterococci*). When no cut-off value was available, or the range of concentrations tested was inappropriate for the recommended value, a cut-off value was defined on basis of the actual MIC distributions obtained in the SVARM programme. The same approach was used when recommended cut-off values would have cut through distributions of MIC in a manner not in agreement with the concept of wild-type distributions, causing an erroneously high frequency of resistance in single a year(s). This applies to ciprofloxacin in *E. coli*.

Also for animal pathogens epidemiological cut-off values issued by EUCAST were used when available. When no cut-off value was available, or the range of concentrations tested was inappropriate for the recommended value, a cut-off value was defined on basis of the actual MIC distributions obtained in the SVARM programme but the clinical breakpoints recommended for animal pathogens by CLSI (2004) were also taken into consideration. It should be understood that epidemiological cut-off values classifies isolates with acquired reduced susceptibility as resistant, which is relevant for monitoring purposes, but that this not always implies clinical resistance.

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. The Dept. of Bacteriology is also accredited for isolation and identification of animal pathogens and *Salmonella* 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 testing of *Brachyspira*, the *B. hyodysenteriae* type strain B78T ATCC 27164T was used for quality control.

The Dept. of Antibiotics participates in several proficiency tests for antimicrobial susceptibility testing. These are arranged either by the Community Reference Laboratory (CRL) or as national studies. Likewise, the Dept. of Bacteriology participates 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 a Microsoft Access database.

For indicator bacteria, data on animal species, date of sampling, abattoir and herd or flock of origin were recorded in an Access database on arrival of samples, and the results of culture identification and susceptibility tests were recorded on completion of testing.

Calculations and analysis of data were performed in the computer programs Microsoft Access, Microsoft Excel, or 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. Values in bold lettering are current (April 2008) epidemiological cut-off values presented by EUCAST, values in italic lettering deviate from values presented by EUCAST for values in normal lettering no EUCAST epidemiological cut-off value is available (See "Susceptibility testing" above for details).

Antimicrobial	*Actinobacillus pleuropneumoniae*	*Brachyspira* spp.	*Enterococcus faecalis*	*Enterococcus faecium*	*Enterococcus* spp. Other than *E. faecalis* and *E.faecium*)	*Escherichia coli* (indicator)	*Escherichia coli* (pathogen)	*Pasteurella* spp.	*Salmonella* spp.	*Staphylococcus intermedius*	*Staphylococcus aureus*	*Streptococcus zooepidemicus*
Ampicillin	>1		**>4**	**>4**	>4	**>8**	**>8**	>1	**>4**			>8
Bacitracin[a]			**>32**	**>32**	>32							
Cefotaxime	>1					**>0.25**		>1	**>0.5**			
Ceftiofur	>0.25					**>1**	**>1**	>0.25	**>2**			
Cefoxitin										>4		
Cephalothin										>2	**>1**	
Chloramphenicol	>2		>32	>32	>32	**>16**		>2	**>16**		**>16**	
Clindamycin										>4	**>0.25**	
Ciprofloxacin	>0.06					*>0.06*		>0.06	**>0.06**	**>1**	**>1**	
Enrofloxacin	>0.25					**>0.12**	**>0.12**	>0.25	>0.25	>0.5		
Erythromycin			>4	>4	>4					*>4*	**>1**	
Florfenicol	>16					**>16**	**>16**	>16	**>16**			>8
Fusidic acid										>4	**>0.5**	
Gentamicin	>8		**>32**	**>32**	>32	**>2**	*>4*	>8	**>2**	>4	**>2**	
Kanamycin			>1024	>1024	>1024	**>8**			>16		**>8**	
Linezolid			**>4**	**>4**	>4							
Nalidixic acid	>16					**>16**		>16	**>16**			
Narasin			>2	*>2*	>2							
Neomycin							**>8**		**>4**			
Nitrofurantoin							*>32*			>32		
Oxacillin										>1	**>2**	
Penicillin	>1							>1		[c]	[c]	>1
Spiramycin												>16
Streptomycin	>32		**>512**	**>128**	>128	**>16**	**>16**	>32	>32	>32		
Sulphametoxazole	>256					>256		>256	>256			
Tetracycline	>2		**>2**	**>2**	**>2**	**>8**	**>8**	>2	**>8**	>8	**>1**	>8
Tiamulin		>2										
Trimethoprim	>4					**>2**	**>2**	>4	**>2**		**>4**	
Trimethoprim & sulphametoxazole[b]							**>1**	>4	*>0.5*	>2		>4
Tylosin		>16										
Vancomycin			**>4**	**>4**	**>4**							
Virginiamycin			**>32**	**>4**	>4							

[a] MIC in U/mL; [b] Concentration of trimethoprim given, tested with sulphamethoxazole in concentration ration 1/20; [c] β-lactamase production.

Appendix 4: Antimicrobial agents licensed

ANTIMICROBIAL AGENTS licensed for therapy in veterinary medicine in Sweden year 2007are 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. 2007. For explanation of ATCvet code, see Appendix 2.

Table AP4 I. Antimicrobial agents authorised for therapeutic use in cattle, sheep, pigs, poultry, horses, dogs and cats in Sweden, 2007. Routes of administration are indicated [a].

		Animal species						
Antimicrobial agent	**ATCvet code**	**Cattle**	**Sheep**	**Pigs**	**Poultry**	**Horses**	**Dogs**	**Cats**
Tetracyclines								
Doxycycline	QJ01A A02			O			O	O
Oxytetracycline	QJ01A A06, QG01A A07	I O U	I U	I O U	O			
Beta-lactams, penicillins								
Ampicillin	QJ01C A01	O		O		O	O	O
Amoxicillin	QJ01C A04	I		I			I O	O
Amoxicillin/Clavulanic acid	QJ01C R02			I			I O	I O
Penicillin G, sodium	QJ01C E01	I		I		I		
Penicillin G, procaine	QJ01C E09/QJ51C E09	IM	I	I		I	I	I
Penicillin G, penetamathydroiodide	QJ01C E90	I						
Beta-lactams, cephalosporins								
Cephalexin	QJ01D B01						O	
Cefadroxil	QJ01D B05						O	O
Ceftiofur	QJ01D D90	I						
Sulphonamides /Trimethoprim								
Sulphadiazine/Trimethoprim	QJ01E W10	I	I	I		I O	O	
Sulphadoxine/Trimethoprim	QJ01E W13	I		I		I		
Sulphonamides								
Sulphaclozin	QP51A G04				O			
Macrolides								
Spiramycin	QJ01F A02	I						
Tulathromycin	QJ01FA94	I		I				
Tylosin	QJ01F A90	I		I O	O		I	I
Lincosamides								
Clindamycin	QJ01F F01						O	O
Aminoglycosides								
Gentamicin	QJ01G B03					I U	I	I
Dihydrostreptomycin (DHS)	QA07A A90	O U	O U	O U		O U	O	O
Fluoroquinolones								
Danofloxacin	QJ01M A92	I						
Difloxacin	QJ01M A94						O	
Enrofloxacin	QJ01M A90	I		I	O		I O	I O
Marbofloxacin	QJ01M A93						O	O
Ibafloxacin	QJ01M A96						O	O
Pleuromutilins								
Tiamulin	QJ01X X92			I O				
Valnemulin	QJ01X X94			O				
Combinations								
Penicillin G, procaine/DHS	QJ01R A01, QJ51R C23	I M	I	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						

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

Appendix 5: References

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